

Psychiatric Aspects of Adult-Onset Hallervorden-Spatz Syndrome: A Report of Two Cases

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ABSTRACT

Psychiatric aspects of adult-onset hallervorden-spatz syndrome: a report of two cases

Hallervorden-Spatz Syndrome (HSS) is a rare, familial, progressive, and ultimately fatal disorder characterized by extrapyramidal rigidity, dysarthria, pyramidal tract involvement, and dementia, with pathological evidence of iron deposition in the globus pallidus and substantia nigra. The diagnosis is usually made using magnetic resonance imaging (MRI), where bilateral high signal intensity in the globus pallidus surrounded by low signal intensity areas is found. This is called an "eye-of-the-tiger" appearance and is considered specific to this disorder. Psychiatric aspects of this syndrome are common and include cognitive decline, personality changes with impulsivity and violent outbursts, depression and emotional lability. Here we report two cases of Hallervorden-Spatz Syndrome with psychiatric presentation.

Keywords: Hallervorden Spatz, neuropsychiatry, psychosis



ÖZET

Erişkin başlangıçlı hallervorden-spatz sendromunun psikiyatrik yönleri: İki olgu sunumu

Hallervorden Spatz Sendromu, nadir görülen, ailesel, ilerleyici ve genellikle ölümcül seyredabilen bir hastalıktır. Extrapiramidal rijidite, dizartri ve demans bulguları ile karakterize, globus pallidus ve substantia nigrada patolojik demir birikimi ile giden bir seyri vardır. Genellikle tanı MRI incelemede bilateral globus pallidusta lokalize olan hiperintens alanların çevrelediği hipointens alanların görülmesi ile konur. Bu görünüme kaplan gözü denilmektedir ve hastalığa spesifiktir. Bu sendromda kognitif yıkımdan kişilik değişikliklerine, dürtüsellik ve şiddet davranışından depresyon ve emosyonel değişikliklere kadar çeşitli psikiyatrik belirtiler görülebilmektedir. Bu sunumda psikiyatrik belirtilerle giden iki Hallervorden Spatz Sendromu olgusunun tartışılması hedeflenmiştir.

Anahtar kelimeler: Hallervorden Spatz, nöropsikiyatri, psikoz

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INTRODUCTION

Hallervorden-Spatz Syndrome (HSS) is a rare, familial, progressive, and ultimately fatal disorder characterized by extrapyramidal rigidity, dysarthria, pyramidal tract involvement, and dementia, with pathological evidence of iron deposition in the globus pallidus and substantia nigra (1). Patients are classified as having either the classic disease (early-onset, which includes both a rapid and progressive type), or the

atypical disease (adult-onset) (2). A definite diagnosis is ascertained by the finding of iron accumulation in the affected regions in postmortem analysis (1). Psychiatric aspects of this syndrome are rare and include cognitive decline, personality changes with impulsivity and violent outbursts, depression and emotional lability (2). Here we report two cases of psychiatric symptoms with depressive and psychotic symptomatology. Especially psychosis may accompany the disorder and may even be the presenting sign in adult patients.

CASE 1

A 32-year-old married housewife was brought to the emergency unit with generalized dystonia, paranoid delusional ideation, depressive mood, irritability, hypomnesia, anxiety, significant speech disturbances, and dysphagia. The neurological examination revealed limited cooperation, bilateral extrapyramidal signs (prominent rigidity and Parkinsonian gait), and pyramidal spasticity with increased tendon reflexes. The onset of her illness had been a year before, with complaints including non-steroid anti-inflammatory drug-resistant headache, vertigo, difficulty in concentrating, and inability to sleep. Due to acute-onset psychiatric signs, such as paranoid delusions, mood disturbances, psychomotor agitation, and auditory-visual complex hallucinations, she had been admitted to a psychiatry outpatient unit and diagnosed with schizophreniform disorder three months before our examination. She was treated with zuclopenthixol decanoate (200mg every two weeks), and her psychotic symptoms partially responded to the treatment. Fifteen days after our initial examination, motor signs consisting of extrapyramidal rigidity, mutism and hypersomnia were observed. During physical examination, common rigidity and restriction in her movements were prominent. In the neurological examination, she was conscious, her cooperation and orientation was limited. Motor activity examination was not possible because of common rigidity of all extremities and marked spasticity of the upper extremities. Leakage of saliva was present, and she did not communicate verbally. No pathological sign was observed in clinical EEG results and cerebrospinal fluid examination. A brain MRI showed low signal intensity in the globus pallidus and substantia nigra bilaterally, consistent with iron deposition (Figure 1).

On the eighth day of hospitalization, she became clinically more unstable, respiratory distress developed, and low arterial O₂ pressure was detected. She was transferred to the intensive care unit. In response to the development of visual hallucinations and agitation in the patient, 100mg/day of oral quetiapine was added to the treatment of baclofen and L-dopa. The patient was

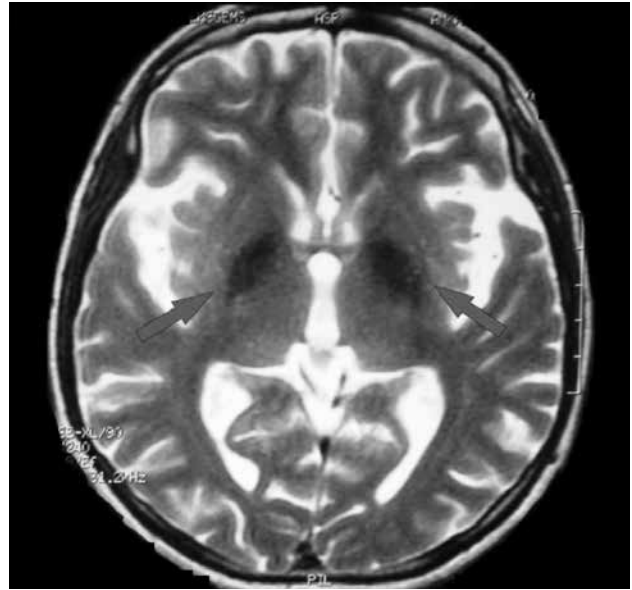


Figure 1: Low signal intensity in the globus pallidus and substantia nigra bilaterally in MRI

discharged since she did not show any improvement in the psychotic symptoms, except for the decrease in psychomotor agitation and partial improvement in spasticity and rigidity. Due to gradually increased difficulty in swallowing, her oral intake became limited and in the second month of follow-up, she was brought to the emergency unit. After being treated in intensive care for 2 days, she became unstable, respiratory dysregulation occurred, and she died.

CASE 2

A 30-year-old married man was referred with a six-year history of hypomnesia, difficulties in concentrating and sleeping, dysarthria and frequent lumbago and intermittent headache. Approximately one year later, his complaints of dysarthria and pain increased gradually, and paranoid ideation, violent behavior, cognitive deterioration, hand tremor complicated the clinical presentation. Complaints including unhappiness, hopelessness, lack of desire, crying during daytime, feeling weakness, balance disorder, and falling occurred in addition to the previous complaints which had also increased.

Initial examination of the patient revealed dysarthria,

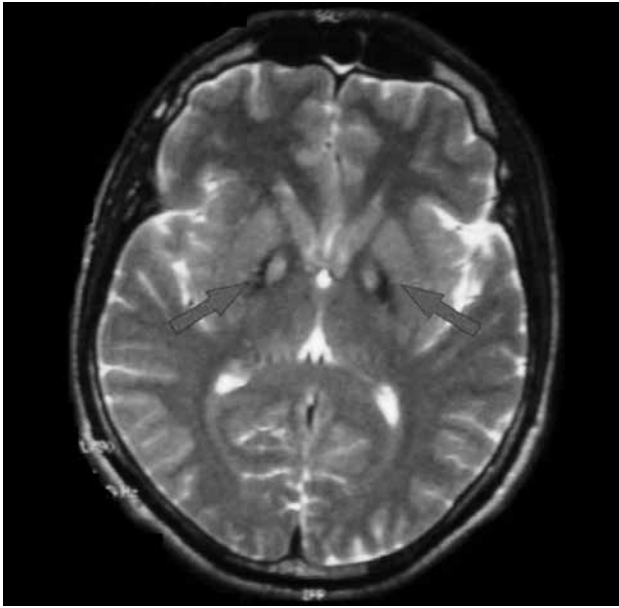


Figure 2: “Eye-of-the-tiger” appearance in the T2A slices of the cranial MRI

extrapyramidal rigidity, bradykinesia, bilaterally hyperactive deep tendon reflexes, tremor in the upper extremities, mild impairment in remote memory and attention tasks, depressive thought content, paranoid-type preoccupations secondary to depressive thought content, depressive mood, and anxious affect. His complaints of hypomnesia and loss of attention showed a gradual increase. Deep tendon reflexes were increased. Resting tremor was observed in his hands, and the cogwheel sign, which is an abnormal rigor in muscle tissue characterized by jerky movements when the muscle is passively stretched, was observed in his right upper extremity with an additional Myerson’s sign, which is a sign of frontal lobe involvement in the basal ganglia disease, repeated blinking of the eyes on tapping the forehead. His speech was dysarthric. Mild impairment was detected in attention tasks and in remote memory using the Wechsler Memory Scale – Revised form. His baseline score on the 17-item Hamilton Depression Rating Scale was 34, indicating severe depressive symptoms. No pathological sign was observed in clinical EEG results and cerebrospinal fluid examination.

In the T2A slices of the cranial MRI, symmetrical hyperintense signal changes and a surrounding

hypointense rim (“eye-of-the-tiger” appearance) were detected in the bilateral globus pallidus (Figure 2).

For his depressive symptoms, 15mg/day (night) of mirtazapine was administered. After approximately four days, the dosage was increased to 30mg/day. After all investigations for differential diagnoses were completed, the patient was discharged on the 18th day of hospitalization, with an invitation for neurological and psychiatric follow-up visits.

DISCUSSION

In this case report involving two patients, we described HSS featuring a case with psychotic symptoms and another case with depressive symptoms. Both were diagnosed with HSS by using imaging methods and progressive examination findings. The clinical phenotype generally falls into one of two categories (2). The classical disease begins with symptoms related to the extrapyramidal system, such as dystonia or dysarthria, and shows a dramatic progression resulting in death. However, atypical disease manifestation, with late onset and symptoms related to extrapyramidal systems, progresses slowly and shows a wide range of clinical heterogeneity. Due to the late age of onset, slow progression of symptoms, presence of speech disorders and psychiatric symptoms, and absence of pigmentary retinopathy in the male case; and the late age of onset, presence of speech disorders and psychiatric symptoms, and absence of pigmentary retinopathy in the female case, both of our cases are included in the atypical disease classification.

In the female case, the onset of symptoms in the third decade of life was contradictory to standard, classical diagnostic criteria. In the literature, however, age of onset for HSS has varied within a wide range, between the ages of 2 and 75 years (7,8). Although no “eye-of-the-tiger” sign was detected in the MRI findings for the female case, she met the criterion of “presence of a hypointense area in the region of basal ganglia involvement”, a supporting feature for diagnosis developed by Swaiman (9). The corticospinal involvement, the progressive intellectual deterioration, and the MRI findings all supported the diagnosis of HSS.

There was another remarkable point: Atypical subjects generally show slow progression; however, our female case showed rapid progression after the beginning of the symptoms. If we consider this fact and similar ones, maybe another, third form to be called mixed type can be described for patients where criteria of diagnosis fit the atypical form, while the clinic progression fits the classical type. In view of the fact that general clinical classification remains the best approach at this time, it seems reasonable to attempt a classification until definitive molecular markers are available (11).

The different MRI findings in the two cases can be explained by genetic factors. The etiopathogenesis of the disease has focused on a pantothenate kinase enzyme 2 (PANK2) gene mutation on chromosome 20. Hayflick et al. (3) investigated the association between the classical MRI pattern and PANK2 gene mutation in 123 patients with HSS who were selected from 98 separate families. The mutation was detected in all patients with the classical disease and one third of patients with atypical disease. The classical “eye-of-the-tiger” sign detected in all MRI data, regardless of the disease classification, was strongly associated with

a pantothenate kinase enzyme defect (3). There was no chromosome analysis data for our patients.

For the etiopathogenesis of the psychiatric symptoms, it would be helpful to investigate the features of the basal ganglia that are involved in HSS. The visual and auditory hallucinations and paranoid delusions observed in the female case could have resulted from the aforementioned disorders. Another mechanism that might explain the occurrence of psychiatric symptoms is the intellectual deterioration seen in HSS, which was observed in both cases. It might resemble the clinical presentation of subcortical dementia, in which psychotic and mood symptoms may ensue (4).

In the literature related to psychiatric symptoms in HSS, there are three case reports presenting psychotic symptoms published in 2003, 2011, and 2013, respectively (4-6).

Although a significant improvement in understanding etiopathogenesis has been achieved since HSS was first diagnosed, we have observed that comorbidity of psychiatric symptomatology is often neglected. Thus, clinicians should be careful when investigating differential diagnoses.

REFERENCES

- Hallervorden J, Spatz H. Eigenartige Erkrankung im extrapyramidalen System mit besonderer Beteiligung des Globus pallidus und der Substantia nigra. *Z Ges Neurol Psychiatr* 1922; 79:254-302. (German) [\[CrossRef\]](#)
- Hayflick SJ. Unraveling the Hallervorden-Spatz syndrome: pantothenate kinase-associated neurodegeneration is the name. *Curr Opin Pediatr* 2003; 15:572-577. [\[CrossRef\]](#)
- Hayflick SJ, Westaway SK, Levinson B, Zhou B, Johnson MA, Ching KH, Gitschier J. Genetic, clinical, and radiographic delineation of Hallervorden-Spatz syndrome. *N Engl J Med* 2003; 348:33-40. [\[CrossRef\]](#)
- Oner O, Oner P, Deda G, Icagasioglu D. Psychotic disorder in a case with Hallervorden-Spatz disease. *Acta Psychiatr Scand* 2003; 108:394-397. [\[CrossRef\]](#)
- Pawar Y, Kalra G, Sonavane S, Shah N. A case of Hallervorden-Spatz disease presenting as catatonic schizophrenia. *Indian J Psychiatry* 2013; 55:386-389. [\[CrossRef\]](#)
- del Valle-López P, Pérez-García R, Sanguino-Andrés R, González-Pablos E. Adult onset Hallervorden-Spatz disease with psychotic symptoms. *Actas Esp Psiquiatr* 2011; 39:260-262.
- Brouwer OF, Laboyrie PM, Peters AC, Vielvoye GJ. Follow-up magnetic resonance imaging in Hallervorden-Spatz disease. *Clin Neurol Neurosurg* 1992; 94(Suppl):57-60. [\[CrossRef\]](#)
- Grimes DA, Lang AE, Bergeron C. Late adult onset chorea with typical pathology of Hallervorden-Spatz syndrome. *J Neurol Neurosurg Psychiatry* 2000; 69:392-395. [\[CrossRef\]](#)
- Swaiman KF. Hallervorden-Spatz syndrome and brain iron metabolism. *Arch Neurol* 1991; 48:1285-1293. [\[CrossRef\]](#)
- Cooper GE, Rizzo M, Jones RD. Adult-onset Hallervorden-Spatz syndrome presenting as cortical dementia. *Alzheimer Dis Assoc Disord* 2000; 14:120-126. [\[CrossRef\]](#)
- Swaiman KF. Hallervorden-Spatz syndrome. *Pediatr Neurol* 2001; 25:102-108. [\[CrossRef\]](#)