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Letter to the Editor (Case report)

Psychosis in a patient with Fabry's disease and treatment with aripiprazole

1. Introduction

Fabry's disease (FD) is an X-linked disorder of glycosphingolipid metabolism resulting from a deficiency of the lysosomal enzyme alpha-galactosidase A (Peters et al., 2001). This enzymatic defect leads to progressive accumulation of neutral glycosphingolipids in most visceral tissues and body fluids. Progressive intracellular accumulation of neutral glycosphingolipids leads to progressive cellular dysfunction and eventually, organ dysfunction (Germain, 2002). Clinical manifestations in patients with this disorder include angiokeratoma, autonomic dysfunction, lifelong debilitating pain, renal failure, progressive neurological and cardiac lesions, and death as a young adult (Germain, 2002).

Except the medical manifestations, there have been case reports of psychiatric disorders developing in patients with FD. In a single case series of 33 men with FD it was found that 18% of the patients had a psychiatric disorder, in most instances depression (Grewal, 1993). There are also case series in the literature describing depression in female patients of FD (Muller et al., 2006; Sadek et al., 2004). Personality changes have also been reported, but without comments on the etiologies of these changes (Steward and Hitchcock, 1968). In a literature review, there was only one report of a patient with FD who presented with schizophrenic symptoms (Liston et al., 1973). Although the authors suggested that this psychosis was an organic psychotic disorder, the nature of brain involvement was unclear. It is now well established that FD also affects the central nervous system (CNS) and a number of brain imaging studies have been carried out (Fellgiebel et al., 2006; Ginsberg et al., 2006). This case report presents the imaging findings of newonset psychosis occurring in a patient with FD and describes the treatment response to the dopamine D2 receptor partial agonist, aripiprazole.

2. Case report

A 35-year-old male was referred by an internist and admitted to our neuropsychiatric facility for the first time with acute psychotic symptoms. Prominent symptoms included auditory hallucinations and delusions of reference. During the interview, his thought processes were loose and disorganized and there was evidence of thought blocking. The patient had been

neglecting his personal hygiene for several days prior to admission. He denied feeling depressed, but showed some somatic symptoms of fatigue and insomnia, which he attributed to his physical discomfort. His past medical history revealed that the diagnosis of FD has been established 3 years earlier by testing leukocyte activity of the lysosomal enzyme alphagalactosidase A and performing a genetic analysis of the alphagalactosidase A gene. During the following years, he irregularly received enzyme replacement therapy. The results of laboratory screening, including hematological analysis, biochemical examination, and urine toxicology screen, were normal. Brain magnetic resonance imaging (MRI) revealed small hyperintense spots in the right thalamus, midbrain, and corona radiata on T2weighted imaging, which were absent in his previous MRI imaging. For treatment of psychotic symptoms, a trial of risperidone with slow titration was started with a dosage of 0.5 mg at bedtime. The dosage was gradually increased to 1 mg within 1 week. Unfortunately, risperidone had to be discontinued due to the side effects of sedation, muscle stiffness, extrapyramidal symptoms, and vision impairment. Subsequently, aripiprazole was initiated, starting with a dosage of 5 mg at bedtime. The patient tolerated this medication and his psychotic symptoms were reduced (PANSS total score improved from 122 to 74 after 2 weeks of treatment). The pain in his hands and feet also responded to treatment with carbamazepine 400 mg per day. After the psychosis was relieved, enzyme replacement therapy was reinstituted for slowing the clinical course of FD. Unfortunately, auditory hallucinations and delusions of reference were exacerbated again 2 months later when he guitted taking medication. By using the same psychotropic medications (aripiprazole and carbamazepine) for his auditory hallucinations, delusion, and pain, the psychotic symptoms remitted gradually.

3. Discussion

To our knowledge, this is the first description of imaging findings of new-onset psychosis occurring in a patient with FD. Brain MRI revealed small hyperintense spots in the right thalamus, midbrain, and corona radiata on T2-weighted imaging. Such spots were absent in the patient's previous MRI scans which suggested that there was a coincidence between psychotic symptoms and changes in the MRI findings. Taken together, our case and previous reports (Danos, 2004) of thalamic lesions in patients with schizophrenic symptoms suggest that the thalamus is a brain region which may be involved in the pathogenesis of psychotic symptoms.

In a literature review, a concept for the pathogenesis of these hyperintense spots on MRI T2-weighted images was formulated (Ginsberg et al., 2006). Glycosphingolipid deposition might increase cerebral blood flow and alter vascular reactivity. Glycosphingolipids might also induce cellular dysfunction leading to increased interstitial pressure and to metabolic vulnerability of these areas. In the order of occurrence, gliosis, demyelination, and increased interstitial water content result in these hyperintense spots.

Our preliminary experience is mixed and not very encouraging with regard to low-dose risperidone leading to prominent extrapyramidal symptoms which were not seen with aripiprazole in the treatment of our patient with FD and brain involvement. Previous reports have indicated some of the risk factors for development of extrapyramidal symptoms in patients receiving antipsychotic medication (Carnahan et al., 2006). These factors include a past history of mood disorder or substance abuse, rapid dosage increase or a large total dose of the drug, advanced age, underlying brain problems, and concurrent anti-dopaminergic medications. Our patient had none of these risk factors except FD-related brain involvement that might have led to the development of prominent extrapyramidal symptoms after low-dose risperidone treatment. Aripiprazole, which is unique among antipsychotics in that it is a partial agonist at the dopamine D2 receptor (Gupta and Masand, 2004), might be a preferred agent for patients with psychosis in the setting of underlying brain problems because its dopamine agonism may prevent worsening of extrapyramidal symptoms that may occur with other antipsychotic agents.

4. Conclusion

In conclusion, this is the first description of imaging findings related to new-onset psychosis in a patient with FD. The evidence from the case presented here suggests that right thalamus involvement might be related to the pathogenesis of psychotic symptoms. It also appears that aripiprazole, which is unique among antipsychotics in that it has partial dopamine agonism, might be a preferred agent for patients with psychosis in the setting of underlying brain problems.

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