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CASE REPORT

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Treatment Dilemma in Juvenile Huntington's Patient Presenting with Psychiatric Symptoms

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ABSTRACT

The Westphal variant of Huntington's disease (HD) is a progressive neurodegenerative disease characterized by a rigid-hypokinetic syndrome rather than choreiform movements. This variant is a distinct clinical entity of HD and is often associated with a juvenile onset of the disease. We present the case of a 13-year-old patient diagnosed with the Westphal variant with an onset at approximately 7 years of age and primarily exhibited developmental delay and psychiatric symptoms. In the light of findings from both physical and clinical examinations, possible difficulties in the diagnosis and treatment of juvenile HD are discussed in here.

Keywords: Chorea, parkinsonism, Westphal variant

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INTRODUCTION

Huntington's disease (HD) is a rare neurodegenerative disease characterized by motor, cognitive, and psychiatric symptoms (1). The inheritance pattern is autosomal dominant, and its worldwide prevalence is 6–14 per 100,000 individuals (1,2). The disease occurs due to CAG trinucleotide expansion in exon 1 of the Huntingtin gene (*HTT*) (2–4). Typically, it emerges with chorea, personality changes and dementia. On the other hand, a syndrome in which rigidity and bradykinesia predominate at the onset of the disease was first described by Westphal in 1883 in a small group of patients (5). Since these rare cases do not present with classical symptoms, diagnosis is difficult and it is important to focus on these patients due to the difficulties that arise during the treatment.

Highlights

- **The Westphal variant is extremely rare.**
- **Choreiform movements may not be seen.**
- **Initial symptoms may only be behavioral changes and parkinsonism.**
- **Typical neuroleptic use should be avoided in patients with parkinsonism.**
- **Family history should be questioned in detail.**

CASE PRESENTATION

A 13-year-old girl was admitted to our clinic two years ago with complaints of declining school performance which started at approximately seven years of age and slowness of movements. Over time, obsessions such as repeated hand washing were also noted. Consequently, the patient was evaluated by a child psychiatrist. She was diagnosed with attention deficit and hyperactivity disorder and obsessive–compulsive disorder. She was prescribed 5 mg aripiprazole and 100 mg fluvoxamine and followed up. After about one year from discontinuing the drugs the patient consulted to our clinic with the complaints of slow movements and falls.

The initial examination revealed that the patient was apathetic, her speech was slow and some words she spoke were incomprehensible. She had moderate hypomimia, bilateral symmetrical bradykinesia and rigidity in all extremities. She had an inversion dystonia in the right foot. There was no tremor. Slight choreic movements were observed on the face and rarely in extremities. The patient had a mild stooped posture but had no loss of postural reflexes. She could walk independently. She had moderate cognitive impairment (Standardized Mini-Mental State Examination Score: 24). Unified Huntington's Disease Rating Scale (UHDRS) part I score was 37 and Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) part III score was 43. Brain magnetic resonance imaging (MRI) showed bilateral putaminal atrophy and increased signals on T2-weighted sequences, similar to the findings obtained in other studies (Fig. 1–3) (6).

Family history revealed that her father and grandfather had undiagnosed, involuntary choreiform movements. The pedigree of the patient is shown below (Fig. 4). Molecular analysis revealed 51 CAG repeats in the father and 71 in our patient in the IT15 gene located on chromosome 4p16.3.

Low-dose levodopa-benserazide treatment was tested on the patient, and moderate improvements in bradykinesia and gait were observed. She was prescribed to take 31.25 mg of levodopa-benserazide and 5 mg

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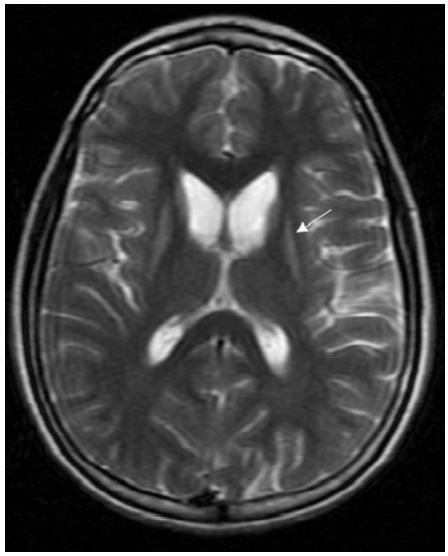

Figure 1. Axial T2-weighted image exhibits atrophy of bilaterally putamen (white arrow).

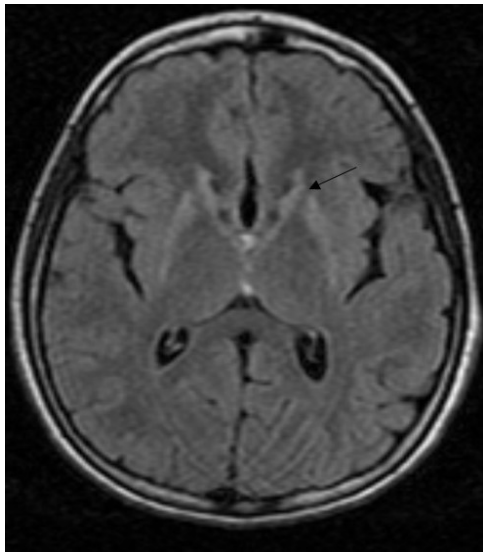

Figure 2. T2-FLAIR image exhibits severe atrophy of the caudat nucleus heads (black arrow).

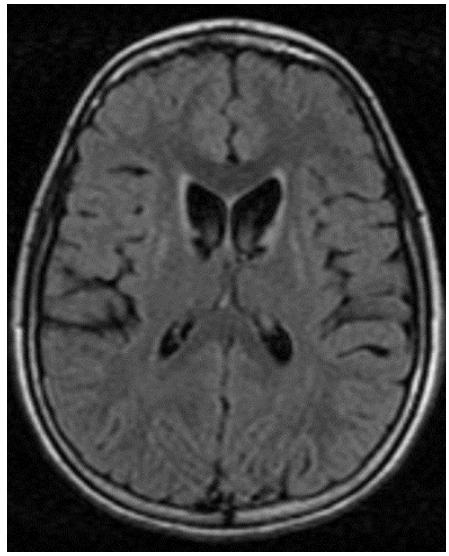

Figure 3. T2-FLAIR image exhibits enlargement of frontal horns due to regional atrophy.

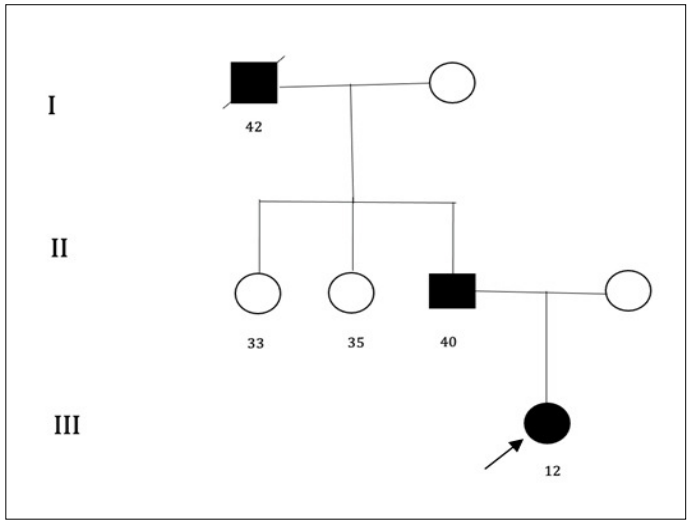

Figure 4. The pedigree of the family, as shown in pedigree disease occurs at a much earlier age with an expanded CAG trinucleotide repeats than their parent which causes more disability and severity (anticipation).

of domperidone three times a day. Motor functions were stable when the patient was evaluated after three months. One year later, the patient was re-evaluated and it was observed that bradykinesia and rigidity had increased, her stooped posture became prominent, and postural reflexes were lost. Left-hand dystonia was observed in addition to the inversion dystonia (MDS-UPDRS part III score: 50, UHDRS part I score: 42). The patient's cognitive impairment had progressed. The dose of levodopa-benserazide was increased to 3×62.5 mg, and a significant improvement was observed in bradykinesia and rigidity with a negligible increase in lower extremity chorea. Writen informed consent was received from the family.

DISCUSSION

Given that the Westphal variant accounts for approximately 10% of HD cases, it is possible to consider the variant as a rare one (7). There is no clear consensus on the treatment of these patients owing to the rarity of the disease; treatment recommendations are based on small case series. The general approach is to start treatment according to the predominant clinical symptoms. Since parkinsonism was dominant in the patient, we initiated the treatment with levodopa-benserazide. Before starting the levodopa-benserazide treatment, the most appropriate dose regimen that provided significant improvement in parkinsonism without exacerbating the choreiform movements was chosen by administering the drug at gradually increasing doses. However, the symptoms progressed over time and the dose of levodopa-benserazide was increased to 3×62.5 mg. The coexistence of chorea and dystonia made it even more difficult to treat the patient. In fact, we tried higher dose than the existing one; however, there was no significant difference in rigidity and bradykinesia when compared to the dose of 62.5 mg, and the patient had an increase in choreiform movements. So, levodopa-benserazide treatment had to be continued at 3×62.5 mg. Exacerbation of chorea and parkinsonism respectively with dopaminergic treatment and dopamine blocking agents used for chorea complicate the treatment. We administered levodopa to our patient since it is the primarily recommended drug for dopaminergic treatment (8).

As the disease progresses; initial symptoms of behavioral changes, walking difficulties, and-other sympoms such as mental deterioration, speech disorders and seizures may occur in children. Antiepileptic treatment was not initiated as the patient did not have any seizures yet, but agents such as valproic acid, which exacerbates parkinsonism, should be avoided as much as possible when antiepileptic treatment becomes necessary (9,10).

In Westphal variant, psychiatric findings can occur before motor symptoms become evident at disease onset (11,12). Indeed, our patient was followed up by the psychiatrist with various psychiatric diagnoses until she consulted to our clinic. She was started on fluvoxamine [selective serotonin reuptake inhibitor (SSRI)] and aripiprazole (antipsychotic). It is known that SSRIs can trigger dystonia and parkinsonism, furthermore there are also fluvoxamine-induced dystonia cases in the literature (13,14). It is also known that aripiprazole can cause serious extrapyramidal side effects and aggravate symptoms in patients with bradykinesia and rigidity (15). These agents should be avoided if possible, and agents with the least risk of causing extrapyramidal symptoms, such as clozapine and quetiapine, should be preferred if treatment is required.

There is another aspect that needs to be considered in the treatment of the cognitive function (10). Anticholinergic agents prescribed for dystonia may also exacerbate the cognitive status of these patients.

As described herein, the clinical course of patients with early-onset HD differs from that of those with adult-onset HD. Before planning treatment, a detailed evaluation of the current findings on the extrapyramidal system, cognitive status, and psychiatric comorbidities should be made. When treating the predominant symptom, care must be taken to avoid exacerbation of other symptoms.

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