

Tardive dyskinesia due to risperidone

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INTRODUCTION

Tardive dyskinesia (TD) is a neuroleptic-induced movement disorder, and is recognised as a late adverse effect of neuroleptic drugs. We report a case of TD associated with risperidone, a new "atypical" antipsychotic drug. Risperidone has a high affinity for D2 dopamine and 5-HT₂ receptors [8]. Thus, it produces less extrapyramidal side effects (EPS) than classical neuroleptics. Also, risperidone was shown to have a beneficial effect on TD [3, 7, 9]. To our knowledge, only four cases have been reported concerning the appearance of TD in relation to risperidone administration [1, 2, 5, 10].

CASE REPORT

A 65-year-old man suffering from major depression with psychotic features was admitted to hospital in September 1996. Twelve years ago, a liver biopsy suggested the presence of chronic active hepatitis. Otherwise his medical history was unremarkable. His history of depression started 4 years ago, when he retired. He felt worthless, expressed depressed mood, complained of loss of interest and pleasure, and withdrew from his family. He spent most of his time in bed and he was very anxious. He also expressed paranoid ideas. Most of them were mood-congruent (ie, he felt guilty about an old story of mistrust in his business, of which he was actually innocent), but also delusions with mood-incongruent content (thinking that his brother was after his money and intended to throw him out of their family business). One year ago, he visit a psychiatrist who prescribed amitriptyline 25 mg/d and perphenazine 4 mg/d. The patient was very uncooperative and took his pills irregularly for 3 months.

His psychiatric condition deteriorated. He became more anxious and paranoid. He visited another doctor who gave him only risperidone 6 mg/d which he took regularly, in the

prescribed dose. With risperidone, his delusional ideas subsided and became more calm. However, he was still withdrawn, with no interest in everyday activities, had psychomotor retardation, and continuously expressed feelings of worthlessness. After 8 months of treatment, another psychiatrist diagnosed major depressive episode, abruptly stopped risperidone and started fluoxetine 20 mg/d and alprazolam 2 mg/d.

In the very first days of risperidone elimination, the patient manifested involuntary perioral movements. Day after day the movements became more pronounced and included chewing and lateral jaw movements. The psychiatrist diagnosed TD and reassured the patient that this side effect would eventually disappear. He also increased the dose of fluoxetine to 40 mg/d. However, after 1 month the patient not only continued manifesting TD symptomatology, but he also manifested signs of tardive Parkinsonism. He had muscle stiffness, cogwheel rigidity, shuffling gait and tremor in both his hands. An anticholinergic agent, biperiden 8 mg/d, had little effect and following a neurological consultation levodopa with carbidopa was introduced. Fluoxetine was reduced to 20 mg/d and levodopa was increased progressively to 500 mg/d.

The patient showed no improvement, and after 6 months he was hospitalised. Levodopa was progressively discontinued and fluoxetine was replaced by mianserin 60 mg/d and venlafaxine 150 mg/d. Also, in order to control the patient's anxiety, after 1 week levomepromazine 25 mg/d and trifluoperazine 2.5 mg/d were introduced. On the 3rd week of hospitalisation improvement in both the psychiatric and the neurological symptomatology became obvious. The patient was discharged when he completed 1 month's hospital treatment, in very good condition. He was no longer depressed or paranoid and had no involuntary movement. His speech was clear and the only Parkinsonian sign present was a thin cogwheel rigidity. During his hospitalisation only an elevation of blood γ GT was noted. Also, the magnetic resonance image (MRI) revealed a degree of brain atrophy and some small ischaemic-type alterations in both parietal lobes.

DISCUSSION

In most reported cases, TD develops after at least 1 year of neuroleptic use. However, in elderly patients and in patients with a cognitive disorder, TD may appear after shorter periods of neuroleptic use. Another risk factor for TD is the presence of mood disorder [6]. Although TD could emerge while the patient is taking a steady dosage of medication, it is more likely to emerge when the dosage is reduced or stopped. All the classical neuroleptics have been associated with TD.

Risperidone is a new antipsychotic drug which acts in both dopamine and serotonin receptors. This combined action allows the drug to be not only more potent in the treatment of negative schizophrenic symptoms, but also to induce less EPS. However, since this drug has an affinity with D2 dopamine striatum receptors, theoretically it has a potential for the production of TD. In our patient this potential was unfortunately accomplished, possibly because he was a high risk patient for TD. He was of advanced age, had cerebral atrophy and some brain alterations of ischaemic type, and suffered from affective disorder. Also, the irregular intake of perphenazine during the months that preceded risperidone ingestion, may have played a role in the sensitisation of the dopamine receptors. Finally, fluoxetine administration may have facilitated the appearance of TD symptomatology, as postulated elsewhere [5]. Moreover, it is known that fluoxetine and other inhibitors of serotonin presynaptic reuptake, may exacerbate motor symptoms when given in combination with antipsychotic medication [4]. Overall, the appearance of TD and Parkinsonian

symptoms in our patient, may reflect in great part some cerebral dysfunction.

Our report is one of the few reports associating TD with risperidone. We believe that as the use of this useful antipsychotic is expanded world-wide, more such cases will be reported. Thus, it would be wise to administer risperidone with caution, similar to the caution required for the classical neuroleptics. Finally, our observations indicate that when risperidone is discontinued, withdrawal must be carried out progressively.

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