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Case Report

Unusual compulsive motor activity during treatment with clothiapine in a mentally retarded adolescent

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Abstract

Atypical antipsychotic agents, specifically those with a high hyposerotonergic activity such as clozapine and clothiapine, have been associated with de novo obsessive–compulsive symptoms. We report the case of a 16-year-old adolescent male with severe mental impairment and disruptive behaviour who developed a compulsive head and body turning disorder on clothiapine. Such a symptom had to be distinguished from epileptic partial seizures; it promptly disappeared with the drug discontinuation.
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Keywords: Mental retardation; Paroxysmal motor activity; Clothiapine

1. Introduction

Anecdotic cases on transient obsessive–compulsive disorders (OCD) during treatment with atypical neuroleptics such as clozapine and clothiapine, have been reported in the recent years [1–4]. In particular, both these drugs share strong antiserotonergic activity that has been hypothesised to be responsible for the development of iatrogenic obsessive–compulsive symptoms [5]. According to that, potent serotonin reuptake inhibitors (SRIs) clearly resulted in the most effective monotherapy for OCD. Further, there is a consistent group of SRI-refractory OCD patients who may respond to dopamine receptor antagonists [6], such as haloperidol and pimozide, thus confirming that any comprehensive theory of the OCD pathophysiology must consider this differential treatment response finding [7].

In this report, we describe the case of an adolescent male with severe mental impairment and disruptive behaviour disorder who developed an unusual paroxysmal motor activity during clothiapine treatment. Such a symptom had to be distinguished from epileptic partial seizures and promptly disappeared with the drug discontinuation.

2. Case study

Patient 1 is a 16-year-old boy, born of non-consanguineous parents. His mother and father were, respectively, 23- and 30 year-old at the time of his birth. The pregnancy was uneventful except for poor fetal movements from the fifth month of gestation. Delivery was at 32 weeks by cesarean section because of partial detachment of placenta; birth weight was 2,150 g and head circumference measured 34 cm (10th centile). There was postnatal cyanosis and Apgar score was 3 and 5 at $1'$ and $5'$, respectively. By 12 months of age, he was exhibiting a severe delay in his motor milestones. Brain magnetic resonance imaging (MRI) performed at age 2.5 years, was normal.

At the age of 3 years, language was absent and the child developed a disruptive behaviour together with aggressive episodes. Both tioridazine and clorpromazine results were unsuccessful; at the age of 5 years clothiapine was tried and the child improved satisfactorily. Upwards of 6–14 years, the patient discontinued any drug therapy, attending fairly well a special educational program in primary school. As soon as he left the primary school for a new boarding-school for handicapped young patients, he started with aggressive behaviour at both home and school together with continuous stereotyped vocalizations and insomnia. Such symptoms did not disappear on leaving the new school and tioridazine associated with lorazepam

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resulted substantially ineffective. Clothiapine treatment (7 mg/day) was initiated on the basis of our good experience with this agent in mentally retarded children with behavioural disorders due to lack of prominent neurological extrapyramidal side effects, typical of most of the clinically used neuroleptics. This treatment was followed by a good clinical improvement evaluated by means of a Clinical Global Impression Scale (range 1–6); in about 6 months the total score switched from 5 to 2. Due to the reappearance of a disruptive behaviour [8] and subcontinuous vocalizations and/or screams, clothiapine daily dose was raised to 13 mg/day (0.16 mg/kg); a few days later, Patient 1 started turning his head and eyes to the right followed by compulsive body rotation lasting about 15–20 min (Fig. 1). Serial interictal EEGs did not show any paroxysmal discharge; as Patient 1 did not comply, ictal EEG recording was not obtained. As behavioural disorder persisted, clothiapine daily dose was raised to 90 mg/day (1.1 mg/kg) by parents on their own; concomitantly, the turning episodes became more frequent, lasting up to 5–6 h. Clothiapine was consequently withdrawn and the turning activity disappeared during the following washout period. Soon afterwards, given a persisting insomnia, clothiapine was tried by parents on their own three times running at the daily dose of 13–15 mg/day, the turning disorder promptly reappearing each time. Once on haloperidol at 6 mg/day, clinical picture improved without abnormal motor episodes.

3. Discussion

In the present report, a compulsive paroxysmal motor activity due to clothiapine therapy in an adolescent with severe mental impairment and behaviour disorder has been described.

Toren et al. [4] had previously reported obsessive–compulsive symptoms in an 8-year-old boy with schizophrenia during daily assumption of the same drug (10 mg/day). The compulsions pertained to washing and cleaning only. They appeared within 2 days after the initiation of clothiapine treatment, lasted unchanged for 2 weeks and then subsided over the following 2 weeks. Compulsive symptoms worsened concomitantly with increasing clothiapine daily dose.

Our patient developed a prolonged motor manifestation represented by ‘turning episodes’, lasting up to 5–6 h, soon after a forced ipsiversive posture of the head and eyes.

These episodes were clearly related to the daily assumption of clothiapine, as they repeatedly appeared at a given dosage and disappeared soon after discontinuing the drug.

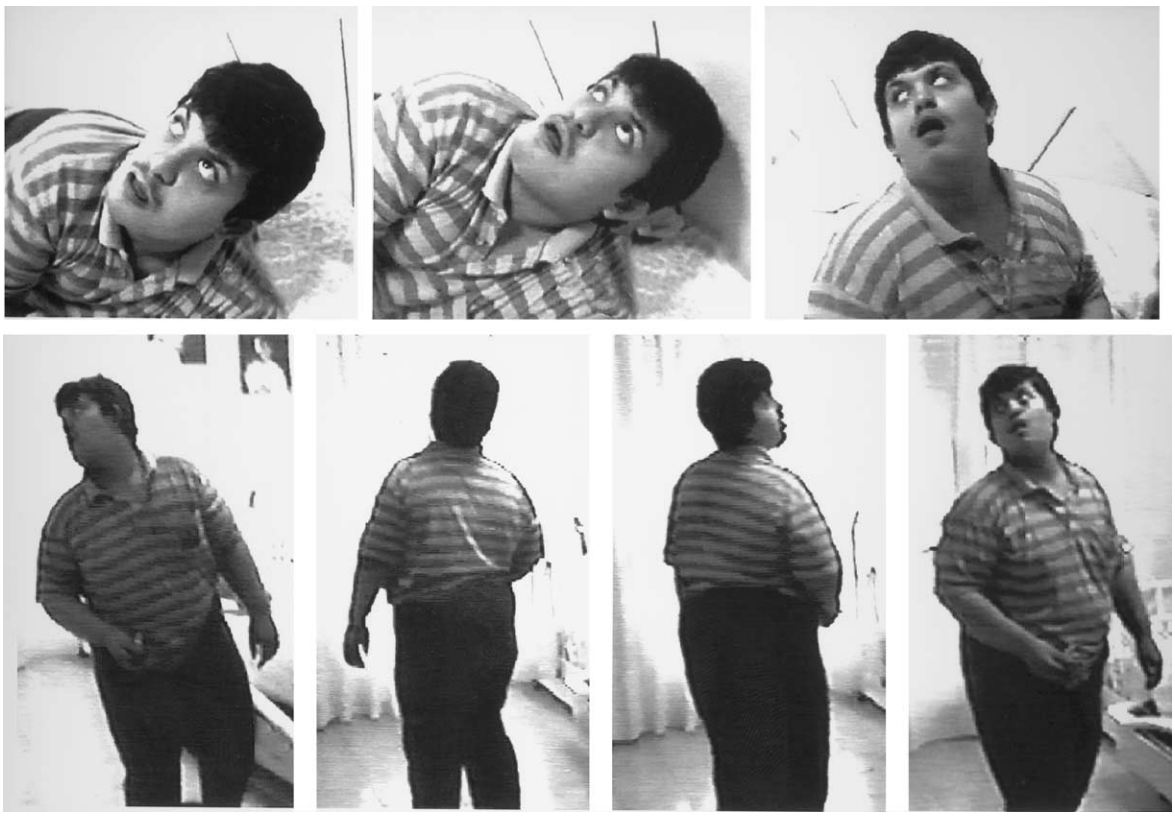

Fig. 1. Photograms showing a ‘paroxysmal turning activity’ lasting more than 3 h (by permission of his guardian because of patient’s privacy).

Furthermore, home-video recordings showing no impairment of consciousness, and normal interictal EEGs, contributed to ruling out epileptic partial seizures.

Occasional reports [2,3] on the emergence of OC symptoms in patients treated with clozapine support the OCD hyposerotonergic hypothesis [5]; the same mechanism can be hypothesised for clothiapine [4]. Our case fits the OCD serotonin hypothesis considering that clothiapine has antagonist activity at D1, D2, 5-HT1a, 5-HT2a/5-HT2c, and 5-HT3 receptors. Further, our patient did not manifest other turning episodes during treatment with haloperidol that is characterised by a moderate antagonistic activity on 5-HT-2 receptor and, conversely, by strong antidopaminergic properties.

This OCD seems clearly dose-dependent in our patient. In fact, parents reported a significant behaviour improvement during the first 6 months of treatment with 7 mg daily dose. By increasing clothiapine dose to 13 mg/day, paroxysmal motor episodes recurred frequently, probably due to increasing hyposerotonergic activity. In the case reported by Toren et al. [4], the OC symptoms gradually subsiding over the following weeks, may be related to the subsensitation of presynaptic receptors. In our patient it was not possible to verify if symptoms would have disappeared because clothiapine was each time discontinued in a few days, due to unacceptable and prolonged 'turning episodes'.

Furthermore, the impairment of the cortical component of the OCD neurobiological pathways represented by the association and limbic areas [9], could explain the absence of structured OC symptoms in a severe mentally retarded patient.

In conclusion, the possible iatrogenic origin of severe compulsive symptoms should be considered in mentally retarded patients treated with atypical antipsychotic agents and, specifically, those with a high hyposerotonergic activity such as clothiapine and clozapine.

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