with IFNo that responded to levodopa (L-dopa) infusion. As in the present patient, RLS often responds to opiates. IFNo can exert direct effects on opiate systems in the brain; however, the interactions are complex, depending on receptor type and brain region.13,14 Because dopaminergic neurotransmission in the basal ganglia can be also modulated by opiate receptors, IFNo may cause RLS via direct or indirect effects on dopaminergic and opiate receptor systems.

IFNo can raise the level of autoantibodies. Although manifestations of elevated autoantibody levels are often subclinical, autoimmune thyroiditis is not uncommon and type I diabetes mellitus has also been reported in association with IFNo.15,16 It could be proposed, therefore, that autoantibodies to a basal ganglia epitope gave rise to reversible RLS during interferon treatment in our patient, similar to the mechanism proposed for choreiform movements in pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections.

IFNo therapy has been associated with akathisia, parkinsonism, and chorea.2,4,6 RLS can now be added to this list. References

after receiving ciprofloxacin 200 mg intravenously twice daily OFD in a young woman with normal renal and liver function had renal impairment; the renal and liver function of the other patients were 85 and 87 years old: 1

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The causality of ofloxacin treatment and OFD was judged as probable by the clinicians caring for this patient. A definite relation of the adverse event to the drug treatment would have required re-challenge. There are no reported cases of OFD due to ofloxacin so far. It is a fluoroquinolone that has a 95% oral bioavailability and superior (up to 50% of the serum concentration) penetration across the blood–brain barrier compared to ciprofloxacin. This feature might increase the likelihood of neurotoxicity, but to date, the reported incidence of CNS adverse events is lower for ofloxacin than for ciprofloxacin.

In vitro studies suggest that fluoroquinolone neurotoxicity may be related to competitive inhibition of γ-aminobutyric acid (GABA) binding to its brain receptor sites, with a resultant hyperexcitable neuronal state. There is considerable evidence for a role of GABAergic dysfunction in the pathogenesis of OFD, and interference with GABAergic neurotransmission is the most likely pharmacological explanation for the predication in this patient. The concomitant use of venlafaxine for several months previously should be considered; it is a strong inhibitor of the neuronal reuptake of serotonin and noradrenaline and a mild to moderate inhibitor of dopamine reuptake. In vitro data indicate that venlafaxine does not block muscarinic, cholinergic, alpha- or beta-receptors, and only weakly reacts with histamine receptors. During premarketing studies in healthy people and patients, extrapyramidal symptoms such as akathisia and dyskinesia were rare adverse effects of venlafaxine (defined as less than 1 in 1,000), even at high doses. There were two cases of extrapyramidal symptoms, both young women who experienced facial grimacing and difficulty speaking after 1 and 2 days of treatment with venlafaxine 37.5 mg daily, a low therapeutic dose. To date, there have been no clinical reports of possible pharmacodynamic or pharmacokinetic interactions between fluoroquinolones and venlafaxine. Nevertheless, in our patient, the treatment with venlafaxine may have raised the susceptibility for ofloxacin-induced neurotoxicity due to decreased dopamine reuptake.

Discussion

OFD is a syndrome consisting of involuntary movements of the face, lips, tongue, and jaw. Facial grimacing and distortions, puckering and pursing of the lips, tongue protrusion, and writhing and opening and closing of the jaw can occur. The predominant movements are choreatic stereotypies, but dystonic movements may also be seen. OFD is often drug-induced, mainly by neuroleptics, or occurs as a part of degenerative diseases of the extrapyramidal system. Rarely, dyskinesia restricted to the facial region may be caused by drugs that are in common use, including antihistamines, anticonvulsants, metoclopramide, anticholinergics, and tricyclic antidepressants. The association of OFD with the use of fluoroquinolones rarely has been described. One patient with liver cirrhosis and partial nephrectomy developed OFD after taking ciprofloxacin 500 mg orally twice daily. Two cases of suspected ciprofloxacin-induced OFD have been reported to the Committee on Safety of Medicine. These patients were 85 and 87 years old: 1 had renal impairment; the renal and liver function of the other patient was not documented. Lee and colleagues described OFD in a young woman with normal renal and liver function after receiving ciprofloxacin 200 mg intravenously twice daily during 2 days for a complicated high urinary tract infection (recommended dose).

The causality of ofloxacin treatment and OFD was judged as probable by the clinicians caring for this patient. A definite relation of the adverse event to the drug treatment would have required re-challenge. There are no reported cases of OFD due to ofloxacin so far. It is a fluoroquinolone that has a 95% oral bioavailability and superior (up to 50% of the serum concentration) penetration across the blood–brain barrier compared to ciprofloxacin. This feature might increase the likelihood of neurotoxicity, but to date, the reported incidence of CNS adverse events is lower for ofloxacin than for ciprofloxacin.

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References