CASE REPORT

Generalised dystonia: clinical diagnosis is possible

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Neurodegeneration with brain iron accumulation type 1 (previously known as Hallervorden-Spatz syndrome) is a rare neurodegenerative disorder characterised by its typical clinical and radiological features. We present a case of an adolescent girl with rapidly progressive dystonia in whom the diagnosis of the above disorder was made prior to radiological investigation. This report has been made to highlight the diagnostic relevance of a good history and clinical examination. This is particularly important in a developing country where diagnostic radiological investigations are expensive.

Introduction

We present an unusual case of generalised dystonia in an adolescent girl. Hallervorden-Spatz syndrome, now known as neurodegeneration with brain iron accumulation type 1 (NBIA type 1), is a rare cause of dystonia. It is classically seen in the first decade with associated corticospinal tract signs and pigmentary retinopathy.

Case report

A 17-year-old girl, the first child born to second-degree consanguineous parents, presented to the general medicine outpatient department in October 2007 with a 6-month history of abnormal movements of all her limbs and trunk, associated with intermittent facial grimacing. The movements were first noted in her upper limbs and gradually progressed to the rest of the body. There was no preceding history of fever, no use of any dopamine receptor blocking drugs, jaundice, psychiatric symptoms, and no motor or sensory deficits. Her siblings had no similar symptoms. She had been treated elsewhere with trihexyphenidyl hydrochloride (Pacitane) for 2 weeks but her symptoms failed to improve. On examination, she had dystonic movements of both the upper and lower limbs with tonic posturing of her wrists and fingers and features of corticospinal tract involvement. A physical examination revealed no limb weakness, sensory deficit or cognitive impairment, and a normal abdomen.

Examination of the eye did not reveal an obvious Kayser-Fleisher (KF) ring. A detailed ophthalmic evaluation showed features consistent with retinitis pigmentosa. A slit lamp examination did not detect a KF ring. We then enquired whether she had any night blindness and she confirmed that she did. It was evident that this adolescent had generalised dystonia. A literature search for reports on the combination of dystonia with retinitis pigmentosa helped us to limit our list of differential diagnoses to NBIA type 1, HARP (hypoprebetalipoproteinaemia, acanthocytosis, retinitis pigmentosa, and pallidal degeneration), and juvenile neuronal ceroid lipofuscinosis. Her clinical presentation did not fit the typical presentation of the latter two conditions, however.

Her investigations, which included those needed to rule out Wilson's disease, a lipid profile, a blood film seeking acanthocytes, and a cerebrospinal fluid analysis were all normal (Table). Magnetic resonance imaging (MRI) of the brain using gadolinium showed bilateral basal ganglia hypodensities with centrally placed areas of central hyperdensity. This sign, also known as the 'eye-of-the-tiger' appearance (Fig), is typically seen in NBIA type 1.[1]

The family was counselled about the progression and prognosis of the disease—she was given a trial of levodopa and bromocriptine but did not show significant improvement after 6 weeks. Due to financial constraints, genetic testing and further therapy could not be offered.

Discussion

Although reports of Hallervorden-Spatz syndrome (now known as NBIA type 1 or pantothenate kinase–associated neurodegeneration) are not uncommon in the literature,

Key words
Dystonia; Iron; Pantothenate kinase-associated neurodegeneration; Retinitis pigmentosa

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TABLE. Results of laboratory tests

Laboratory test*	Value
Hb	149 g/L
MCV	87.5 fL
Blood film	Normocytic, normochromic, negative for acanthocytes
Serum creatinine	79.6 μmol/L
TSH	2.8 mIU/L
Serum calcium	2.3 mmol/L
Serum phosphorous	1.2 mmol/L
Liver function tests	
Total bilirubin	6.8 μmol/L
Direct bilirubin	3.4 μmol/L
Total protein	86 g/L
Albumin	44 g/L
SGOT	31 U/L
SGPT	21 U/L
Alkaline phosphatase	55 U/L
Lipid profile	
Serum cholesterol	4.2 mmol/L
Serum TAG	0.6 mmol/L
HDL	0.9 mmol/L
LDL	2.4 mmol/L
HIV ELISA	Negative
VDRL	Non-reactive
CSF glucose	2.6 mmol/L
CSF protein	380 mg/L
CSF total counts	4 lymphocytes/ x 10^9/L
Serum ceruloplasmin	159 U/L
Serum copper	15.4 μmol/L
Urine copper	68 μg/24 hrs
ANA	Negative

* Hb denotes haemoglobin, MCV mean corpuscular volume, TSH thyroid-stimulating hormone, SGOT serum glutamic-oxaloacetic transaminase, SGPT serum glutamate pyruvate transaminase, TAG triacylglycerol, HDL high-density lipoprotein, LDL low-density lipoprotein, HIV ELISA enzyme-linked immunosorbent assay of human immunodeficiency virus, VDRL Venereal Disease Research Laboratories, CSF cerebrospinal fluid, and ANA antinuclear antibodies

this case report illustrates that a thorough clinical examination and history can ascertain the diagnosis without resorting to expensive imaging modalities. This needs to be kept in mind in a developing country where the burden of poverty is high.

Hallervorden and Spatz originally described this syndrome in a family of 12 in which five of the siblings had increasing dysarthria and progressive dementia; at autopsy brown discolouration of the globus pallidus and substantia nigra was noted.[2] This disorder has been found to be associated with a mutation in the pantothenate kinase gene (*PANK2*).[3,4]

以臨床症狀診斷全身肌張力障礙病是可行的

腦內高鐵聚合一型的神經退行性病變（過往被稱為Hallervorden-Spatz綜合徵）是一種具特殊臨床及影像學特徵的疾病。本文報告一名患有進行性肌張力障礙的年青女性，其病情迅速惡化，在未進行影像學研究前，我們已診斷病人患上此症。本報告顯示仔細研究病人的病歷及臨床資料有助診斷，這對於未能負擔昂貴影像學研究的發展中國家來說尤其重要。

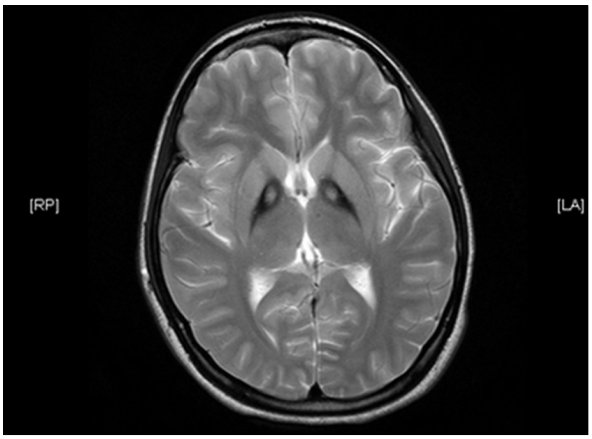

FIG. Magnetic resonance imaging of the brain with gadolinium showing bilateral basal ganglia hypodensities with central hyperdensity: the 'eye-of-the-tiger' sign

Clinically, there are three classes of NBIA type 1—'classic', 'atypical', or 'intermediate'.[5] Patients in the classic form present within the first decade of life and progress to loss of ambulation after approximately 15 years. The atypical form appears in the second decade with patients complaining of slow progression, speech and psychiatric disorders. Unlike the classic variety, they maintain functionality in their activities of daily living even after 15 years. The intermediate category comprises two groups of patients: one with early onset and slow progression, and the other with later onset and rapid progression. All patients have the 'eye-of-the-tiger' sign on MRI.[1] Our patient was classified as having the atypical form of NBIA type 1, because she was 17 years of age and her symptoms had progressed over 6 months.

While the 'eye-of-the-tiger' sign has been observed in patients with *PANK2* mutations, other disorders share similar radiological features. These include: (1) extrapyramidal parkinsonian disorders, including cortical-basal ganglionic degeneration, early-onset levodopa-responsive Parkinsonism, and Steele-Richardson-Olszewski syndrome (progressive supranuclear palsy)[6]; and (2) non-*PANK* disorders with brain iron accumulation such as neuroferritinopathy and aceruloplasminaemia.[7]

The pathogenesis of this disorder is increased amounts of brain iron, which has been shown to be associated with neurodegeneration in the presence of reactive oxygen species.[8] The other disorders of adult onset which share a similar pathogenesis include neuroferritinopathy[9] and aceruloplasminaemia.[10] These disorders can be distinguished from NBIA type 1 on the basis of the clinical presentation and the results of genetic testing.

Treatment of this condition remains directed toward managing symptoms. Systemic chelating agents such as desferrioxamine have been used in an attempt to remove excess iron from the brain, but these have not proved beneficial. Other agents that have been tried in this group of patients include a combination of levodopa and bromocriptine, anticholinergics such as trihexyphenidyl, and botulinum toxin injection into severely affected muscles. Continuous intrathecal baclofen infusion has also been tried for refractory generalised dystonia. Surgical procedures, used to manage severe dystonia, have achieved only partial relief of symptoms.[11]

This case has been highlighted to demonstrate the value of a good history and clinical examination in the diagnosis of this rare cause of dystonia.

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