Primary growth hormone insensitivity (Laron syndrome) and acquired hypothyroidism: a case report.

Cotta OR, Santarpia L, Curtò L, Aimaretti G, Corneli G, Trimarchi F, Cannavò S.

Department of Medicine and Pharmacology, University of Messina, Messina, Italy. cannavos@unime.it.

ABSTRACT: INTRODUCTION: Primary growth hormone resistance or growth hormone insensitivity syndrome, also known as Laron syndrome, is a hereditary disease caused by deletions or different types of mutations in the growth hormone receptor gene or by post-receptor defects. This disorder is characterized by a clinical appearance of severe growth hormone deficiency with high levels of circulating growth hormone in contrast to low serum insulin-like growth factor 1 values.

CASE PRESENTATION: We report the case of a 15-year-old Caucasian girl who was diagnosed with Silver-Russell syndrome at the age of four and a half years. Recombinant growth hormone was administered for 18 months without an appropriate increase in growth velocity. At the age of seven years, her serum growth hormone levels were high, and an insulin-like growth factor 1 generation test did not increase insulin-like growth factor 1 levels (baseline insulin-like growth factor 1 levels, 52 µg/L; reference range, 75 µg/L to 365 µg/L; and peak, 76 µg/L and 50 µg/L after 12 and 84 hours, respectively, from baseline). The genetic analysis showed that the patient was homozygous for the R217X mutation in the growth hormone receptor gene, which is characteristic of Laron syndrome. On the basis of these results, the diagnosis of primary growth hormone insensitivity syndrome was made, and recombinant insulin-like growth factor 1 therapy was initiated. The patient's treatment was well tolerated, but unexplained central hypothyroidism occurred at the age of 12.9 years. At the age of 15 years, when the patient's sexual development was almost completed and her menstrual cycle occurred irregularly, her height was 129.8 cm, which is 4.71 standard deviations below the median for normal girls her age.

CONCLUSION: The most important functional tests for the diagnosis of growth hormone insensitivity are the insulin-like growth factor 1 generation test and genetic analysis. Currently, the only effective treatment is daily administration of recombinant insulin-like growth factor 1 starting from early childhood. However, these patients show a dramatically impaired final height. In our case, unexplained central hypothyroidism occurred during treatment.
Detection of antipituitary and antihypothalamus antibodies to investigate the role of pituitary or hypothalamic autoimmunity in patients with selective idiopathic hypopituitarism.


Department of Clinical and Experimental Medicine and Surgery, F. Magrassi, A. Lanzara, Second University of Naples, Naples, Italy. annamaria.debellis@unina2.it

OBJECTIVE: Antipituitary (APA) but not antihypothalamus antibodies (AHA) have been investigated in patients with idiopathic hypopituitarism. This study searched for APA and AHA in some of these patients to investigate whether pituitary or hypothalamic autoimmunity could play a role in their pituitary dysfunction.

DESIGN: Sixty-six patients with selective idiopathic hypopituitarism were studied: 27 with ACTH deficiency, 20 with GH deficiency and 19 with hypogonadotrophic hypogonadism. Twenty patients with hypopituitarism secondary to hypophysectomy and 50 healthy subjects were enrolled as controls.

MEASUREMENTS: Antipituitary and AHA were evaluated by indirect immunofluorescence in sera of patients and controls. Positive sera were retested by a four-layer double immunofluorescence to identify the cells targeted by these antibodies.

RESULTS: Antipituitary were present at high titre in 4 of 27 patients with ACTH deficiency (14.8%), 4 of 20 with GH deficiency (20%) and 5 of 19 with hypogonadotrophic hypogonadism (26%) and targeted, respectively, corticotrophs, somatotrophs and gonadotrophs. AHA were found at high titre only in 5 patients with ACTH deficiency (18.5%), mostly targeting corticotropin-releasing hormone-secreting cells; none of these 5 patients resulted positive for antipituitary antibodies. Among the controls, only 1 hypophysectomized patient resulted APA positive at low titre.

CONCLUSIONS: Our results suggest that in patients with selective idiopathic hypopituitarism, detection of APA or AHA could better characterize an autoimmune process involving the pituitary or hypothalamus, respectively. In particular, detection of antibodies targeting selectively ACTH-secreting or corticotrophin-releasing hormone-secreting cells may differentiate, respectively secondary from tertiary variants of autoimmune hypoadrenalism.

PMID: 21521324 [PubMed - in process]


Assessment of the awareness and management of sleep apnea syndrome in acromegaly. The COM.E.TA (Comorbidities Evaluation and Treatment in Acromegaly) Italian Study

Pagina 2
Cannavo S, until 2011


Department of Internal Medicine, General Hospital, v. Monte Grappa 30, 31044 Montebelluna, Italy. ernesto.demenis@ulssasolo.ven.it

Erratum in

In 2007 the Italian COM.E.T.A. (COMorbidities Evaluation and Treatment in Acromegaly) study group started to assess the application in a clinical setting of the Versailles criteria for management of acromegaly complications by a first questionnaire focusing on cardiovascular co-morbidities. A further questionnaire on sleep apnea syndrome (SAS) was delivered by the COM.E.T.A. study group to 107 endocrine centers in Italy. The results of our survey suggest that SAS is a well-known comorbidity even if its estimated prevalence is lower than in the literature. Polysomnography is the preferred tool for diagnosis. Control of SAS is considered relevant both for quality of life and co-morbidities. Continuous positive airway pressure is the cornerstone of therapy, but patients’ acceptance may be critical. Control of GH/IGF-I secretion is important to improve SAS. Management of SAS requires cooperation between specialists.

PMID: 21406941 [PubMed - indexed for MEDLINE]


Pregnancy after azathioprine therapy for ulcerative colitis in a woman with autoimmune premature ovarian failure and Addison’s disease: HLA haplotype
OBJECTIVE: To present a case of fertility restored by azathioprine treatment in a woman with autoimmune premature ovarian failure, Addison's disease, and ulcerative colitis, and to study the genetic background of the three autoimmune diseases.

DESIGN: Case report.

SETTING: Endocrinology and Immunology Units of an university hospital.

PATIENT(S): A 30-year-old woman with autoimmune premature ovarian failure, Addison's disease, and ulcerative colitis.

INTERVENTION(S): Azathioprine has been administered as immunosuppressive treatment.

MAIN OUTCOME MEASURE(S): We performed analysis of human leukocyte antigens expression on lymphocytes and genomic haplotype of the patient.

RESULT(S): The human leukocyte antigen haplotype of the patient was consistent with the haplotypes predisposing for the three autoimmune diseases, as reported in the literature. The administration of azathioprine restored regular menses and allowed uneventful pregnancy.

CONCLUSION(S): This is the first clinical evidence of association of immunosuppressive azathioprine treatment and restored ovarian function and fertility in a woman with autoimmune premature ovarian failure. In this patient, the haplotype was associated with susceptibility to autoimmune premature ovarian failure, Addison's disease, and ulcerative colitis.

PMID: 21367409 [PubMed - indexed for MEDLINE]


Increased prevalence of restless legs syndrome in patients with acromegaly and effects on quality of life assessed by Acro-QoL.


Department of Medicine and Pharmacology, Section of Endocrinology, University of Messina, AOU Policlinico G. Martino, Via Consolare Valeria, 1, 98125, Messina, Italy, cannavos@unime.it.

Restless legs syndrome (RLS), a neurological sensory-motor disorder characterized by a compelling urge to move the limbs during the night, is a sleep disturbance that impairs quality of life. Prevalence of RLS and consequences on quality of life were investigated in acromegalic patients. Fifty-six patients (20 men, 55.0 ± 1.6 years), 22 with active acromegaly (group 1) and 34 with controlled
disease (group 2), and 95 controls (35 men, 52.9 ± 1.1 years) were evaluated by a structured sleep interview concerning insomnia, circadian sleep disorders and excessive diurnal sleepiness (EDS). The Epworth Sleepiness Scale (ESS) questionnaire was administered to those reporting EDS. Patients were investigated by RLS diagnostic interview and International Restless Leg Syndrome-Rating Scale (IRLS-RS). Quality of life was investigated by AcroQoL questionnaire. RLS was diagnosed in 21% of acromegalics and in 4% of controls (P < 0.002). Prevalence of RLS and mean IRLS-RS was higher in group 1 than in group 2 (P < 0.05). Prevalence of insomnia (P < 0.0002) and of EDS (P < 0.05) and mean ESS score (P < 0.01) were higher in RLS-positive than in RLS-free acromegalics. Video-PSG showed that mean sleep latency (P < 0.01), micro-arousal index (P < 0.05) and wakefulness after sleep onset (P < 0.01) were higher, whereas sleep efficiency (P < 0.01) was lower, in RLS-positive than in RLS-free patients. Global and physical AcroQoL scores were significantly lower in RLS-positive than in RLS-free acromegalics (P < 0.01 and P < 0.001, respectively). Prevalence and severity of RLS is increased in patients with active acromegaly and impacts negatively on their physical performances, dramatically impairing quality of life.

PMID: 21328081 [PubMed - in process]


Effects of high-dose octreotide LAR on glucose metabolism in patients with acromegaly inadequately controlled by conventional somatostatin analog therapy.


Department of Medical and Surgical Sciences, University of Brescia, 25125 Brescia, Italy.

OBJECTIVE: In this study, the effect of high-dose octreotide LAR on glucose metabolism in patients with acromegaly was investigated.

DESIGN: A post-hoc analysis of a clinical trial enrolling 26 patients with acromegaly not controlled by standard maximal somatostatin analog (SSAs) dose and randomized to receive high-dose (60 mg/28 days) or high-frequency (30 mg/21 days) octreotide i.m. injection (octreotide LAR) for 6 months.

METHODS: Glucose metabolic status was defined as worsened when a progression from normoglycemia to impaired fasting glucose (IFG) or from IFG to diabetes occurred or when an increase of HbA1c by at least 0.5% was demonstrated. An improvement of glucose metabolism was defined in the presence of a regression from IFG to normoglycemia and/or when HbA1c decreased by at least 0.5%.

RESULTS: Glucose metabolic status remained unchanged in a majority of patients (16/26 patients, 65.3%), worsened in six patients, and improved in four patients. Pre-existing metabolic status did not predict worsening of glucose metabolism, which, conversely, was significantly related to persistent biochemical activity of the disease. In fact, patients with worsened glucose metabolism exhibited a
Cannavo S, until 2011

less frequent decrease in serum GH and IGF1 levels, compared with patients with improved or unchanged glucose metabolism (2/6 vs 18/20; P=0.01).

CONCLUSION: An increase in octreotide LAR dose or frequency did not impact on glucose metabolism in most patients. Worsening of glucose metabolic status occurred in close relation with persistently uncontrolled acromegaly.

PMID: 21212103  [PubMed - indexed for MEDLINE]


Temozolomide-induced shrinkage of a pituitary carcinoma causing Cushing's disease--report of a case and literature review.


Department of Medicine and Pharmacology, Section of Endocrinology, Erasmus Medical Center, Rotterdam, The Netherlands. curto.loren@libero.it

Temozolomide (TMZ) is an alkylating chemotherapeutic agent that has recently been used in some cases as a new therapeutic tool for pituitary carcinomas and aggressive pituitary adenomas. In this report, we present the case of effective TMZ treatment in a 42-year-old man with ACTH-secreting carcinoma. The tumor grew progressively over 4 years, from 2.2 to 31.1 cm³, despite three surgical approaches and γ-knife treatment. Ki-67 increased from 2 to 18%. An intradural metastasis at the foramen magnum was detected by MRI after the third operation. Thereafter, four cycles of 5-day TMZ administration (200 mg/m²/day during the first, and 150 mg/m²/day during the following cycles) induced dramatic tumor size reduction (>90%). Clinical conditions improved progressively and, after 17 months from the beginning of TMZ administration, the patient is still alive. The treatment was well tolerated except for a transient thrombocytopenia (grade 4 WHO).

PMID: 21057727  [PubMed - indexed for MEDLINE]


N-terminal pro-brain natriuretic peptide determination as a possible marker of cardiac dysfunction in patients with adrenal disorders.

Iorio L, Rigolini R, Costa E, Cotta O, Cannavò S, Ambrosi B.

Comment on


PMID: 20671412  [PubMed - indexed for MEDLINE]
OBJECTIVE: Despite the contribution of national registries and population-based reports, data concerning the epidemiology of acromegaly is scanty. In addition, the role of the environmental context has not been investigated.

DESIGN: Epidemiology of acromegaly was studied in the province of Messina (Sicily, Italy), focusing on the influence of environmental factors.

METHODS: Four zones, characterized by different degrees of exposition to environmental toxins due to industrial pollution, were identified in the province: area A (76,338 inhabitants), area B (287,328 inhabitants), area C (243,381 inhabitants), and area D (47,554 inhabitants) at low, middle-low, middle, and high industrial density respectively. We identified all acromegalic who were born and resided in the province of Messina, among patients either referred to our endocrine unit or referred elsewhere but recorded in the archives of the provincial healthcare agency.

RESULTS: In the province of Messina, we found 64 patients (2 in area A, 24 in area B, 28 in area C, and 10 in area D). Macroadenomas were 60%, the male/female ratio was 1, and mean age at diagnosis (±s.e.m.) was 45.4±1.6 years. Overall, prevalence was 97 c.p.m. in the province (26 c.p.m. in area A, 84 c.p.m. in area B, 115 c.p.m. in area C, and 210 c.p.m. in area D). Risk ratio (RR), calculated in every area assuming area A as a reference, showed an increased risk of developing acromegaly in people residing in area D (RR=8.03; P<0.0014).

Conclusion: This study confirms the prevalence of acromegaly reported recently. The increased risk of developing this disease in area D suggests that the pathogenetic role of environmental context needs to be better evaluated.

PMID: 20621957 [PubMed - indexed for MEDLINE]
Assessment of coronary calcium deposits (CCD) by coronary computed tomography (CT) was recently introduced for evaluation of risk to develop events related to coronary heart disease (CHD). We investigated occurrence of CCD in 19 hypopituitary patients (patients), 34 healthy (H) subjects (H controls) and 36 patients with a similar rate of diabetes mellitus and hypertension (morbid, M), but without pituitary diseases (M controls). Patients were replaced with L-thyroxine, cortone acetate, sex hormones and/or desmopressin, but never with GH. Unenhanced coronary CT was performed by 16-row multislice scanner. Framingham score (FS) was calculated and CCD were measured by Agatston score (AS) in all subjects. AS>10 indicates increased CHD risk. CCD and AS >10 were detected in 50% and 33% of patients, respectively. Prevalence of CCD and mean AS were higher in patients than in H and M controls. In patients, AS was negatively dependent on IGF-I levels (p<0.01) and IGF-I SD (p<0.05), and AS >10 was associated with occurrence of hypertension (p<0.02) and hyperinsulinism (p<0.05). Men and women showed the same prevalence of AS >10 (25 vs 31%). FS and AS correlated significantly (rs=0.33, p<0.001), but CCD were detected also in 3/11 patients with low FS. In conclusion, 58% of patients were at CHD risk on the basis of increased FS and/or AS, above all if they were hypertensive and/or showed hyperinsulinism. CCD were detected also in patients with low FS. CHD risk is higher in women. Risk of CCD is increased in patients with low IGF-I levels.

PMID: 20511726  [PubMed - indexed for MEDLINE]


Predictive role of the immunostaining pattern of immunofluorescence and the titers of antipituitary antibodies at presentation for the occurrence of autoimmune hypopituitarism in patients with autoimmune polyendocrine syndromes over a five-year follow-up.


Department of Clinical and Experimental Medicine and Surgery, F. Magrassi, A. Lanzara, Second University of Naples, via Pansini N. 5, 80131 Naples, Italy.

CONTEXT: Antipituitary antibodies (APA) are frequently present in patients with autoimmune polyendocrine syndrome (APS). DESIGN: The aim was to evaluate the predictive value of APA for the occurrence of hypopituitarism. A total of 149 APA-positive and 50 APA-negative patients with APS and normal pituitary function were longitudinally studied for 5 yr.

METHODS: APA, by indirect immunofluorescence, and anterior pituitary function
were assessed yearly in all patients. The risk for developing autoimmune pituitary dysfunction was calculated using survival and multivariate analysis.

RESULTS: Hypopituitarism occurred in 28 of 149 (18.8%) APA-positive patients but in none of the 50 APA-negative patients. The immunostaining pattern in APA-positive patients involved either isolated pituitary cells [type 1 pattern; n=99 (66.4%)] or all pituitary cells [type 2 pattern; n=50 (33.6%)]. All patients developing pituitary dysfunction throughout the study span had a type 1 pattern. Kaplan-Meier curves for cumulative survival showed a significantly higher rate for developing hypopituitarism in relation to positive APA tests (P<0.005), pattern of immunostaining (P<0.0001), and APA titers (P<0.000001). Cox regression analysis in APA-positive patients with a type 1 pattern demonstrated a significantly (P<0.0001) higher risk for the onset of hypopituitarism in relation to increasing titers of APA.

CONCLUSIONS: APA measurement by immunofluorescence may help to predict the occurrence of hypopituitarism but only when considering the immunostaining pattern and their titers. Combined evaluation of these parameters allows identifying patients at higher risk for pituitary autoimmune dysfunction, thus requiring a strict pituitary surveillance to disclose a preclinical phase of hypopituitarism and possibly interrupt therapeutically the progression to clinically overt disease.

PMID: 20501686 [PubMed - indexed for MEDLINE]

Primary empty sella: Why and when to investigate hypothalamic-pituitary function.


Department of Medical and Surgical Sciences, University of Brescia, Italy.
a.giustina@libero.it

PMID: 20208457 [PubMed - indexed for MEDLINE]

Lymphocytic hypophysitis: differential diagnosis and effects of high-dose pulse steroids, followed by azathioprine, on the pituitary mass and endocrine abnormalities--report of a case and literature review.

Curtò L, Torre ML, Cotta OR, Losa M, Terreni MR, Santarpia L, Trimarchi F, Cannavò S.

Department of Medicine and Pharmacology - Section of Endocrinology, University of Messina, Italy. endocrinologia@unime.it
We report on a man with a progressively increasing pituitary mass, as demonstrated by MRI. It produced neurological and ophthalmological symptoms, and, ultimately, hypopituitarism. MRI also showed enlargement of the pituitary stalk and a dural tail phenomenon. An increased titer of antipituitary antibodies (1:16) was detected in the serum. Pituitary biopsy showed autoimmune hypophysitis (AH). Neither methylprednisolone pulse therapy nor a subsequent treatment with azathioprine were successful in recovering pituitary function, or in inducing a significant reduction of the pituitary mass after an initial, transient clinical and neuroradiological improvement. Anterior pituitary function evaluation revealed persistent hypopituitarism. AH is a relatively rare condition, particularly in males, but it represents an emerging entity in the diagnostic management of pituitary masses. This case shows that response to appropriate therapy for hypophysitis may not be very favorable and confirms that diagnostic management of nonsecreting pituitary masses can be a challenge. Clinical, imaging, and laboratory findings are useful for suggesting the diagnosis, but pituitary biopsy may be necessary to confirm it.

PMID: 20098956  [PubMed - indexed for MEDLINE]


Lipoatrophy in GH deficient patients treated with a long-acting pegylated GH.


Department of Endocrinology and Reproductive Medicine, GH Pitié Salpêtrière, Centre de Référence des Maladies Endocriniennes Rares de la Croissance, Université Paris VI Pierre et Marie Curie, 47-83, Boulevard de l'Hôpital, 75651 Paris Cedex 13, France. philippe.touraine@psl.aphp.fr

OBJECTIVE: Changes observed during adult GH deficiency (GHD) are most often reversed with the administration of recombinant human GH (rhGH). To avoid daily injections, a long-acting GH molecule has been obtained by covalent binding of polyethylene glycol (PEG) with rhGH (PEG-GH), allowing weekly s.c. injections. This study was designed to assess its efficacy and safety, in adult GHD subjects.

DESIGN AND METHODS: This was a randomized, double-blind, placebo-controlled, multiple-dose, parallel group study. Subjects were recruited from 34 centers. A total of 105 subjects with GHD were assigned a treatment. They received 6 weekly injections of either PEG-GH or placebo. Subjects were randomized into one out of
Cannavo S, until 2011

four treatment groups (Groups A-D) or placebo (Group E). Groups A, B, and C received 1, 3, and 4 mg PEG-GH respectively, for the first 3 weeks followed by 2, 6, and 8 mg PEG-GH respectively, for the remaining 3 weeks. Group D received 4 mg PEG-GH for 6 weeks. Group E received placebo. The study was suspended because of the development of lipoatrophy in certain subjects and restarted with an injection rotation plan, before being terminated due to further subjects developing lipoatrophy.

RESULTS: A total of 13 cases of injection-site lipoatrophy were reported, of which ten were in females and three occurred after the first injection; all cases were independent of PEG-GH dose or IGF1 levels, either basal or under treatment.

CONCLUSION: The unpredictable occurrence of injection-site lipoatrophy with weekly long-acting pegylated GH molecules may be a limiting factor for their development.

PMID: 19654233  [PubMed - indexed for MEDLINE]


Dissociated responsiveness of a growth hormone- and thyrotropin-secreting pituitary adenoma to octreotide-long-acting release therapy: the intriguing case of Mister B.

Curtò L, Ragonese M, Losa M, Trimarchi F, Cannavò S.

PMID: 19609104  [PubMed - indexed for MEDLINE]


Unusual endocrine and somatic phenotypic abnormalities in a 14-year-old boy with classic Klinefelter syndrome (47,XXY).

Curtò L, Messina MF, Trimarchi F, Cannavò S.

PMID: 19542758  [PubMed - indexed for MEDLINE]


Unusual magnetic resonance imaging finding in a male with lymphocytic hypophysitis mimicking a pituitary tumor.

Curtò L, Granata F, Torre ML, Trimarchi F, Cannavò S.

PMID: 19498319  [PubMed - indexed for MEDLINE]

High-dose intramuscular octreotide in patients with acromegaly inadequately controlled on conventional somatostatin analogue therapy: a randomised controlled trial.


Department of Medical and Surgical Sciences, University of Brescia, 25123 Brescia, Italy. a.giustina@libero.it

OBJECTIVE: In acromegaly, 25-50% of patients respond inadequately to conventional long-acting somatostatin analogue (SSA) therapy. Response may be improved by increasing SSA frequency or dose. This study evaluated the biochemical efficacy and safety of high-dose octreotide in patients with acromegaly.

DESIGN: A 24-week prospective, multicentre, randomised, open-label trial conducted from 12 December 2005 to 23 October 2007 in patients with persistently uncontrolled acromegaly despite \( \geq 6 \) month conventional SSA therapy.

METHODS: Patients with \( > or =50\% \) reduction in GH levels during previous SSA treatment were randomised to high-dose (60 mg/28 days) or high-frequency (30 mg/21 days) octreotide i.m. injection. Primary end-points were week 12 and 24 reduction in serum IGF1 and GH from baseline. Secondary end points included IGF1 normalisation and tumour shrinkage rates, and safety/tolerability evaluations.

RESULTS: Significantly, more patients (10 out of 11) achieved week 24 IGF1 reduction in the high-dose than the high-frequency group (8 out of 15; \( P<0.05 \)). In the high-dose group only, week-24 IGF1 values were significantly reduced (\( P=0.02 \)) versus baseline. Normalisation of IGF1 occurred only with the high-dose regimen (4/11; \( P=0.02 \)). Out of 14 patients experiencing adverse events, 5 reported drug-related gastrointestinal effects. No dose-response relationship was seen. Safety parameters were similar between treatment groups, apart from a slight decrease in HbA1c in the high-dose group only.

CONCLUSION: High-dose octreotide treatment is safe and effective (normalisation of IGF1 levels) in a subset of patients with active acromegaly inadequately controlled with long-term SSA. Individualised octreotide doses up to 60 mg/28 days may improve outcomes of SSA therapy.

PMID: 19465485 [PubMed - indexed for MEDLINE]


Non-functioning pituitary adenomas infrequently harbor G-protein gene mutations.

Ruggeri RM, Santarpia L, Curtò L, Torre ML, Galatioto M, Galatioto S, Trimarchi F, Cannavo S.

Department of Medicine and Pharmacology, Section of Endocrinology, University of Messina, 98125 Messina, Italy. rmruggeri@unime.it
BACKGROUND: Mutations of the genes encoding the alpha subunit of the stimulatory G protein (Gs) and of the inhibiting Gi2 protein (GNAS1 and GNAI2 genes, respectively) have been described in various endocrine neoplasias, including pituitary tumors.

AIM: To search for mutations of GNAS1 and GNAI2 in a continuous series of non-functioning pituitary adenoma (NFPA) patients neurosurgically treated.

SUBJECTS AND METHODS: The surgical samples of 22 patients who have been defined and characterized on a clinical, biochemical, histological, and immunohistochemical point of view have been processed for investigating the presence of the above mutations by PCR amplification of the hot spots exons 8 and 9 of GNAS1, and exons 5 and 6 of GNAI2, followed by direct sequencing. Moreover, the promoter region of GNAI2, in order to assess the prevalence of single nucleotide polymorphisms (SNP), was investigated in the same series.

RESULTS: A CGT>TGT mutation at codon 201 of GNAS1 gene in a single case of NFPA was found, but no mutation of GNAI2A was demonstrated.

CONCLUSIONS: This finding suggests and confirms that G-protein mutations are rare and not crucial in NFPA development. Additionally, we found a silent SNP at codon 318 in the promoter of the Gi2alpha gene in one out of the 22 NFPA.

PMID: 19169048 [PubMed - indexed for MEDLINE]


Patients with craniopharyngiomas: therapeutical difficulties with growth hormone.

Cannavò S, Marini F, Trimarchi F.

Section of Endocrinology, Department of Medicine and Pharmacology, University of Messina, 98125 Messina, Italy. cannavos@unime.it

Craniopharyngioma (CP) is a rare and benign tumor of the pituitary region. It is the second cause of hypopituitarism in children and the third in adults. Multiple pituitary deficiencies or panhypopituitarism and diabetes insipidus are very frequent and their prevalence increases significantly after neurosurgery. In patients with GH deficiency (GHD), recombinant GH (rGH) replacement is recommended, after a near complete surgical excision of CP and exclusion of tumor progression. The risk of CP recurrence or progression due to rGH therapy is unproven. Treatment with rGH improves significantly the quality of life (QoL), although body composition and lipid abnormalities are not modified. At the data lock 2003, in the Hypopituitary Control and Complications Study (HypoCCS) Italian Database 90 patients with CP were included. Adulthood onset (AO) hypopituitarism had been diagnosed in two/thirds of them. They had worse QoL than their childhood onset (CO)-counterpart. During 3-yr rGH treatment mean body mass index, fat mass percentage, and both hip and waist circumferences decreased significantly only in CO patients. Accordingly, total cholesterol and triglycerides decreased, and HDL-cholesterol increased significantly in CO- but not in AO-patients. Analysis of dose titration showed that CO- were treated with higher rGH doses than AO-patients.
PMID: 19020388 [PubMed - indexed for MEDLINE]


Confirmation of local amino acid sequence homology between human prolactin and the amyloid-related proteins.

Benvenga S, Cannavò S, Trimarchi F, Guarneri F.

PMID: 18985456 [PubMed - indexed for MEDLINE]


Assessment of the awareness and management of cardiovascular complications of acromegaly in Italy. The COM.E.T.A. (COMorbidities Evaluation and Treatment in Acromegaly) Study.


Department of Medical and Surgical Sciences, University of Brescia, Brescia, Italy. a.giustina@libero.it

Erratum in
J Endocrinol Invest. 2008 Dec;31(12):IV.
BACKGROUND: During the course of acromegaly, cardiovascular, respiratory, and metabolic co-morbidities contribute to enhanced mortality. In 2002, the Pituitary Society and the European Neuroendocrine Association sponsored a Consensus Workshop in Versailles during which guidelines for diagnosis and treatment of co-morbidities in acromegaly were defined. However, as for other guidelines previously issued in the field, no data are available on their clinical application.

AIM: The aim of this work coordinated by the Italian Study group on co-morbidities evaluation and treatment in acromegaly (COM.E.T.A.) was to assess, on a national basis, the application in the clinical practice of the Versailles criteria for diagnosis and treatment of cardiovascular comorbidities in acromegaly.

MATERIALS AND METHODS: In January 2007 an ad hoc designed questionnaire was sent by mail to 130 endocrine Centers in Italy.

RESULTS: The guidelines have been generally well perceived and translated in clinical practice. Specifically: 1) echocardiography is considered the mainstay for the diagnosis and follow-up; 2) ambulatory blood pressure monitoring and blood lipid assessment are performed in most hypertensive patients; 3) most endocrinologists directly manage hypertension and are aware of the uncertainty of the effect of the control of the disease on blood pressure levels; 4) ACE inhibitors and angiotensin receptors blockers are first-choice anti-hypertensive treatment; 5) approximately half of the centers consider somatostatin analogues of paramount relevance for biochemical control of disease; 6) awareness that left ventricular hypertrophy and heart failure are the most relevant cardiovascular complications is high although the impact of ischemic, arrhythmic, and valvular complications on prognosis is less well perceived.

CONCLUSION: The results of the present survey suggest that previously issued guidelines are generally carefully followed in the clinical practice. On the other side, a certain lack of awareness of emerging aspects of the cardiovascular comorbidities of acromegaly confirms the necessity of periodically updating the guidelines based on the availability of new clinical information.

PMID: 18852535 [PubMed - indexed for MEDLINE]

Large genomic deletions in AIP in pituitary adenoma predisposition.

Department of Medical Genetics, Biomedicum Helsinki, University of Helsinki, 00014 Helsinki, Finland.

CONTEXT: Germline mutations in AIP have been recently shown to cause pituitary adenoma predisposition (PAP). Subsequently, many intragenic germline mutations have been reported, both in familial and in sporadic settings.

Pagina 15
Cannavo S, until 2011

OBJECTIVE: Our objective was to evaluate the possible contribution of large genomic germline AIP deletions, an important mutation type in tumor predisposition syndromes, in PAP.

DESIGN: Here, we applied the multiplex ligation-dependent probe amplification assay to examine whether large genomic AIP or MEN1 alterations account for a subset of PAP cases.

PATIENTS: The study was performed on familial and sporadic pituitary adenoma cases of European origin, which had previously tested negative for germline AIP and MEN1 mutations by sequencing.

RESULTS: Two of 21 pituitary adenoma families (9.5%) were found to harbor an AIP deletion. No copy number changes were detected among 67 sporadic pituitary adenoma patients. No MEN1 deletions were found.

CONCLUSIONS: The present study shows that large genomic AIP deletions account for a subset of PAP. Therefore, in suspected PAP cases undergoing counseling and AIP genetic testing, multiplex ligation-dependent probe amplification could be considered if direct sequencing does not identify a mutation.

PMID: 18628514 [PubMed - indexed for MEDLINE]


Soluble adhesion molecules levels in patients with Cushing's syndrome before and after cure.

Ermetici F, Malavazos AE, Corbetta S, Eller-Vainicher C, Cannavò S, Corsi MM, Ambrosi B.

Endocrinology Unit, Department of Medical and Surgical Sciences, IRCCS Policlinico San Donato, University of Milan, Milan, Italy.

OBJECTIVE: Patients with Cushing's syndrome (CS) show a high prevalence of cardiovascular risk factors and atherosclerosis, persisting even after cure. Soluble intercellular adhesion molecule-1 (sICAM-1) and vascular cell adhesion molecule-1 (sVCAM-1) are surrogate markers of endothelial function involved in the initiation of atherosclerosis. This study aimed to evaluate sICAM-1 and sVCAM-1 levels in patients with CS before and after successful cure.

SUBJECTS AND METHODS: sICAM-1 and sVCAM-1 levels were evaluated in 28 patients with active CS and in 12 patients with Cushing's disease (CD), 6-12 months after disease remission. Body mass index (BMI), blood pressure, glucose, serum lipids, ACTH, cortisol and urinary free cortisol (UFC) were measured in basal conditions in all patients.

RESULTS: At baseline, sICAM-1 levels positively correlated with BMI (r=0.443, p<0.01), while no correlations between sICAM/sVCAM levels and ACTH, cortisol or UFC were found. Plasma ACTH, serum cortisol, and UFC levels significantly decreased in 12 cured patients, but ICAM-1 and VCAM-1 levels were unchanged (12.7+/-1.8 vs 10.1+/-0.9 ng/ml and 33.5+/-4.4 vs 35.8+/-4.0 ng/ml, respectively). Obesity, hypertension, and impaired glucose metabolism persisted 1 yr after the biochemical cure of hypercortisolism. A significant reduction in
ICAM-1 levels was observed in 4 out of 12 cured patients as well as a remission from diabetes, hypertension or obesity.

CONCLUSIONS: ICAM/VCAM-1 levels show a great variability in patients with active CS, not correlated with cortisol levels, and are slightly modified in some cured patients with CD. The persistence of obesity, hypertension, and impaired glucose metabolism may be responsible for the maintenance of a subclinical endothelial dysfunction, making these subjects still at high cardiovascular risk and needing a long-term follow-up.

PMID: 18560255  [PubMed - indexed for MEDLINE]


Aryl hydrocarbon receptor interacting protein (AIP) gene mutation analysis in children and adolescents with sporadic pituitary adenomas.


Department of Medical Genetics, Genome-scale Biology Research Program, University of Helsinki, Helsinki, Finland.

OBJECTIVE: Pituitary adenomas occur rarely in childhood and adolescence. Pituitary adenoma predisposition (PAP) has been recently associated with germline mutations in the aryl hydrocarbon receptor interacting protein (AIP) gene. The aim of the study was to examine the proportion of germline AIP mutations in apparently sporadic paediatric pituitary adenomas.

DESIGN: Genomic DNA was analysed for mutations in the AIP gene, by PCR amplification and direct sequencing.

PATIENTS: A population-based cohort consisting of 36 apparently sporadic paediatric pituitary adenoma patients, referred to two medical centres in Italy, was included in the study. Patients were either less than 18 years at diagnosis, or showed clinical evidence of adenoma development before the age of 18 years.

RESULTS: A heterozygous in-frame deletion Y248del (c.742_744delTAC) was identified in one GH-secreting adenoma patient. Loss of heterozygosity (LOH) analysis of tumour DNA revealed the loss of the wild-type allele. First degree relatives carrying the mutation were clinically unaffected.

CONCLUSIONS: While mutations were absent in non-GH-secreting adenoma patients, germline AIP mutations can be found in children and adolescents with GH-secreting tumours, even in the absence of family history. The present study reports the AIP mutation analysis results on patients of a single ethnic origin. Clearly, further studies are needed to improve our knowledge on the role of AIP in paediatric pituitary adenomas.

PMID: 18410548  [PubMed - indexed for MEDLINE]
Evaluation of myocardial fibrosis by imaging techniques in acromegaly.
Romanello G, Di Bella G, Minutoli F, Cannavo S.
Comment on
PMID: 18394020  [PubMed - indexed for MEDLINE]

Dopamine D2 receptor gene polymorphisms and response to cabergoline therapy in
patients with prolactin-secreting pituitary adenomas.
Filopanti M, Barbieri AM, Angioni AR, Colao A, Gasco V, Grottoli S, Peri A,
Baglioni S, Fustini MF, Pigliaru F, Monte PD, Borretta G, Ambrosi B, Jaffrain-Rea
A.
Department of Medical Sciences, University of Milan, Endocrine and Diabetes Unit
Fondazione Ospedale Maggiore IRCCS, Milan, Italy.
Dopamine-agonist cabergoline (CB) reduces prolactin (PRL) secretion and tumor
size in 80% of patients with prolactin-secreting adenomas (PRL-omas) by binding
type 2 dopamine receptor (DRD2). The mechanisms responsible for resistance to CB
remain largely unknown. To assess the association of DRD2 with sensitivity to CB,
TaqI-A1/A2, TaqI-B1/B2, HphI-G/T and NcoI-C/T genotypes were determined in a
cross-sectional retrospective study, including 203 patients with PRL-oma. DRD2
alleles frequencies did not differ between patients and 212 healthy subjects.
Conversely, NcoI-T allele frequency was higher in resistant rather than
responsive patients, considering both PRL normalization (56.6 vs 45.3%, P=0.038)
and tumor shrinkage (70.4 vs 41.4%, P=0.006). Finally, [TaqI A1-/TaqI B1-/Hphl
T-/NcoI T-] haplotype was found in 34.5% of patients normalizing PRL with < or =3
mg/week of CB vs 11.3% of resistent (P=0.021). In conclusion, resistance to CB
was associated with DRD2 NcoI-T+ allele, consistent with evidence suggesting that
this variant may lead to reduction and instability of DRD2 mRNA or protein.
PMID: 18332900  [PubMed - indexed for MEDLINE]

Atrial parasystole in left ventricular noncompaction: a morphofunctional study by
echocardiography and magnetic resonance imaging.
Isolated left ventricular noncompaction is a recently recognized age-independent cardiac genetic disorder caused by heterogeneous defects in endo-myocardial morphogenesis. Transthoracic echocardiography and cardiac magnetic resonance are the most reliable techniques to make a diagnosis of the disease, noninvasively. Arrhythmic atrial and ventricular disorders have been reported in 20-50% of these patients. The morphological and functional findings are described in a young woman in whom the exclusive clinical sign of isolated ventricular noncompaction was an atrial parasystole.

PMID: 18301148  [PubMed - indexed for MEDLINE]


Hypophosphatemia as unusual cause of ARDS in Cushing's syndrome secondary to ectopic CRH production. A case report.

Mondello S, Fodale V, Cannavò S, Aloisi C, Almoto B, Buemi M, Santamaria LB.

Department of Internal Medicine, Psychiatric and Anesthesiological Sciences, University of Messina, School of Medicine, Policlinico Universitario G.Martino, 98125 Messina, Italy.

Hypophosphatemia is an unusual cause of acute respiratory distress syndrome (ARDS). We describe a hypophosphatemia-related ARDS case report of a 50-year-old woman with ACTH dependent Cushing's syndrome secondary to ectopic CRH production. The patient clinically showed hypotension tachypnea and increasing dyspnea. Laboratory data showed carbohydrate intolerance, severe hypokalemia, and hypophosphatemia. Arterial blood gases measurement revealed hypocapnia and elevation in bicarbonate values. Chest X-ray showed diffuse bilateral alveolar infiltrates similar to acute pulmonary edema and Kerley's striae. Chest CT scan evidenced diffuse ground glass opacification, bilateral patchy consolidation, and fibrosis, compatible with the recovery phase of ARDS. Clinical symptoms and laboratory examinations supported the diagnosis of ARDS. The patient was managed with supplemental potassium, octreotide, and oxygen therapy. Hypophosphatemia was managed by treating the underlying disorder. Successive surgical removal of the adrenal gland led to complete resolution of Cushing's syndrome. In conclusion, although rare and associated with specific risk factors, hypophosphatemia should be suspected in patients who develop unexplained ARDS.

PMID: 18264630  [PubMed - indexed for MEDLINE]

Pegvisomant in acromegaly: why, when, how.


Department of Molecular and Clinical Endocrinology and Oncology, University Federico II of Naples, Naples, Italy.

PMID: 17923803  [PubMed - indexed for MEDLINE]


MRI finding of simultaneous coexistence of growth hormone-secreting pituitary adenoma with intracranial meningioma and carotid artery aneurysms: report of a case.

Curto L, Squadrito S, Almoto B, Longo M, Granata F, Salpietro F, Torre ML, Marini F, Trimarchi F, Cannavo S.

Department of Medicine and Pharmacology, Unit of Endocrinology, University of Messina, Messina, Italy. curto.loren@libero.it

Coexistence of pituitary adenoma, intracranial meningioma and cerebral aneurysm has never been described. We report on a patient with GH-secreting pituitary macroadenoma associated with a right frontal meningioma and with two intracavernous asymptomatic aneurysms. A 61-year-old woman was referred to our Endocrine Unit 13 years after a right frontal craniotomy for a pituitary tumour. Endocrine investigation showed high levels of IGF-1 (560 ng/ml) and increased basal serum GH (56 ng/ml) levels, not suppressed after OGTT. MRI showed persistence of a homogeneously enhancing intra- and suprasellar lesion, compressing the visual pathways, with bilateral intracavernous invasion and simultaneous coexistence of a right intracavernous internal carotid artery (ICA) aneurysm in direct contact with the pituitary tumour. Somatostatin analog treatment normalized GH and IGF-1 levels. Eight months later, the patient underwent a balloon ICA occlusion with disappearance of the right ICA aneurysm. One year later, a new MRI confirmed the presence of the pituitary mass showing also a right intracranial frontal meningioma and a new ICA aneurysm on the left side. Previous studies have suggested that prolonged GH hypersecretion could play a role in the genesis of intracranial aneurysms, inducing atherosclerotic and/or degenerative modification of the arterial walls. Other aetiological factors include a mechanical effect due to a direct contact between adenoma and aneurysm. Coexistence of pituitary adenoma and intracranial meningioma is a rare event, but also for this association it has been suggested that GH or other growth factors could play a role in appearance or in growth of meningioma. In our case, meningioma appeared and grew, despite the effective treatment of acromegaly.
Hypopituitarism findings in patients with primary brain tumors 1 year after neurosurgical treatment: preliminary report.


Division of Endocrinology, Institute of Internal Medicine, Catholic University of Sacred Heart, 00189 Rome, Italy. laurademarinis@yahoo.it

Hypopituitarism represents the consequence of many conditions, in both the adult and child population. It may occur after neurosurgical treatment of brain tumors arising near sella turcica. Much more attention has been focused on lesions far from the hypothalamic-pituitary region as possible causes of pituitary impairment, validating the concept of the particular fragility of these structures. The aim of this study was to evaluate pituitary function in particular GH deficiency (GHD) in patients submitted to neurosurgery for benign tumors of the central nervous system (CNS) not involving hypothalamic-pituitary region. We observed 37 patients with benign brain tumors [13 males, 24 females, age: 54.6+-13.9 yr; body mass index (BMI): 25.1+-4.0 kg/m2] performing a basic evaluation of the pituitary function and a dynamic test of the GH/IGF-I axis [GHRH (1 microg/kg iv)+arginine (0.5 g/kg iv) test] for 3 and 12 months after the neurosurgical treatment. Some degree of hypopituitarism was shown in 16 patients (43.2%) at the 3-months follow-up. Hypogonadism was present in 4 patients, hypoadrenalism in another 4 and hypothyroidism in 2. Two patients showed mild hyperprolactinemia and no patients had diabetes insipidus. Seven patients (18.9%) were GH deficient (peak GH <16.5 microg/dl). At 12 months retesting, some degree of hypopituitarism was confirmed in 8 patients, hypogonadism in 2 and hypothyroidism in one; no patients showed hypoadrenalism and GHD was present in 5. This data suggests that hypopituitarism of various degree may develop in patients who are submitted to neurosurgery for primary brain tumors, even far from hypothalamic-pituitary region.

PMID: 16840829 [PubMed - indexed for MEDLINE]
CONTEXT: Coronary atherosclerosis in acromegaly was not extensively investigated in the literature until now. At autopsy, it was demonstrated in about 20% of patients with long-lasting disease, and myocardial infarction was reported as cause of death in a quarter of acromegalics.

OBJECTIVE: The objective of the study was to evaluate coronary atherosclerosis in a cohort of acromegalics with controlled or uncontrolled disease.

DESIGN: Coronary risk was evaluated by the Framingham algorithm, according to the Framingham score (FS). Patients were stratified into low (<6%), intermediate (6-20%), and high (>20%) midterm risk. Coronary calcium deposits were detected by multidetector computed tomography and measured by the Agatston algorithm. Coronary artery calcium [Agatston score (AS)] was quantified at the level of left main artery, left anterior descendent artery, left circumflex artery, right coronary artery, and posterior descendent artery. Total AS values in healthy persons are less than 50 (aged < 60 yr) and less than 300 (age ≥ 60 yr).

PATIENTS: Thirty-nine patients (12 males and 27 females, aged 53.0 +/- 2.1 yr) were evaluated. In each patient, the mean of at least four determinations of serum IGF-I, assayed during the last 2 yr before study, was normalized for the age-matched normal range, and the result was presented as sd value (IGF-I sd). On the basis of serum IGF-I sd, acromegaly was considered controlled (< or =1.9 sd; n = 24) or uncontrolled (> or = 2.0 sd; n = 15).

RESULTS: The FS was intermediate in 12 and high in two acromegalics. Overall, the FS was not correlated with serum GH values and IGF-I sd. Mean FS was not significantly different between patients with controlled and uncontrolled acromegaly. Total AS was increased in nine patients, most frequently in left anterior descendent, left circumflex, and left main arteries. In these nine patients, mean AS was similar in individuals with controlled and those with uncontrolled acromegaly, and the rate of 17% patients with controlled disease having increased AS was not statistically different from the rate of 33% uncontrolled acromegalics. Total AS was increased in six of 12 males and in three of 27 females (chi(2) 7.1, P < 0.01). Overall, total AS correlated with FS (r(2) = 0.4, P < 0.0002) but not age, body mass index, disease duration, indexed left ventricular mass, serum cholesterol, triglycerides, GH, or IGF-I levels. Increased AS was more frequently observed in acromegalics with diabetes mellitus (chi(2) = 5.2, P < 0.05) or hypertension (chi(2) = 9.8, P < 0.002) but not in smokers (chi(2) = 1.34, P = NS). Seven of nine patients with coronary calcium deposits had a FS greater than 6%. In six of 13 patients with FS greater than 6%, multidetector computed tomography did not demonstrate coronary calcifications.

CONCLUSIONS: In our study, the integrated evaluation of FS and AS showed that 41% of acromegalics are at risk for coronary atherosclerosis and that coronary calcifications were evident in about half of them despite the fact that myocardial infarction was not more frequent in acromegalic patients than the general population. Moreover, the control of acromegaly did not influence significantly the extent of coronary atherosclerosis.
34. BMC Endocr Disord. 2006 Feb 28;6:1.

Echocardiographic assessment of subclinical left ventricular eccentric hypertrophy in adult-onset GHD patients by geometric remodeling: an observational case-control study.


Clinical and Experimental Department of Medicine and Pharmacology, Cardiology Unit, University Hospital of Messina, Messina, Italy. cesaredeggregorio@alice.it

BACKGROUND: Most patients with growth hormone deficiency (GHD) show high body mass index. Overweight subjects, but GHD patients, were demonstrated to have high left ventricular mass index (LVMi) and abnormal LV geometric remodeling. We sought to study these characteristics in a group of GHD patients, in an attempt to establish the BMI-independent role of GHD.

METHODS: Fifty-four patients, 28 F and 26 M, aged 45.9 +/- 13.1, with adult-onset GHD (pituitary adenomas 48.2%, empty sella 27.8%, pituitary inflammation 5.5%, cranio-pharyngioma 3.7%, not identified pathogenesis 14.8%) were enrolled. To minimize any possible interferences of BMI on the aim of this study, the control group included 20 age- and weight-matched healthy subjects. The LV geometry was identified by the relationship between LVMi (cut-off 125 g/m2) and relative wall thickness (cut-off 0.45) at echocardiography.

RESULTS: There was no significant between-group difference in resting cardiac morphology and function, nor when considering age-related discrepancy. The majority of patients had normal-low LVM/LVMi, but about one fourth of them showed higher values. These findings correlated to relatively high circulating IGF-1 and systolic blood pressure at rest. The main LV geometric pattern was eccentric hypertrophy in 22% of GHD population (26% of with severe GHD) and in 15% of controls (p = NS).

CONCLUSION: Though the lack of significant differences in resting LV morphology and function, about 25% of GHD patients showed high LVMi (consisting of eccentric hypertrophy), not dissimilarly to overweight controls. This finding, which prognostic role is well known in obese and hypertensive patients, is worthy to be investigated in GHD patients through wider controlled trials.

PMCID: PMC1483822
PMID: 16507109 [PubMed]


Hypopituitarism induced by traumatic brain injury in the transition phase.

Traumatic brain injury (TBI) has been associated with hypothalamic-pituitary dysfunction in general and GH deficiency (GHD) in particular; the consequences of this on growth and development are likely to be critical in children and adolescents in the so-called "transition phase". In order to verify the consequences of TBI on pituitary function in the transition phase, we studied a population of adolescents and young adults 3 and 12 months after brain injury [no. = 23, 9 females, 14 males; age: 16-25 yr; body mass index (BMI): 21.9 +/- 0.6 kg/m2]. At 3 months, hypopituitarism was present in 34.6%. Total, multiple and isolated deficits were present in 8.6, 4.3 and 21.7%, respectively. Diabetes insipidus (DI) was present in 8.6% patients and mild hyperprolactinemia in 4.3%. At 12 months, hypopituitarism was present in 30.3%. Total, multiple and isolated deficits were present in 8.6, 4.3 and 17.4%, respectively. DI was present in 4.3% of patients and mild hyperprolactinemia in 4.3%. Total hypopituitarism was always confirmed at retesting. Multiple and isolated hypopituitarism were confirmed in 0/1 and 2/5, respectively. Two/23 patients showed isolated hypopituitarism at 12 months only; 1 patient with isolated at 3 months showed multiple hypopituitarism at retesting. GHD and secondary hypogonadism were the most common acquired pituitary deficits. These results show the high risk of TBI-induced hypopituitarism also in the transition age. Thus it is recommended that pediatric endocrinologists follow-up pituitary function of children and adolescents after brain injuries.

PMID: 16483176  [PubMed - indexed for MEDLINE]


Residual pituitary function after brain injury-induced hypopituitarism: a prospective 12-month study.


Division of Endocrinology and Metabolism, Department of Internal Medicine, University of Turin, C.so Dogliotti, 14, 10126 Turin, Italy.

CONTEXT: Traumatic brain injury (TBI) and subarachnoid hemorrhage (SAH) are conditions at high risk for the development of hypopituitarism.

OBJECTIVE: The objective of the study was to clarify whether pituitary deficiencies and normal pituitary function recorded at 3 months would improve or worsen at 12 months after the brain injury.

DESIGN AND PATIENTS: Pituitary function was tested at 3 and 12 months in patients...
Cannavo S, until 2011
who had TBI (n = 70) or SAH (n = 32).
RESULTS: In TBI, the 3-month evaluation had shown hypopituitarism (H) in 32.8%.
Panhypopituitarism (PH), multiple (MH), and isolated (IH) hypopituitarism had
been demonstrated in 5.7, 5.7, and 21.4%, respectively. The retesting
demonstrated some degree of H in 22.7%. PH, MH, and IH were present in 5.7, 4.2,
and 12.8%, respectively. PH was always confirmed at 12 months, whereas MH and IH
were confirmed in 25% only. In 5.5% of TBI with no deficit at 3 months, IH was
recorded at retesting. In 13.3% of TBI with IH at 3 months, MH was demonstrated
at 12-month retesting. In SAH, the 3-month evaluation had shown H in 46.8%. MH
and IH had been demonstrated in 6.2 and 40.6%, respectively. The retesting
demonstrated H in 37.5%. MH and IH were present in 6.2 and 31.3%, respectively.
Although no MH was confirmed at 12 months, two patients with IH at 3 months
showed MH at retesting; 30.7% of SAH with IH at 3 months displayed normal
pituitary function at retesting. In SAH, normal pituitary function was always
confirmed. In TBI and SAH, the most common deficit was always severe GH
deficiency.
CONCLUSION: There is high risk for H in TBI and SAH patients. Early diagnosis of
PH is always confirmed in the long term. Pituitary function in brain-injured
patients may improve over time but, although rarely, may also worsen. Thus,
brain-injured patients must undergo neuroendocrine follow-up over time.

PMID: 16144947  [PubMed - indexed for MEDLINE]

Hypopituitarism and rare dermatological diseases: an intriguing case of xanthoma
dissemminatum.
Curtò L, Cannavò SP, Lentini M, Cannavò S.
PMID: 15963073  [PubMed - indexed for MEDLINE]

Effectiveness of long-term rosiglitazone administration in patients with
Cushing's disease.
Cannavò S, Arosio M, Almoto B, Dall'Asta C, Ambrosi B.
Comment on
PMID: 15963072  [PubMed - indexed for MEDLINE]


Pagina 25
This short review summarizes the results of treatments now available in Italy for the management of GH and IGF-I excess due to primary pituitary somatotroph adenoma, which accounts for over 99% of cases of acromegaly. Goals of treatment of acromegaly should now include, in addition to the reduction of tumor bulk and symptomatic relief, the lowering of GH circulating concentrations to below a critical level (2.5 microg/l, "safe" GH), the normalization of serum IGF-I concentrations according to age, improvement (or at least not worsening) of co-morbidities (diabetes mellitus, hypertension, cardiomyopathy, sleep-apnea), the decrease of the risk of premature mortality. Surgery, radiation (fractionated conventional radiotherapy and radiosurgery) and medical treatments with dopamine agonists and somatostatin analogs are the available options that are discussed in detail. The treatment of acromegaly must be tailored to the needs of the individual patient. Age, tumor size and invasiveness, GH concentrations, the patient's general medical conditions, presence and severity of co-morbidities, availability of local resources such as an expert neurosurgeon or gamma-knife radiosurgery, and of course the informed wishes of the patient are all factors that must be taken into account. For most patients the treatment will be multimodal. However, despite criteria and guidelines based on continuously emerging information about the management of acromegaly, patient outcomes are still less than desirable, with 10 to 20% of patients with uncontrolled disease, despite the use of all available therapies. This underscores the need for the quick introduction in clinical practice of the new therapies.

PMID: 15497658 [PubMed - indexed for MEDLINE]
patients does not routinely include neuroendocrine evaluations.

AIM: To clarify the occurrence of hypopituitarism in patients after traumatic brain injury (TBI) or subarachnoid haemorrhage (SAH) 3 months after the BI.

SUBJECTS AND METHODS: The occurrence of hypopituitarism in conscious patients after traumatic brain injury [TBI, n = 100, 31 women, 69 men; age 37.1 +/- 1.8 years; body mass index (BMI) 23.7 +/- 0.4 kg/m(2); Glasgow Coma Scale (GCS) 3-15] or subarachnoid haemorrhage [SAH, n = 40, 14 men, 26 wpmen, 51.0 +/- 2.0 years; 25.0 +/- 0.6 kg/m(2); Fisher's scale 1-4] was studied in a multicentre study 3 months after the BI. All patients underwent wide basal hormonal evaluation; the GH/IGF-I axis was evaluated by GHRH + arginine test and IGF-I measurement.

RESULTS: In TBI patients, some degree of hypopituitarism was shown in 35%. Total, multiple and isolated deficits were present in 4, 6 and 25%, respectively.

Diabetes insipidus was present in 4%. Secondary adrenal, thyroid and gonadal deficit was present in 8, 5 and 17%, respectively. Severe GH deficiency (GHD) was the most frequent pituitary defect (25%). In SAH patients, some degree of hypopituitarism was shown in 37.5%. Despite no total hypopituitarism, multiple and isolated deficits were present in 10 and 27.5%, respectively. Diabetes insipidus was present in 7.5%. Secondary adrenal, thyroid and gonadal deficit was present in 2.5, 7.5 and 12.5%, respectively. Severe GHD was the most frequent defect (25%).

CONCLUSIONS: TBI and SAH are conditions associated with high risk of acquired hypopituitarism. The pituitary defect is often multiple and severe GHD is the most frequent defect. Thus neuroendocrine evaluations are always mandatory in patients after brain injuries.

PMID: 15355447  [PubMed - indexed for MEDLINE]


Effects of chronic administration of PPAR-gamma ligand rosiglitzone in Cushing's disease.


Endocrinology Unit, Department of Medical and Surgical Sciences, University of Milan, Istituto Policlinico San Donato, San Donato Milanese, Milan, Italy. bruno.ambrosi@unimi.it

OBJECTIVE: Rosiglitzone, a thiazolidinedione compound with peroxisome proliferator-activated receptor-gamma (PPAR-gamma)-binding affinity, is able to suppress adrenocorticotropic hormone (ACTH) secretion in treated mice and in AtT20 pituitary tumor cells. These observations suggested that thiazolidinediones may be effective as therapy for Cushing's disease (CD).

PATIENTS AND METHODS: Rosiglitzone (8 mg/day) was administered to 14 patients with active CD (13 women, one man, 18-68 years). Plasma ACTH, serum cortisol (F) and urinary free cortisol (UFC) levels were measured before and then monthly during rosiglitzone administration.
RESULTS: In six patients a reduction of ACTH and F levels and a normalization of UFC were observed 30-60 days after the beginning of rosiglitazone administration: there was a significant difference between basal and post-treatment values for UFC (1238 +/- 211 vs 154 +/- 40 nmol/24 h, P<0.03), but not for ACTH (15.9 +/- 3.7 vs 7.9 +/- 0.9 pmol/l) and F levels (531 +/- 73 vs 344 +/- 58 nmol/l). Two of six cases, followed up for 7 months, showed a mild clinical improvement. Eight patients were nonresponders after 30-60 days of rosiglitazone treatment: their ACTH, F and UFC levels did not differ before and during drug administration. Immunohistochemical analysis of pituitary tumors removed from two responder and two nonresponder patients showed a similar intense immunoreactivity for PPAR-gamma in about 50% of cells.

CONCLUSIONS: The administration of rosiglitazone seems able to normalize cortisol secretion in some patients with CD, at least for short periods. Whether the activation of PPAR-gamma by rosiglitazone might be effective as chronic pharmacologic treatment of CD needs a more extensive investigation through a randomized and controlled study.

PMID: 15296471  [PubMed - indexed for MEDLINE]


Baseline and CRH-stimulated ACTH and cortisol levels after administration of the peroxisome proliferator-activated receptor-gamma ligand, rosiglitazone, in Cushing's disease.


Department of Medicine and Pharmacology, Unit of Endocrinology, University of Messina, Messina, Italy. salvatorecannavo@hotmail.com

Comment in

The ability of acute rosiglitazone administration in influencing ACTH/cortisol secretion in basal conditions and after CRH stimulation was studied in patients with Cushing's disease. Ten patients (8 women and 2 men, aged 18-65 yr) with Cushing's disease were enrolled in the study: 6 of them had previously undergone unsuccessful surgery and 4 were untreated. Plasma ACTH and serum cortisol levels were evaluated at serial time points for 3 h during saline infusion and after the administration of rosiglitazone (8 mg, po) and for 1 h after the injection of CRH (1 microg/kg iv) given alone or 30 min following rosiglitazone administration. The 4 tests were performed in all subjects in randomized order on different days. No significant difference was observed between the pattern of hormone secretion during saline alone and after rosiglitazone, as evaluated by two-way analysis of variance (ANOVA). The integrated areas under the curves (AUCs) were also not significantly different (ACTH: 5683 +/- 1038 vs 6111 +/- 1007 pg/ml/180 min; cortisol: 2333 +/- 267 vs 2902 +/- 486 microg/dl/180 min). In addition, there was
Cannavo S, until 2011

no difference for ACTH and cortisol responses to CRH given either alone or after rosiglitazone, when evaluated as peak, increment or AUC; the pattern of the responses analyzed by two-way ANOVA was also similar. In conclusion: 1) the administration of a single dose of rosiglitazone did not decrease ACTH/cortisol levels or blunt their response after CRH injection; 2) the activation of PPAR-gamma receptors by rosiglitazone seems unable to affect ACTH and cortisol secretion, at least in acute conditions, in patients with ACTH-secreting pituitary adenomas.

PMID: 15279069 [PubMed - indexed for MEDLINE]


Correlation between endocrinological parameters and acne severity in adult women.

Borgia F, Cannavò S, Guarneri F, Cannavò SP, Vaccaro M, Guarneri B.

Institut of Dermatology, University of Messina, University Hospital G. Martino, Messina, Italy. Ist.Dermatologia@unime.it

Many studies demonstrate increased androgen levels and high prevalence of polycystic ovaries in women affected by acne. We evaluated the relationship between clinical features, ultrasonographic data on polycystic ovaries and hormonal parameters in 129 women >17 years of age with acne. Serum levels of androgens of ovarian and adrenal origin were measured. Menstrual cycle regularity, hirsutism, body mass index and ultrasonographic evaluation of ovaries were recorded. Raised levels of at least one androgen were evident in a majority of our patients. Only 19% of them had polycystic ovary syndrome. Hirsutism and acne severity correlated negatively with serum sex hormone-binding globulin (SHBG) levels (p<0.05). No correlation between acne severity and hirsutism was found. In post-pubertal women, severity of acne seems to depend on peripheral hyperandrogenism, with a negative relationship between the acne severity and serum SHBG levels. We strongly recommend the evaluation of serum SHBG levels in women with acne in order to select patients who can have a better response to appropriate hormonal regimes.

PMID: 15202836 [PubMed - indexed for MEDLINE]


Severe head trauma in patients with unexplained central hypothyroidism.


Sezione di Endocrinologia del Dipartimento Clinico Sperimentale di Medicina e
OBJECTIVE: Since Cushing's disease due to large pituitary tumors is rare, we evaluated biochemical characteristics at entry and the results of first surgical approach and of adjuvant therapeutic strategies during a long-term follow-up period.

DESIGN: We studied 26 patients (nine male, 17 female; 42.5+-12.7 years, mean+-s.e.) with ACTH-secreting pituitary macroadenoma (tumor diameter: 11-40 mm).

METHODS: At entry, plasma ACTH, serum cortisol and 24-h urinary free cortisol (UFC) levels were measured in all patients, a high-dose dexamethasone (DEXA) suppression test was evaluated in 22 cases and a corticotrophin releasing hormone (CRH) test in 20 cases. Patients were re-evaluated after operation and, when not cured, they underwent second surgery, radiotherapy and/or ketoconazole treatment.
The follow-up period was 78+/-10 months.

RESULTS: Before surgery, dexa decreased ACTH (>50% of baseline) in only 14/22 patients. The CRH-stimulated ACTH/cortisol response was normal in six patients, impaired in six patients and exaggerated in eight patients. After operation eight patients were cured, nine had normalized cortisol levels and nine were not cured. Pre-surgery, mean ACTH values were significantly higher in the not cured patients than in those normalized (P<0.05) and cured (P<0.01); the ACTH response to CRH was impaired in only six patients of the not cured group. The tumour diameter was significantly less in cured patients (P<0.02) and in normalized patients (P<0.05) than in the not cured ones. Magnetic resonance imaging (MRI) showed invasion of the cavernous sinus in 2/9 normalized, and in 6/9 not cured patients. After surgery, ACTH, cortisol and UFC were significantly lower than at entry in cured and in normalized patients, but not in not cured patients. In the cured group, the disease recurred in one patient who was unsuccessfully treated with ketoconazole. In the normalized group, a relapse occurred in eight patients: radiotherapy and ketoconazole induced cortisol normalization in one case, hypoadrenalism in one case and were ineffective in another one, while five patients were lost at follow-up. In the not cured group, eight patients underwent second surgery, radiotherapy and/or ketoconazole, while one patient was lost at follow-up. These therapies induced cortisol normalization in two patients and hypoadrenalism in one.

CONCLUSIONS: (i) A sub-set of patients with ACTH-secreting pituitary macroadenoma showed low sensitivity to high doses of dexamethasone and to CRH, (ii) pituitary surgery cured Cushing's disease in a minority of patients, (iii) high baseline ACTH levels, impaired ACTH response to CRH, increased tumor size or invasion of the cavernous sinus were unfavourable prognostic factors for surgical therapy, and (iv) second surgery, radiotherapy and/or ketoconazole cured or normalized hypercortisolism in half of the patients with recurrence or not cured.

PMID: 12943521  [PubMed - indexed for MEDLINE]


Clinical presentation and outcome of pituitary adenomas in teenagers.

Cannavò S, Venturino M, Curtò L, De Menis E, D'Arrigo C, Tita P, Billeci D, Trimarchi F.

Department of Medicine and Pharmacology, Section of Endocrinology, University of Messina, Messina, Italy. endocrinolog@hotmail.com

OBJECTIVE: Pituitary adenomas rarely occur in childhood and adolescence, but their mass effect and endocrine abnormalities can compromise both quality and length of life. In this study we evaluated the symptoms at onset and the long-term consequences induced in teenagers by functioning or nonfunctioning pituitary adenomas. DESIGN AND PATIENTS: Clinical, biochemical and neuroradiological data of 44 young patients (12 males and 32 females, aged 16.3 +/- 1.9 years at diagnosis) with
Cannavo S, until 2011

Pituitary adenomas were evaluated retrospectively at baseline and after therapy. Patients underwent surgery, radiotherapy and/or medical treatment depending on clinical history and endocrine secretion of the tumour. Follow-up ranged from 8 to 252 months (median 55 months).

MEASUREMENTS: Baseline and dynamic pituitary function were evaluated in all cases at diagnosis and after treatments. Magnetic resonance imaging (MRI) or computed tomography (CT) scan were performed before therapy and during follow-up. Hormone levels were measured using commercial radioimmunologic or immunoradiometric methods.

RESULTS: Pituitary macroadenomas (group 1) or microadenomas (group 2) were found in 61% and 39% of cases, respectively. Overall, 68% were PRL-secreting, 7% GH-secreting, 5% ACTH-secreting and 20% nonfunctioning. The most frequent symptoms at onset were oligoamenorrhea (62%) and galactorrhoea (59%) in the girls, and headache (58%) in the boys. Pubertal development was delayed in 12/27 (44%) cases with macroadenoma. Growth failure was observed in 4/44 (9%) patients (3 in group 1 and 1 in group 2). At diagnosis, hypopituitarism was detected in 10/27 (37%) patients with macroadenoma. Surgery alone cured 4/18 (22%) and 4/9 (44%) patients in group 1 and group 2, respectively. Adjuvant therapies (second surgery and/or radiotherapy and/or medical treatment) cured the disease in 2/13 (15%) patients with macroadenoma and allowed a persistent normalization in other 4/13 (31%) and 2/4 (50%) cases in group 1 and group 2, respectively. Medical treatment alone cured 2/9 (22%) patients with PRL-secreting macroadenoma and normalized PRL levels in another six (66%) with macroprolactinoma and in 2/7 (28%) patients with microprolactinoma.

CONCLUSION: Delay of growth was rarely observed in teenagers with pituitary adenomas. At the onset of the disease, many girls complained of oligoamenorrhea and galactorrhoea, while headache and delay of pubertal development were the symptoms more frequently referred by boys. Surgery alone was effective in a minority of patients and adjuvant therapies were helpful to obtain the remission of the disease in many cases. In patients with PRL-secreting pituitary adenoma, medical treatment, both as first choice or as adjuvant therapy, normalizes serum PRL levels in 14/27 (52%) cases.

PMID: 12641637  [PubMed - indexed for MEDLINE]


Twelve months of treatment with octreotide-LAR reduces joint thickness in acromegaly.


Department of Molecular and Clinical Endocrinology, Federico II University of Naples, Via S. Pansini 5, 80131 Naples, Italy. calao@unina.it

OBJECTIVE: To evaluate the role of age, gender, duration and control of acromegaly on the reversibility of arthropathy.

Pagina 32
Cannavo S, until 2011

PATIENTS AND DESIGN: 30 de novo patients with active acromegaly, 30 cured patients and 30 healthy subjects were studied in a tranverse and an open longitudinal study design.

METHODS: Shoulder, wrist and knee thickening was measured by ultrasonography at study entry in all 90 subjects and after 12 Months of treatment with octreotide-LAR (OCT-LAR) at a dose of 10-40 mg every 28 days in the 30 de novo patients.

RESULTS: Thickness at all joint sites was greater in the active than in the cured patients and controls (P<0.001), and was greater in the cured patients than in the controls (P<0.001). There was no gender difference, but joint thickness was less in the patients with disease duration >10 Years. Age significantly correlated with wrist (r=-0.55; P<0.001), right knee (r=-0.45; P=0.01), and left knee thickness (r=-0.42; P=0.02) in patients with active disease, and with wrist thickness (r=0.88; P<0.0001) in controls. Twelve Months of OCT-LAR treatment led to disease control in 18 patients (60%). There was a decrease in the thickness of the shoulder (15.1+/-3.2%), wrist (20.5+/-3.1%), right knee (22.2+/-3.4%) and left knee (18.2+/-2.8%) in all patients but the reduction in joint thickness at all sites was greater in the patients with controlled disease after OCT-LAR treatment than in the uncontrolled patients (P<0.01). Shoulder and right knee thickening normalized in respectively 11 (61.1%) and 16 (88.9%) well-controlled patients.

CONCLUSIONS: Growth hormone and insulin-like growth factor-I (IGF-I) suppression by 12 Months' OCT-LAR treatment is accompanied by a significant decrease in the thickness of both weight-bearing and non-weight-bearing joints (mainly in patients whose disease is controlled) regardless of disease duration. These findings suggest that tissue hypertrophy in the context of the acromegalic arthropathy can be improved by suppressing IGF-I levels.

PMID: 12534355 [PubMed - indexed for MEDLINE]


Raloxifene and pituitary secretion in post-menopausal women.


Department of Internal Medicine, University of Messina, Messina, Italy. alasco@unime.it

PMID: 12508935 [PubMed - indexed for MEDLINE]


Effects of long-lasting raloxifene treatment on serum prolactin and gonadotropin levels in postmenopausal women.
OBJECTIVE: To evaluate the effects of a 6 month administration of raloxifene hydrochloride, a selective estrogen receptor modulator which was recently approved for the prevention of osteoporosis, on serum gonadotropin and prolactin (PRL) levels and on TRH-stimulated PRL responsiveness in postmenopausal women who have not undergone estrogen replacement therapy.

DESIGN AND METHODS: Sixteen healthy postmenopausal women were divided into two groups on the basis of their bone status, evaluated by dual energy X-ray absorptiometry at the lumbar level. Eight women (chronological age 52.4 +/- 4.1 (s.d.) years, menopausal age 42.4 +/- 3.9 years), in whom T-score L2-L4 was less than -2.5 s.d., were treated with raloxifene (60 mg p.o.) administered daily for 6 months (group 1), while the other eight women (chronological age 52.6 +/- 2.5 years, menopausal age 42.1 +/- 3.6 years), in whom the T-score L2-L4 ranged between -1 and -2.5 s.d., were used as a control group (group 2). Serum PRL, FSH, LH and 17beta-estradiol (E2) levels were evaluated at baseline and after 3 and 6 months of treatment. In all subjects, PRL responsiveness to TRH (200 microg i.v.) administration was evaluated at baseline and at the end of the study.

RESULTS: At baseline, mean PRL, LH and FSH levels were not significantly different in the two groups (PRL 133.6 +/- 21.7 vs 136.7 +/- 28.1 mIU/l (NS), LH 25.1 +/- 6.8 vs 24.4 +/- 6.7 mIU/ml (NS), FSH 74.4 +/- 25.0 vs 71.1 +/- 24.1 mIU/ml (NS), in group 1 and group 2 respectively). No significant variations in serum FSH and LH values, in either group, or in serum PRL levels in group 2, were observed at the 3 and 6 month examinations. On the contrary, serum PRL values decreased significantly in group 1 after 3 months (100.1 +/- 47.7 mIU/l, P<0.05) and 6 months (81.5 +/- 30.2 mIU/l, P<0.001). At baseline, no significant differences were observed in the TRH-stimulated serum PRL peak between the groups (1015.4 +/- 30.5 vs 1030.2 +/- 25.7 mIU/l in group 1 and in group 2 respectively), while it decreased significantly at the 6 month examination in group 1 (770.5 +/- 47.4 mIU/l, P<0.001) and it was significantly lower than in group 2 (1068.1 +/- 301.8 mIU/l, P=0.02). Serum E2 was not detected at baseline and at each examination, in all patients.

CONCLUSIONS: The decrease of PRL values induced by long-term raloxifene administration in postmenopausal women could be explained by a direct antiestrogenic effect of raloxifene on lactotrope cells or by the recently suggested increase of opiateergic tone on the hypothalamic-pituitary region.

PMID: 12370106  [PubMed - indexed for MEDLINE]


Impairment of GH secretion in adults with primary empty sella.

Primary empty sella (PES) is generally not associated with overt endocrine abnormalities, although mild hyperprolactinemia and, in children, deficient GH secretion have been reported. The aim of this multi-center collaborative study was to evaluate basal and stimulated GH secretion in a large series of adult PES patients. The study group consisted of 51 patients [41 women and 10 men, age range: 20-78 yr; (mean +/- SD) 47 +/- 11 yr]; results were compared with those in normal subjects (Ns) (Ns: no. = 110, 55 women, age: 20-50 yr, 37 +/- 14 yr), and in hypopituitaric patients (HYP) with GH deficiency (HYP: no. = 44, 17 women, age: 20-72, 49 +/- 16 yr). Baseline IGF-I levels and GH responses to insulin-induced hypoglycemia (insulin tolerance test, ITT) and/or GHRH + arginine (ARG) stimulation tests were evaluated. PES patients were also subdivided according to BMI in lean (BMI <28 kg/m\(^2\) no. = 22) or obese (BMI >28 kg/m\(^2\) no. = 29). PES patients had serum total IGF-I concentrations (mean +/- SE: 142.2 +/- 9.6 ng/ml) higher than HYP patients (77.4 +/- 6.4 ng/ml, p < 0.001), but lower than Ns (213.3 +/- 17.2 ng/ml, p < 0.005), with no differences between lean and obese PES subjects. The increase in serum GH concentrations following ITT and/or GHRH + ARG stimulation tests, although higher than that observed in HYP patients, was markedly reduced with respect to Ns. No difference was observed in the GH response to provocative tests between lean and obese PES patients. When individual GH responses to ITT or GHRH + ARG were taken into account, a large proportion of PES patients (52% after ITT, 61% after GHRH + ARG) showed a GH peak increase below the 1st centile of normal limits. Serum IGF-I levels in PES patients with blunted GH responses to provocative tests were significantly (p < 0.001) lower in PES patients with normal GH responses, and a positive correlation was observed between IGF-I levels and serum GH peak concentrations after GHRH + ARG. In conclusion, the results of the present study provide evidence that adult PES patients often have an impairment of GH secretion, as indicated by the blunted GH response to ITT and GHRH + ARG provocative tests, and by the reduction in serum IGF-I levels. These changes are independent of body mass.

PMID: 12030603 [PubMed - indexed for MEDLINE]


Abnormalities of hypothalamic-pituitary-thyroid axis in patients with primary empty sella.

Primary empty sella (PES) is a very frequent neuroradiological finding in the general population, that can induce hypopituitarism. Some studies focused on the association of PES with GH deficiency (GHD) or hypogonadotropic hypogonadism (HH), while data regarding the involvement of hypothalamic-pituitary-thyroid (HPT) axis, despite sporadic reports of central hypothyroidism, or the occurrence of hypoadrenalism (HA) are scanty. In this study, thyroid function and TSH response to exogenous TRH injection (TRH/TSH) were investigated in 43 patients [10 men and 33 women; aged (mean +/- SD), 48 +/- 12 yr] with PES: 22 patients had total and 21 partial PES. Forty healthy subjects (9 men and 31 women; aged 46 +/- 12 yr) were enrolled as a control group. Central hypothyroidism was found only in 2/43 cases, whereas one patient showed primary hypothyroidism. In euthyroid patients, mean serum TSH levels were significantly lower than controls (TSH: 1.0 +/- 0.7 vs 1.4 +/- 0.6 mU/l, p<0.01) and 79% of them showed abnormal TRH/TSH responses (TRH test was performed in 34 euthyroid patients: 17 cases with total and 17 cases with partial PES), but mean serum free T4 (FT4) and free T3 (FT3) values were not significantly lower than controls (FT4: 15.9 +/- 0.4 vs 15.0 +/- 2.1 pmol/l, p=NS; FT3: 5.3 +/- 1.2 vs 5.8 +/- 1.5 pmol/l, p=NS). Moreover, no significant differences were evident in mean serum TSH, FT4 and FT3 between patients with total and partial PES (TSH: 1.1 +/- 0.7 vs 0.9 +/- 0.8 mU/l, p=NS; FT4: 16.3 +/- 2.6 vs 15.7 +/- 2.2 pmol/l, p=NS; FT3: 5.4 +/- 1.3 vs 5.2 +/- 0.8 pmol/l, p=NS) and the TRH/TSH peak was impaired or exaggerated/delayed in 9 and 3 patients with total and in 12 and 3 cases with partial PES. No significant differences in the prevalence of abnormal TRH/TSH responsiveness were found between patients with partial or total PES (chi2=1.6, p=NS). Other impairment of pituitary function was detected in 23/43 patients: GHD was present in 15 cases, HH in 11 and central HA in 5 patients. Isolated or combined hypopituitarism was present in 17 and in 6 patients, respectively. In conclusion, pituitary dysfunction is very frequent in patients with PES, but central hypothyroidism occurs rarely. The entity of arachnoid herniation into the sellar fossa does not play a significant role on the degree of HPT axis dysfunction.

PMID: 11936465  [PubMed - indexed for MEDLINE]
Cannavo S, until 2011
156.2 cm (+1.0 SD), weight 20.7 kg, BMI 16.0 (-0.04 SD), and many phenotypic abnormalities: long eyelashes, large bulbous nose with broad nasal bridge, short philtrum, moderately broad mouth, tooth folding and malocclusion, posteriorly rotated ears, low posterior hair line, short neck, clinodactyly of the 5th finger and hyperextensible finger joints. Diffused hyperpigmentation and hypertrichosis with sporadic pubic terminal hairs, but neither clitoromegaly nor other signs of hyperandrogenism and/or precocious puberty, were observed (T1, P1). Carpal bone evaluation showed a delayed bone age (TW2: 5-5/10, -3.6 yr) and the statural age/bone age ratio was 1.1. Other dysmorphic syndromes were excluded on the basis of clinical evidence, also evaluated by a computer-assisted search (P.O.S.S.U.M. version 3.5, 1992). Analysis of chromosome 22 by the FISH method, using specific probes Cos29 and Tuple1, excluded microdeletions in the region 22q11.2, typical of Velo-cardio-facial syndrome. In this case, we report the impairment of serum GH responsiveness (GH baseline values: 0.2-1.9 ng/ml) to the administration of oral 150 microg clonidine [peak 4.7 ng/ml, normal values (nv)>10 ng/ml] and oral 4 mg dexamethasone (8.1 ng/ml, nv=10 ng/ml). Moreover, the evaluation of spontaneous 24-h GH secretion (Carmeda AB, Stockholm, Sweden) showed low mean GH levels (1.75 ng/ml, nv>3.0 ng/ml), with a maximum sleep-related peak of 2.8 ng/ml. Serum IGF-1 values were in the low-normal range (80-176 ng/ml, nv 133-626 ng/ml). While in FHS the cranio-facial features minimize with advancement of age, the impairment of growth velocity is permanent and results in severe dwarfism. In our case, treatment with recombinant GH (0.10 U/kg/day), administered by a needle-free device, induced a dramatic increase of growth velocity, increasing the height from -2.8 to -1.9 SD after 18 months, thus indirectly confirming a role of GH deficiency in the pathogenesis of FHS dwarfism.

PMID: 11883867 [PubMed - indexed for MEDLINE]


Exercise-related female reproductive dysfunction.

Cannàvò S, Curtò L, Trimarchi F.

Department of Medicine and Pharmacology, Section of Endocrinology, University of Messina, Italy. endocrinologi@hotmail.com

Clinical or biochemical abnormalities of gonadal function, consisting of delayed puberty, luteal phase deficiency, oligo-amenorrhea or anovulation, occur in girls and women participating in strenuous sports. The evidence of a causal relationship between athletic activity and menstrual dysfunction has led to increased interest, also because the number of women who practice sports has increased rapidly. The pathogenesis of exercise-related female reproductive dysfunction (ERFRD) is not completely clarified. The heterogeneity of sports practice, the role of overtraining and other factors, as adequate calorie balance or the assumption of exogenous steroids, could play a primary role in the comprehension of the pathogenic mechanisms of reproductive dysfunction. The

Pagina 37
interest of physicians about ERFRD is also due to the consequences of reduced gonadal function on women's health. Apart from some short-term transient effects (i.e. on muscle, genito-urinary tract or behavior), hypoestrogenemia can induce long-term deleterious effects, as premature osteoporosis and lifelong impairment of skeletal structure. In view of the possible short-term (infertility) and long-term (osteoporosis) consequences of ERFRD, correct physical training and adequate diet approach are mandatory to prevent or to revert neuroendocrine abnormalities so frequently reported in girls and women participating in recreational or competitive athletic activities.

PMID: 11765055  [PubMed - indexed for MEDLINE]


Effectiveness of slow-release lanreotide in previously operated and untreated patients with GH-secreting pituitary macroadenoma.

Cannavò S, Squadrito S, Curtò L, Almoto B, Trimarchi F.

Cattedra di Endocrinologia, University of Messina, Italy.
endocrinologi@hotmail.com

The aim of this study was to verify whether treatment with slow-release lanreotide (SRL) before surgery is useful in the management of patients with GH-secreting pituitary macroadenoma. Twenty untreated acromegalics were enrolled randomly in two groups. Ten patients (group 1: 2 males and 8 females aged 44.5 +/- 4.3 years) underwent surgery via transsphenoidal access. Only one of them was cured by surgery, whereas the other nine were treated with SRL. In the other ten patients (group 2: 3 males and 7 females aged 43.2 +/- 12.3 years), transsphenoidal surgery followed SRL treatment. Surgery induced the normalization of GH and IGF-1 levels in four group 2 patients - three of them had shown an evident shrinkage of the tumor after SRL treatment. After surgery, group 1 showed a significant decrease of mean IGF-1 (580 +/- 63 vs. 789 +/- 64 ng/ml, p < 0.02), but not of GH values (26.1 +/- 9.8 vs. 44.8 +/- 19.3 ng/ml, NS); the cured patient was excluded from the following evaluations. Group 2 showed an evident, but not significant, decrease of both GH and IGF-1 values compared to values measured at the end of medical treatment (GH: 22.4 +/- 9.7 vs. 7.7 +/- 4.7 ng/ml, NS. IGF-1: 570 +/- 69 vs. 402 +/- 58 ng/ml, NS). Gonadal, thyroid and adrenal impairment was evident in six, four and no patients in group 1 and in three, two and one patients in group 2, respectively. SRL 30 mg was administered every 14 days for three months and then every 10 days until the 6th month. Before SRL treatment, mean GH and IGF-1 levels did not differ significantly in group 1 vs. group 2 (GH: 29.3 +/- 10.5 vs. 43.4 +/- 22.0 ng/ml; IGF-1: 633 +/- 38 vs. 778 +/- 83 ng/ml). In group 1, a significant decrease of serum GH, but not of IGF-1 levels, was achieved at the end of 1st trimester of SRL (GH: 17.6 +/- 5.4 ng/ml, p < 0.05. IGF-1: 540 +/- 48 ng/ml, NS), whereas a significant decrease in both GH and IGF-1 values was evident during the 2nd trimester (GH: 6.1 +/- 3.0 ng/ml, p < 0.05. IGF-1: 433 +/- 74 ng/ml, p < 0.02). Serum GH levels, measured during the
2nd trimester of SRL therapy, were also significantly lower than levels measured at the end of the 1st trimester (p < 0.05). Group 2 serum GH and IGF-1 levels were not significantly decreased at the end of the 1st trimester (GH: 27.2 +/- 12.1 ng/ml, NS. IGF-1: 698 +/- 74 ng/ml, NS), whereas only serum IGF-1 (570 +/- 69 ng/ml, p < 0.05) was significantly reduced during the 2nd trimester of SRL (GH: 22.4 +/- 9.7 ng/ml, NS). Serum GH and IGF-I fell in the normal range in 4 patients in group 1 and one in group 2 at the end of the second trimester of SRL therapy. Independently of the trial applied, the mean clinical score level ameliorated significantly in both groups (group 1: p < 0.0005; group 2: p < 0.0001). In both groups, the proportion of patients complaining of headache and tissue swelling and the score level of headache, tissue swelling and excessive sweating decreased significantly. In group 1 the score level of fatigue and arthralgia also decreased significantly. In conclusion, this study proves that in patients with GH-secreting pituitary macroadenoma: (i) surgery followed by SRL induces a better clinical and biochemical status than SRL alone; (ii) SRL treatment before surgery ameliorates the clinical and biochemical outcome and reduces the prevalence of hypopituitarism due to surgery.

PMID: 11607883 [PubMed - indexed for MEDLINE]


Results of a two-year treatment with slow release lanreotide in acromegaly.

Cannavò S, Squadrito S, Curtò L, Almoto B, Vieni A, Trimarchi F.

Cattedra di Endocrinologia, University of Messina, Italy.
endocrinologi@hotmail.com

In this open sequential study we evaluated the long-term effectiveness and tolerability of the i.m. administration of slow release lanreotide 30 mg (SRL) in 18 acromegalics (7 M/11 F, age 50.9 +/- 12.7 yr). Baseline mean GH and IGF-1 levels were 15.8 +/- 6.6 ng/ml and 702 +/- 74 ng/ml, respectively. Four hours, 1, 7, and 14 days after SRL, mean GH levels were 8.9 +/- 5.9 (p < 0.005), 11.4 +/- 6.9 (p < 0.05), 9.1 +/- 4.5 (p < 0.05), and 9.1 +/- 4.1 ng/ml (p < 0.05), respectively; and the IGF-1 values at 1, 7, and 14 days were 624 +/- 77 (p < 0.05), 555 +/- 83 (p < 0.001), and 467 +/- 58 ng/ml (p < 0.0001), respectively. Four hours after SRL administration GH was < 2.5 ng/ml in 11 patients and decreased 85% of the basal value, without normalizing, in another case. In the following 2 weeks, 7 and 2 patients maintained GH < 2.5 ng/ml or < 50% of baseline; 3 and 2 of them attained IGF-1 values in the normal range or < 50% of basal levels. A patient developed acute pancreatitis after the injection of the drug and therefore stopped the treatment. Another patient did not continue SRL, and she was turned on octreotide, s.c. administered (OCT), because only the latter treatment ameliorated significantly the headache. In 16/18 patients the treatment was continued until the 24th month. SRL was administered every 14 days until the 24th month in 3 cases, whereas in 13 patients the dose schedule was increased every 10 days since the 7th month because they did not normalize serum GH and IGF-1 levels. In these 16 patients
baseline GH and IGF-1 levels were 10.0 +/- 2.5 ng/ml and 671 +/- 75 ng/ml, respectively. At the 1st, 3rd, and 6th month of treatment mean GH levels fell to 5.4 +/- 1.4 (p < 0.05), 5.3 +/- 1.8 (p < 0.05), and 5.0 +/- 1.6 (p < 0.05) ng/ml, respectively; and IGF-1 declined to 511 +/- 87 (p < 0.005), 565 +/- 85 (p < 0.05), and 525 +/- 94 (p < 0.01) ng/ml, respectively. Throughout the first semester GH was < 2.5 ng/ml in 5 patients and decreased > 50% in another three. IGF-1 levels normalized in 3/5. Throughout the following 18 months of treatment, mean GH (3.4 +/- 1.0 ng/ml) and IGF-1 (413 +/- 75 ng/ml) values decreased significantly in comparison with both the baseline concentrations (GH p < 0.01, IGF-1 p < 0.001) and the levels measured during the 1st semester of treatment (GH p < 0.05, IGF-1 p < 0.001). GH remained < 2.5 ng/ml in 11 patients, and in 8/11 cases IGF-1 fell in the normal range. Serum GH and IGF-1 levels decreased by more than 50% of baseline levels in 2 other cases. At MRI, pituitary adenoma was no longer evident in one patient previously treated with OCT and significantly decreased in another patient previously treated with surgery plus radiotherapy, as well as in a patient previously untreated. During treatment the percentage of patients complaining of headache and fatigue decreased significantly (chi2, p < 0.05 and p < 0.0005, respectively). Overall, the headache (p < 0.005), arthralgia (p < 0.05), and paresthesia (p < 0.01) ameliorated significantly. Ultrasound scan showed gallbladder sludge or sand-like stones in 5/11 patients. This study, which is one of the longest surveys on a relatively large series of acromegals treated with SRL, confirms the long-term effectiveness of this drug for the treatment of patients with active acromegaly. SRL decreases significantly GH and IGF-1 in most cases and induces the shrinkage of the pituitary tumor in some patients previously either untreated or both treated for acromegaly. SRL improves significantly clinical symptoms and it is well tolerated.

PMID: 10898551 [PubMed - indexed for MEDLINE]

Goiter and impairment of thyroid function in acromegalic patients: basal evaluation and follow-up.

Cannavò S, Squadrito S, Finocchiaro MD, Curtò L, Almoto B, Vieni A, Trimarchi F.
Cattedra di Endocrinologia, University of Messina, Italy.
endocrinologi@hotmail.com

AIMS: We evaluated morphological, biochemical and cytological thyroid parameters in acromegalic patients, investigated before and after treatment for acromegaly.

PATIENTS: 28 acromegals were investigated before and, in 18 cases, after 2-7 years of therapy. Fourteen patients were from areas of moderate iodine deficiency in Southern Italy. One patient underwent thyroidectomy before entering this study.

RESULTS: 19 patients were euthyroid (FT4: 17.7 +/- 0.8 pmol/l and FT3 4.6 +/- 0.2 pmol/l), but TSH was undetectable in 5/19. Among them, TRH-stimulated TSH increase was absent/impaired or exaggerated/delayed in 9 and one cases,
respectively. Decreased FT3 and/or FT4 values with low/normal TSH values were detected in 7 cases; TRH-stimulated TSH response was absent/impaired in 2 patients and exaggerated/delayed in another two. Increased free T4 and free T3 concentrations with undetectable TSH levels were found in one. Two euthyroid patients had high TPOAb levels. Goiter was diagnosed in 21 cases and nodules were found in 14/21. 99Tc scintiscan showed "cold" areas in 13/14 cases and a "hot" nodule in the hyperthyroid patient. Acromegalis from iodine deficient areas showed a not significant increase of prevalence of goiter (86 vs. 71 %) and of mean thyroid volume (35 +/- 7 vs. 28 +/- 4 ml, NS), compared to others. Thyroid volume (TV) did not correlate with GH, IGF-1 and TSH levels, the area under the curve of insulin-increase during OGTT, the age of patients or the duration of acromegaly. Fine needle aspiration biopsy (FNAB), performed in 11/14 patients with nodular goiter, showed colloid nodules in 8 cases, hyperplastic nodules in 2 and an adenomatous nodule in one. Neurosurgery, radiotherapy or medical treatment for acromegaly induced a significant decrease of mean GH and IGF-1 levels (21.5 +/- 8.5 vs. 12.9 +/- 9.6 ng/ml, p< 0.005 and 747 +/- 94 vs. 503 +/- 88 ng/ml, p < 0.02, respectively), but both GH and IGF-1 values normalized only in 3 cases. No significant variation of mean TSH levels was found. Although TV normalized in 3 patients, ultrasound evaluation showed a not significant decrease of mean TV and no changes in the diameter and number of nodules. FNAB was unchanged.

CONCLUSIONS: Our results suggest that, despite no correlation between serum GH and IGF-1 levels and thyroid volume being found, a decrease in serum GH and IGF-1 levels has favourable effects on thyroid status.

PMID: 10871160 [PubMed - indexed for MEDLINE]


Cabergoline: a first-choice treatment in patients with previously untreated prolactin-secreting pituitary adenoma.

Cannavò S, Curtò L, Squadrito S, Almoto B, Vieni A, Trimarchi F.

Cattedra di Endocrinologia, Università di Messina, Italy. salcan@mbox.vol.it

Cabergoline (CAB) treatment is an effective, safe and well tolerated approach for hyperprolactinemia. We investigated the efficacy of 24-month treatment with CAB in 37 patients with previously untreated PRL-secreting pituitary adenoma and evaluated the hormonal and neuroradiological changes after the discontinuation of long-term therapy. Eleven patients with macroprolactinoma (1M/10F) and 26 with microprolactinoma (4M/22F) started treatment taking 0.25 mg CAB twice a week for 4 weeks. The dose was increased stepwise in 0.5 mg increments until reaching lowest maximally effective and tolerated dose. CAB was withdrawn before the end of the study in 6 women who became pregnant and in one patient who showed a slight increase of the macroadenoma at MRI. During treatment, PRL levels decreased significantly in macro (11.1 +/- 1.1 vs 407.8 +/- 98.3 microg/l, p<0.001) and microprolactinomas (11.1 +/- 1.6 vs 193.8 +/- 23.4 microg/l, p<0.05) and normalized in all macro and in 23/26 microprolactinomas. In 3 cases PRL levels
Cannavo S, until 2011
decreased but did not normalize because the appearance of side effects, such as
nausea or hypotension, prevented the increase of the dose of CAB. The effective
dose of drug correlated significantly with basal serum PRL levels (p<0.05) and
with the pituitary tumor size (p<0.05). A significant decrease of the mean
adenoma size was evident for macro (6.9+/−1.8 vs 16.0+/−1.8 mm, p<0.001) and
microprolactinomas (3.0+/−0.5 vs 6.5+/−0.4 mm, p<0.001) at MRI. The tumor
disappeared in 4 macroadenomas and in 11 microadenomas after 12 months of
treatment. CAB withdrawal was followed by serum PRL increase in 13 cases after 3
months, in 6 after 6 months, in 2 after 9 months, and in one patient at the 12th
month. Five patients showed normoprolactinemia with negative MRI after one year.
Regular menses were restored in 7/10 macroadenomas and in all
oligo-amenorrhoic patients with microadenoma; serum testosterone levels
normalized in 2/3 hypogonadic men. Five out of 6 women become pregnant and had
uneventful pregnancies which resulted in deliveries of normal babies. In
conclusion, this study confirms the effectiveness and safety of CAB for patients
with PRL-secreting pituitary adenoma and suggests that it can be considered a
first choice treatment.

PMID: 10401709  [PubMed - indexed for MEDLINE]

Shrinkage of a PRL-secreting pituitary macroadenoma resistant to cabergoline.
Cannavò S, Bartolone L, Blandino A, Spinella S, Galatioto S, Trimarchi F.
Cattedra di Endocrinologia, University of Messina, Italy.

Cabergoline decreases both serum PRL levels and size of prolactinomas, including
some tumors resistant to other dopamine-agonists. It is common observation that
the shrinkage of the adenoma is preceded by suppression of PRL levels. A minority
of patients, who do not show a significant decrease of PRL after a short trial
with dopamine-agonists, undergoes neurosurgery or radiotherapy. We report on the
case of a 14-year-old girl with a huge prolactinoma who showed, during
cabergoline treatment (0.5 mg twice a week), a significant shrinkage of the
pituitary mass but no decrease of the very high PRL values. She was referred to
us after partial removal of the suprasellar extension of the pituitary tumor. The
post-surgical evaluation showed very high PRL levels (9352 microg/l; 20941
microg/l before surgery), which did not decrease during the 2-year treatment with
cabergoline (nadir value: 8735 microg/l). However, one month after the beginning
of therapy, MRI showed a significant shrinkage of the tumor (tumor volume 5.7 ml,
compared with 45.1 ml prior to surgery and 24.4 ml after surgery). Subsequently
MRIs demonstrated a progressive reduction of the size with a complete
disappearance of the suprasellar and parasellar tissue (tumor volume 1.8, 0.9 and
0.2 ml, at 3, 6 and 12 months, respectively). The MRI performed at the 24th month
showed a secondary empty sella, with residual tumor tissue in the right
sphenoidal sinus. Increasing cabergoline, up to 3 mg a week, failed to induce any
decrease of PRL levels. In conclusion, in such macroprolactinomas the shrinkage
of tumor is not strictly correlated with (or it is partially dissociated from) the inhibition of PRL hypersecretion. The choice of other therapeutic options in cabergoline-resistant macroprolactinomas needs careful neuroradiological evaluation after a short trial of pharmacological treatment.

PMID: 10342366 [PubMed - indexed for MEDLINE]


Unusual MRI finding of multiple adenomas in the pituitary gland: a case report and review of the literature.

Cannavò S, Curtò L, Lania A, Saccomanno K, Salpietro FM, Trimarchi F.

University of Messina, Italy. salcan@tim.it

The simultaneous occurrence of multiple adenomas in the pituitary gland is a rare event. We report the coexistence of three non functioning pituitary microadenomas in a 37-year-old woman, referred to us for oligomenorrhea and headache. Biochemical evaluation revealed prolactin (131 U/liters), follicle-stimulating hormone (4.1 U/liters), luteinizing hormone (3.9 U/liters), 17beta-estradiol (74 pg/mL), free (2.0 pg/mL) and total testosterone (0.5 ng/mL), dehydroepiandrosterone-sulfate (3.5 microg/mL), 17OH-progesterone (0.8 ng/mL), cortisol (13.1 microg/dL), free triiodothyronine (4.8 pmol/L), free thyroxine (18.5 pmol/liters), thyrotropin (1.6 mU/L), and growth hormone (0.2 ng/mL) levels in the normal range, as for as the response to dynamic endocrine tests. MRI showed an enlarged sella turcica, occupied by three distinct hypointense areas that measured less than 5 mm in diameter in the left, medium and right side of the pituitary, respectively. This finding was confirmed 6 months later by a second MRI that revealed also a light increase in microadenomas dimensions. The patient, therefore, underwent neurosurgery by transfenoidal approach. Histologic examination showed no morphologic differences between the specimens obtained from the different microadenomas. Immunohistochemistry evaluation revealed a positive staining for the common alpha-subunit of glycoproteic hormones and negative for the other pituitary hormones tested, while electron microscopy showed cells with a poor secretory apparatus and a variable grade of cell differentiation. In conclusion, we report the fifth case described with multiple pituitary adenomas diagnosed in vivo and the first with three coexisting tumors revealed by MRI before neurosurgery. The occurrence of multiple pituitary tumors emphasizes the role of pituitary and extrahypophisal factors in the clonal expansion of genetically altered cells.

PMID: 10231191 [PubMed - indexed for MEDLINE]

Octreotide and lanreotide treatment in active acromegaly.

Cannavò S, Fazio R, Squadrito S, Trimarchi F.

Comment on

PMID: 9215324 [PubMed - indexed for MEDLINE]


Granulomatous sarcoidotic lesion of hypothalamic-pituitary region associated with Rathke's cleft cyst.

Cannavò S, Romano C, Buffa R, Faglia G.

Cattedra di Endocrinologia, Università di Messina, Italy.

The association of large pituitary mass, lack of clinical syndromes of pituitary hypersecretion, hypopituitarism and visual field defects suggests the diagnosis of nonfunctioning pituitary adenoma, but the same characteristics can be present in patients affected by other tumorous lesions, cysts, inflammatory processes or vascular disease. The management of these patients depends on a correct diagnosis. A 53-year-old woman was admitted for nausea, vomiting and severe hypotension. For three months she had complained of weakness, sleepiness, skin-dryness and loss of weight. Imaging and endocrine evaluations revealed an intra and extrasellar mass causing hypopituitarism without diabetes insipidus. Histological examination of the tissue obtained at transsphenoidal surgery showed a Rathke's cleft cyst, surrounded by areas of noncaseous granulomatous tissue with scattered multinucleated giant cells of foreign body type, similar to a sarcoid lesion. Other systemic sarcoidosis localizations were absent. After two years of full well-being, the patient reported a sudden visual impairment, due to sarcoidosis involvement of the prechiasmatic tract of the optic nerve, that promptly improved with corticosteroid treatment. This report emphasizes the overlap of signs and symptoms between non functioning tumors and nontumoral masses of hypothalamic-pituitary region and underlines the fact that a correct diagnosis is feasible only on histopathological basis. Although, occasionally, the coexistence of Rathke'cyst with pituitary adenoma has been reported, to the best of our knowledge, this is the first report of the association between Rathke's cleft cyst and noncaseating granuloma tissue. Finally, the remission of neurological symptoms following corticosteroid therapy confirms this treatment as a valid medical approach and suggests its use in a short therapeutic trial when the diagnosis is doubtful.

PMID: 9125487 [PubMed - indexed for MEDLINE]

Coexistence of growth hormone-secreting pituitary adenoma and intracranial meningioma: a case report and review of the literature.


Cattedra di Endocrinologia, Università di Messina, Italy.

The simultaneous occurrence of a pituitary adenoma and an intracranial meningioma is a rare event. We report the coexistence of an eosinophilic pituitary adenoma and an endotheliomatous meningioma, in the sellar region, and evaluate their endocrine, neuro-radiological and immunohistochemical pattern. A 47-year-old woman affected by acromegaly was referred to us. Serum GH level was 82 ng/ml and remained unresponsive to both OGTT (75 g per os) and iv. GHRH 1-29 (100 micrograms); IGF-1 was 807 ng/ml. Eight hours after acute sc administration of octreotide (100 micrograms) GH returned to normal levels (2.3 ng/ml). CT scan showed a large intra- and suprasellar mass involving the right cavernous sinus, with a retrostellar extension along the tentorium. A slight and inhomogeneous enhancement, with a periferal rim of bright signal was apparent at MRI. Conversely, the retrostellar component showed a bright homogeneous enhancement. The patient, therefore, underwent neurosurgery. Histological examination revealed the coexistence of 2 types of tissue: areas of endotheliomatous meningioma were interspersed among sheets of acidophilic adenoma tissue. Immunohistochemical analysis was performed in order to determine the relationship between the two masses: a positive staining for GH was shown in the areas of adenoma, as against for GHRH, neither in the adenomatous tissue nor in the slices of meningioma. Although MRI showed a latero-sellar post-surgical residual of meningioma, serum GH value was < 1 ng/ml. In conclusion, the relationship between the GH-secreting adenoma and the meningioma is unclear; however the GH-hypersecretion is not induced by a hypothetic GHRH-activity from the meningioma.

PMID: 8282967  [PubMed - indexed for MEDLINE]


Effectiveness of computer-assisted perimetry in the follow-up of patients with pituitary microadenoma responsive to medical treatment.

Cannavó S, De Natale R, Curtó L, Li Calzi L, Trimarchi F.

Cattedra di Endocrinologia, University of Messina, Italy.
MEASUREMENTS: We used computed tomodensitometry, Goldman perimeter and computer-assisted perimetry.

RESULTS: The patients were divided into three groups according to their response to medical treatment as proved by computed tomodensitometry which revealed the disappearance of the tumour in four prolactinomas (group 1), a reduction > 40% in three prolactinomas and in three acromegalics (group 2) and no significant variation in the diameter of the adenoma in three prolactinomas and in four acromegalics (group 3). Comparison by the paired t-test of the visual fields before and after treatment revealed a significant positive change (P < 0.01) for all patients in groups 1 and 2 and for one patient in group 3, with disappearance of the scotomas in all cases in group 1 and in two cases in group 2. Visual field defects were detected by means of the Goldman perimeter in only one patient with prolactinoma and in two acromegalics, although the computer-assisted perimetry showed that, in 15 out of 17 patients, visual impairment was unilateral and in all cases the presence of relative scotomas was concentrated in the upper temporal quadrant. The visual defects observed with computer-assisted perimetry and the pituitary tumour dimension evaluated with computed tomodensitometry did not show significative correlations (r = 0.059, P NS).

CONCLUSIONS: Computer-assisted perimetry was most useful in the diagnosis and follow-up of patients with pituitary adenoma, especially in the evaluation of small masses without subjective symptoms of visual loss, when the Goldman perimeter does not usually allow us to recognize minimal chiasmatic involvements or the improvement of visual field as a result of the medical therapy.

PMID: 1395066 [PubMed - indexed for MEDLINE]


[Acromegalic cardiopathy: a morphofunctional study with color-Doppler echocardiography].

[Article in Italian]


Cattedra di Endocrinologia, Università degli Studi di Messina.

We used color-Doppler echocardiography in an investigation of cardiac morphology and function to verify the cardiac anatomic and functional changes in acromegalic patients with or without hypertension and hyperlipemic states. Fifteen patients with growth hormone-secreting pituitary adenoma (mean age: 47.9 years) and 15 healthy control subjects were studied. We measured serum growth hormone (GH), somatomedin-C, cholesterol, triglyceride levels and carried out echocardiographic studies of the following cardiac morpho-functional parameters: left ventricular diameter, volume, mass and wall systolic stress. Serum GH and somatomedin-C levels were significantly higher in acromegalic patients than in controls (p < 0.001 and p < 0.001 respectively). Echocardiography evidenced increased left
ventricular mass (60% of the acromegalic patients; p < 0.05) and increased wall systolic stress (53.3%; p < 0.05). Color-Doppler analysis evidenced abnormal diastolic function in 8 acromegalic patients (p < 0.001). We thus conclude that the most characteristic feature of acromegalic heart disease is left ventricular involvement, diastolic dysfunction, increased left ventricular mass or wall systolic stress. The pathogenesis is most probably multifactorial: essential hypertension, associated with slow and progressive evolution of heart disease, appears to be a determining factor.

PMID: 1457253  [PubMed - indexed for MEDLINE]


Effectiveness of computer-assisted perimetry in the diagnosis of pituitary adenomas.

Cannavó S, De Natale R, Princi P, Li Calzi L, Aragona A, Trimarchi F.

Istituto Pluridisciplinare di Clinica Medica e Terapia Medica Generale e Speciale, University of Messina, Italy.

Computer-assisted perimetry (CP) is a new method which quantifies the differential light sensitivity threshold and allows the statistical analysis of the data. It offers advantages as compared with manual methods. This study has been carried out in 27 patients with pituitary adenomas (four males and 23 females; 13 with prolactinomas; six with acromegaly, four with Cushing's disease and four with non-secreting adenomas). A skull X-ray and a computed tomodensitometry (CT), a manual Goldman perimeter and a computer assisted visual field examination were performed in all cases. The presence of a pituitary tumour was suggested by the X-ray and by the CT in 12 and 23 patients respectively out of the 27: the CT scan revealed a suprasellar extension in seven cases. Visual field defects were detected by means of the Goldman perimeter in six patients and by means of the computer-assisted technique in 25/27. The effectiveness of this new technique was proved by the concordance with the CT scan results in 21 cases and by the histological examination of the four adenomas which were not apparent at CT scan. A significant difference was found for both eyes (right eye, chi squared = 258, P less than 0.001; left eye, chi squared = 295.0, P less than 0.001) between patients and controls. No correlation existed between visual defects and the pituitary size apparent at CT scan. Six patients were evaluated with the CT and CP after 1 year of bromocriptine treatment; a slight reduction of size was documented with the CT in four cases, whereas a significant positive change in visual acuity was observed in five patients. (ABSTRACT TRUNCATED AT 250 WORDS)

PMID: 2697478  [PubMed - indexed for MEDLINE]

Cannavò S, Li Calzi L, Trimarchi F.

Primary hypothyroidism may be associated with enlargement of the sella turcica, due to thyrotroph hyperplasia, in its turn due to the lack of feedback control by thyroid hormones. It may develop independently of the severity or of the duration of thyroid failure. A 42-year-old woman was referred to us. She presented us with a CT scan compatible with a pituitary microadenoma, in the left part of the sella. The patient showed obvious signs of myxedema, due to subtotal thyroidectomy which had been performed 14 months before, because of the presence of multinodular goiter. After operation, the patient has been discontinuously and inappropriately treated with desiccated thyroid. She complained of headache, nausea, galactorrhea without amenorrhea. Serum T4 (0.8 micrograms/dl), serum T3 (47 ng/dl) and TSH (174.5 +/- 60.1 mU/l: M +/- SD of 4 assays) were compatible with primary hypothyroidism as confirmed by TSH hyper-response to i.v. TRH (200 micrograms) and i.v. domperidone (10 mg), and by the normal TSH decrease after orally administered 2.5 mg bromocriptine or 90 min continuously infused 800 micrograms GHRH. Moreover, an abnormal GH response to TRH was observed, whereas basal and appropriately stimulated PRL levels were normal. Serum alpha-subunit was marginally high (5.92 ng/ml), but alpha-subunit/TSH molar ratio fell within the normal range (0.1 molar ratio). Complete suppression of basal and TRH stimulated TSH values was achieved after a 14-day L-T3 (120 micrograms per day) and 4-month L-T4 (200 micrograms per day) administration. L-T4 treatment, first administered at suppressive doses (200 micrograms per day for 4 months) and subsequently at substitutive doses (150 micrograms per day for 2 months), induced complete remission of symptoms along with normalization of the CT scan picture.

PMID: 2622426 [PubMed - indexed for MEDLINE]


Echocardiographic evaluation in acromegalic patients.

Cannavò S, Cavalli G, Aragona A, Trimarchi F.

PMID: 2976073 [PubMed - indexed for MEDLINE]


Abnormal responses to vasoactive intestinal peptide and corticotropin releasing hormone during the spontaneous remission of Cushing's disease.

Pagina 48
Abnormalities in hypothalamic-pituitary adrenal axis function were demonstrated by measuring plasma adrenocorticotropin abnormal concentrations following Vasoactive Intestinal Peptide (VIP) and Corticotropin Releasing Hormone (CRH) administration during a phase of remission of Cushing's disease in a 45-year-old female patient. When observed 80 days after the first examination, the patient no longer showed cushingoid features and serum cortisol and plasma ACTH were not abnormally high. VIP infusion (75 micrograms during 12 min) induced a significant increase in serum cortisol and ACTH plasma levels with respect to the normal unresponsiveness. Exaggerated plasma ACTH response to CRH (50 micrograms iv) was also observed. We conclude that the study of ACTH and cortisol response to VIP and CRH may be useful in revealing Cushing's disease even during a remission phase of the disorder.

PMID: 2850311  [PubMed - indexed for MEDLINE]


Failure of praziquantel treatment in cerebral cysticercosis. A case report.
Salpietro F, Caruso G, Cipri S, Gambardella G, Cannavò S.

Clinica Neurochirurgica, Università di Messina.

A case of cerebral cysticercosis unsuccessfully treated by Praziquantel is reported. Some diagnostic aspects stressing the role of epidemiologic criteria and neuroradiological evaluation as well as the limits of treatment are discussed.

PMID: 3454362  [PubMed - indexed for MEDLINE]


Abnormal daily periodicity of serum thyrotropin (TSH) and evidence for defective TSH suppression in a case of non-neoplastic syndrome of inappropriate TSH secretion.
Benvenga S, Sobbrio GA, Vermiglio F, Li Calzi L, Cannavò S, Consolo F, Trimarchi F.

A non-neoplastic syndrome of inappropriate secretion of TSH (ITSHS) was diagnosed in a hemithyroidectomized and clinically euthyroid 44-yr-old man, who also
Cannavo S, until 2011 exhibited limping (Perthes' disease), genu valgum, pes supinatus and lateral nystagmus. Computed tomography demonstrated an enlarged sella turcica due to empty sella. Baseline serum T3, T4, free T3, free T4 and TSH fluctuated between 179 and 274 ng/dl, 6.0 and 13.2 micrograms/dl, 4.2 and 6.0 pg/ml, 7.6 and 15.3 pg/ml, and 4.3 and 33.0 microU/ml, respectively. Serum alpha-TSH subunit was repeatedly normal (0.36-0.69 ng/ml) over the follow-up period (greater than 3 yr). No changes in serum liver enzymes and lipids were observed after thyroid hormone administration, whereas red blood cell glucose-6-phosphate dehydrogenase (G-6-PD) and urinary OH-proline were slightly enhanced during 120 micrograms/day L-T3 regimen. This also resulted in an inappropriately normal glucagon-stimulated cAMP levels. Tachycardia was experienced only during L-T3 and very high L-T4 dose treatments. Therefore, the patient showed some evidence for thyroid hormone peripheral refractoriness. Patient's TSH was physiologically responsive to agents (thyrotropin releasing hormone, methimazole, the dopamine antagonists domperidone and sulpiride) known to elicit its release into circulation, while it responded paradoxically to those which normally inhibit TSH secretion. In fact, the infusion of somatostatin (320 micrograms/h) or dopamine (4 micrograms/Kg/min), and the oral administration of bromocriptine or nomifensine (two dopamine agonists) or corticosteroids (dexamethasone) provoked an unexpected elevation of both unstimulated and TRH-stimulated TSH levels.(ABSTRACT TRUNCATED AT 250 WORDS)

PMID: 3584859 [PubMed - indexed for MEDLINE]