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


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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 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 5.5% of TBI with no deficit at 3 months, IH was recorded at retesting. In 5.5% of TBI with no deficit at 3 months, IH was recorded at 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]
**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]

27.

**Therapy for the syndromes of GH excess.**


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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]

28.

**Traumatic brain injury and subarachnoid haemorrhage are conditions at high risk for hypopituitarism: screening study at 3 months after the brain injury.**
OBJECTIVE: Acquired hypopituitarism in adults is obviously suspected in patients with primary hypothalamic-pituitary diseases, particularly after neurosurgery and/or radiotherapy. That brain injuries (BI) can cause hypopituitarism is commonly stated and has been recently emphasized but the management of BI 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 women, 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 rosiglitazone in Cushing’s disease.


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OBJECTIVE: Rosiglitazone, 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: Rosiglitazone (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 rosiglitazone 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]

30.

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


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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 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.

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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.


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PMID: 15144914 [PubMed - indexed for MEDLINE]

Prolactin is an amyloid-related protein.

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Comment on:
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]

36.


**Clinical presentation and outcome of pituitary adenomas in teenagers.**

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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 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 oligoamenorrhoea (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 oligoamenorrhoea 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.
Objectives: To evaluate the role of age, gender, duration and control of acromegaly on the reversibility of arthropathy. Patients and Design: 30 de novo patients with active acromegaly, 30 cured patients and 30 healthy subjects were studied in a transverse 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.
Effects of long-lasting raloxifene treatment on serum prolactin and gonadotropin levels in postmenopausal women.


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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]
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/M2 no.=22) or obese (BMI >28 kg/m2 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.


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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]

42.


Abnormalities of GH secretion in a young girl with Floating-Harbor syndrome.


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We present a 9.1-year-old girl of Calabrian (Italy) ancestry, with clinical features (cranio-facial dysmorphism, short stature with delayed bone age and speech delay) suggesting the diagnosis of Floating-Harbor syndrome (FHS). Physical examination showed: height 113.9 cm (-2.9 SD), with a parent's target of 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]

43.


**Exercise-related female reproductive dysfunction.**

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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 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]

44.


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

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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 acromegals were enrolled randomly in two groups. Ten patients (group 1: 2 males and 8 females aged 44.5 +/- 4.3 years) underwent surgery via transsphe noidal 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), transsphe noidal 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 the 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-1 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.

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45.


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

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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 acromegals (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 acromegalics 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]

46.


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

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AIMS: We evaluated morphological, biochemical and cytological thyroid parameters in acromegalic patients, investigated before and after treatment for acromegaly. PATIENTS: 28 acromegalics 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. Acromegals 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]

47.


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

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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 macroadenoma (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<0.005) and normalized in all macro and in 23/26 microprolactinomas. In 3 cases PRL levels 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 macroprolactinomas and in all oligo-amenorrhoic patients with microadenoma; serum testosterone levels normalized in 2/3 hypogonadal 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]

48.


Shrinkage of a PRL-secreting pituitary macroadenoma resistant to cabergoline.

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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 the 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]

49.


Unusual MRI finding of multiple adenomas in the pituitary gland: a case report and review of the literature.
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 extrahypophiseal factors in the clonal expansion of genetically altered cells.

PMID: 10231191 [PubMed - indexed for MEDLINE]

50.


Octreotide and lanreotide treatment in active acromegaly.

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

Comment on:


PMID: 9215324 [PubMed - indexed for MEDLINE]

51.


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

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

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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's 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]

52.


Early-onset cerebellar ataxia, myoclonus and hypogonadism in a case of mitochondrial complex III deficiency treated with vitamins K3 and C.


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A 16-year-old girl presented with early-onset cerebellar ataxia, myoclonus, elevated lactic acidosis and hypogonadotropic hypogonadism. Muscle biopsy specimens revealed fibres with a "ragged" appearance with increased mitochondria and lipid droplets. Biochemical investigation revealed a deficiency of complex bc1 (complex III) of the mitochondrial respiratory chain. Genetic analysis did not show either deletions or known mutations of mitochondrial DNA (mtDNA). Phosphorus magnetic resonance spectroscopy (31P-MRS) showed defective energy metabolism in brain and gastrocnemius muscle. A decreased phosphocreatine (PCr) content was found in the occipital lobes accompanied by normal inorganic phosphate (Pi) and cytosolic pH. These findings represented evidence of a high cytosolic adenosine diphosphate concentration and a relatively high rate of metabolism accompanied by a low phosphorylation potential. Muscle 31P-MRS showed a high Pi content at rest, abnormal exercise transfer pattern and a low rate of PCr post-exercise recovery. These findings suggested a deficit of mitochondrial function. Therapy with vitamins K3 and C normalized brain 31P-MRS indices, whereas it did not affect muscle bioenergetic metabolism. In this patient, the endocrinological disorder is putatively due to a mitochondrial cytopathy. Although an unknown mtDNA mutation cannot be ruled out, the genetic defect may lie in the nuclear genome.
53.


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]

54.


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

Cannavò S, De Natale R, Curtò L, Li Calzi L, Trimarchi F.

Cattedra di Endocrinologia, University of Messina, Italy.

DESIGN: Patients were studied before and after 1 year of bromocriptine or 6 months of SMS 201-995 treatment, for prolactinomas or GH-secreting adenomas, respectively. PATIENTS: Seventeen patients with intrasellar pituitary tumour (ten prolactinomas, all females; seven GH-secreting
adenomas, four males and three females) and the presence of relative or absolute scotomas, were examined. 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, PNS). 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]

55.


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

Cannavò 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.


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 GHIRH. 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]

58.


Echocardiographic evaluation in acromegalic patients.

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

PMID: 2976073 [PubMed - indexed for MEDLINE]

59.


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

Cannavò S, Li Calzi L, Aragona A, Trimarchi F.

Istituto di Clinica Medica e Terapia Medica, UniversitÃ  di Messina, School of Medicine, Italy.

Abnormalities in hypothalamic-pituitary adrenal axis function were demonstrated by measuring plasma adrenocorticotropic 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]

60.
Failure of praziquantel treatment in cerebral cysticercosis. A case report.

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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.

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A non-neoplastic syndrome of inappropriate secretion of TSH (ITSHS) was diagnosed in a hemithyroidectomized and clinically euthyroid 44-yr-old man, who also 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)

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