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CASE REPORT

Two cases of risperidone-induced tardive dyskinesia and a review of the literature

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Summary – A case in which a 26 year old patient with undifferentiated schizophrenia, showing abnormal oral, lingual and jaw movements suggestive of tardive dyskinesia during a dose reduction of risperidone, is presented. A second case, relating to a 39 year old married woman diagnosed as having a DSM-IV schizophreniform disorder is also presented. These two cases are discussed in relation to the existing literature. © 1999 Elsevier, Paris

risperidone / tardive dyskinesia

INTRODUCTION

Risperidone is a new and atypical antipsychotic agent [1], and its therapeutic action is probably linked to a dual antagonistic effect on 5-HT_2 and D_2 receptors [2, 3]. In low doses it offers the advantage of a decreased incidence of extrapyramidal side-effects compared with conventional antipsychotics [4, 5]. It has also been shown that risperidone possesses antidyskinetic properties [6, 7]. Despite this, risperidone can cause tardive dyskinesia (TD) in some patients, although its relative risk remains to be established [5]. Here, we report two new cases of tardive dyskinesia during treatment with risperidone.

CASE REPORT

Case 1

Mrs C is a 26 year old single unemployed woman with a seven year history of DSM-IV undifferentiated schizophrenia. In the past she received trifluoperazine at 20 mg/d and haloperidol at 15 mg/d with good therapeutic effect. The two neuroleptics induced moderate to severe extrapyramidal side-effects for which anti-cholinergic drugs were prescribed with beneficial effect. In October 1995, following a reduction of haloperidol, she developed psychotic symptomatology with bizarre ideas, auditory hallucinations, inappropriate affect, irritability, and talkativeness. The haloperidol dose was increased to 20 mg/d and the patient's condition improved over the next three weeks. In December 1995, she visited the Outpatients Department of the Athens University Department of Psychiatry at the Eginition Hospital. She had marked extrapyramidal symptoms and negative symptoms were very prominent in her symptomatology. For these two reasons haloperidol was discontinued and risperidone titrated over three days to 6 mg/d was given. She remained on this regimen for eight months without extrapyramidal symptoms. Within this time, negative symptomatology gradually reduced and she became markedly more functional. Reduction of risperidone to 4.5 mg/d was advised. Two weeks later, the patient visited the outpatients department and reported involuntary movements of the lips, the tongue, and the jaw. These movements of mild-to-moderate intensity appeared during the first days of risperidone reduction. The patient was advised to discontinue risperidone over four days, and within three weeks there was no evidence

of neurological symptomatology. Computerized axial tomography scans showed no abnormalities.

Case 2

P.M., a 39 year old married female blue-collar worker was described as sociable, active, and pleasant. One year before visiting the outpatients department she developed delusional ideas of influence, auditory hallucinations, tension, and insomnia and insisted that she could read other people's minds. She came to believe that her employer had put a spell on her. She was diagnosed as having a DSM-IV schizophreniform disorder. She was hospitalized for 20 days, during which period haloperidol at 40 mg/d, thioridazine at 400 mg/d, and biperiden at 6 mg/d were administered with a beneficial effect. She remained on this regimen for eight months before the psychiatrist she visited discontinued all medication and put her on risperidone at 6 mg/d. Approximately three months following the initiation of risperidone she developed involuntary movements of the lips, the tongue, and the jaw with marked difficulty in her speech. She was then advised to reduce the risperidone dose to 3 mg daily. By the second week, improvement in the involuntary movements was observed for the first time. By the fourth week the movements were markedly diminished, and by the eighth week they had disappeared completely. On follow-up two months later, the patient remained asymptomatic with respect to both her psychotic symptoms and her abnormal movements. She was kept on risperidone at 3 mg/d.

DISCUSSION

There are ten reports in the literature (six men, four women; nine adults, one adolescent) of patients who developed tardive dyskinesia while taking risperidone [8-17]. In four of these cases the dose was low, ranging from 1 mg to 4 mg daily, and in all four cases fluoxetine (n = 3) and paroxetine (n = 1) were administered concurrently with risperidone. These drugs have been implicated along with the other SSRIs in the exacerbation of motor symptoms when given in combination with antipsychotics [18]. In the case of our patient, risperidone was given as monotherapy and the dose was as high as 6 mg/d, as was the case with three of the patients reported previously.

Tardive dyskinesia has been associated with the long-term use of classical antipsychotics, although a definite relationship has not been established [19]. In addition to our case 1, a long history of exposure to conventional antipsychotics has been reported in six out of the ten cases in the literature. It is to be noted that these patients had no evidence of tardive dyskinesia before the introduction of risperidone. Sensitization of the dopamine receptors by conventional antipsychotics should be considered as a contributor to the development of tardive dyskinesia. However, this could not be the case with our case 2 who had only eight months of exposure to antipsychotics. Other risk factors in these two patients include female gender and extrapyramidal side-effects [20].

In the case of both patients, the movement disorders began less than one year after starting risperidone treatment, and this is in keeping with five other patients reported in the literature. Two of these patients were elderly and the other three were young, as in the cases reported here. However, all of the patients met the diagnostic criterion of the American Psychiatric Association task force [21], which requires at least three months of total cumulative antipsychotic exposure. Previous authors have proposed the term 'early onset dyskinesia' for these cases [15].

The abnormal movements of tardive dyskinesia often appear when the patients have their dosage of antipsychotic medication decreased or discontinued. Dyskinesias with this pattern of abnormal movements have been referred to as withdrawal-emergent dyskinesias, and it has been noted that they remit spontaneously in a few weeks or months [22]. This was the case with the first case reported above, and with another patient reported by Sakkas et al. [16], but not in the case reported by Anand and Dewan [9]. Contrary to this, our case 2 was a patient who manifested dyskinetic movements while on a steady dose of risperidone for over three months. Reduction of risperidone was associated with a marked improvement of involuntary movements. How did this improvement occur? One could consider the possibility that improvement was in fact a spontaneous phenomenon, unrelated to the reduction of risperidone.

According to Gutierrez-Esteinou and Grebb [23], the risk of tardive dyskinesia in patients receiving risperidone is 0.3% per treatment year, compared to an annual incidence of 5–10% in patients taking conventional antipsychotics. Clearly the association of tardive dyskinesia with risperidone is infrequent. However, this possibility should not be disregarded, particularly in patients exposed to long-term neuroleptic treatment.

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