Late adult onset chorea with typical pathology of Hallervorden-Spatz syndrome

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Abstract

Senile chorea is a well recognised but poorly understood clinical entity characterised by a slowly progressive, generalised chorea in elderly people without mental deterioration or a clear underlying cause. The Hallervorden-Spatz syndrome is typically thought of as a paediatric condition with extrapyramidal features and dementia. However, it has been described in adults usually presenting with parkinsonism plus dementia. An elderly woman with slowly progressive chorea without dementia was found at postmortem to have the pathological features originally described by Hallervorden and Spatz. This association has not previously been reported.

(J Neurol Neurosurg Psychiatry 2000;69:392–395)

Keywords: Hallervorden-Spatz syndrome; neurodegeneration with brain iron accumulation type 1; senile chorea

The diagnosis of Hallervorden-Spatz syndrome encompasses a considerable range of disorders, all with the core pathological features of iron deposition, axonal spheroids, and gliosis of the pallidum and substantia nigra.1 2 It has recently been reclassified as “neurodegeneration with brain iron accumulation type 1 (NBIA-1)” however, most authors continue to use the original terminology. Most cases with this pathology begin in childhood or early adolescence with extrapyramidal dysfunction and dementia, and follow a relentlessly progressive course.1 Adults onset cases have been described but typically have prominent dementia associated with parkinsonism.1 3 5 Chorea, although commonly described in paediatric cases, is not found in isolation and has not been reported in adults with the pathological features originally described by Hallervorden and Spatz. We report on a patient with the clinical diagnosis of “senile” or late adult onset chorea who was found to have this pathological diagnosis on postmortem examination.

Case report

A 76 year old woman was referred with a 1 year history of unsteady gait and unusual movements of her head and upper limbs that had been noticed by her family. Her medical history included myocardial infarction 20 years previously with mild congestive heart failure, peripheral vascular disease, and arthritis. Her medications were digoxin, furosemide, and ibuprofen. There was no known neuroleptic or toxic exposure, no history of Sydenham’s chorea or rheumatic fever, and no family history of abnormal movements.

Her initial mental status examination showed an alert, fully oriented woman with only mild difficulty in tasks of attention. Her motor examination was normal except for the mild generalised choreic movements. The rest of her neurological examination, including extraocular movements, was normal except for slight unsteadiness when walking and mild difficulty with tandem gait.

Laboratory investigations including complete blood count, blood smear, thyroid studies, liver function tests, erythrocyte sedimentation rate, ceruloplasmin, antinuclear antibodies, anticardiolipin antibodies, and rheumatoid factor were normal. Huntington’s disease molecular genetic testing for the CAG trinucleotide repeat expansion was negative (number of repeats=23 and 21). Neuropsychological testing disclosed only mild decline in cognitive functioning and was considered not to be consistent with any significant degree of dementia. Head MRI, done 2 years after the onset of her chorea, demonstrated decreased signal intensity in the putamen, caudate, substantia nigra, and dentate nuclei bilaterally (fig 1). There were also multiple small non-specific focal white matter lesions seen in the centrum semiovale and periventricular regions bilaterally. She was diagnosed as having “senile chorea” with the MRI findings thought to represent iron deposition in the basal ganglia of unknown cause.

Her chorea slowly increased in severity and 5 years after her first assessment reserpine (2 mg/day) was initiated with moderate improvement in her chorea. Two years later tetrabenazine (75 mg/day) was substituted with further benefit because of concerns that the reserpine may have been exacerbating her increasing postural instability. She required placement in a nursing home 8 years after the onset of her chorea because of the worsening postural stability and her increasing number of falls. She was last examined at this time and had moderate head rocking movements with mild
generalised chorea that increased with movement. She continued to have only minor memory difficulties. She died suddenly at the age of 85, 9 years after the onset of her chorea.

**NEUROPATHOLOGICAL FINDINGS**

Neuropathological examination was confined to the right half of the brain. External examination of the cerebral convexity showed no significant cortical atrophy but there were two small areas of subarachnoid haemorrhage in the right occipital and superior parietal areas. Coronal sections through the cerebral hemisphere showed a slight flattening of the head of the caudate nucleus. The medial segment of the globus pallidum had a cribiform appearance. The entorhinal cortex was thinner than normal and there was mild atrophy of the amygdala. A small area of cortical infarction was seen underlying the area of subarachnoid haemorrhage in the right superior parietal area. A large haemorrhage measuring $3.5 \times 4.0 \times 8.0$ cm was noted in the occipital lobe extending into the posterior temporal area. Horizontal sections through the brainstem were unremarkable with the substantia nigra and locus ceruleus well pigmented. Sagittal sections through the cerebellum were unremarkable, including the dentate nucleus. Microscopic examination showed severe neuronal loss in the globus pallidus, predominantly in the medial segment, with abundant neuroaxonal spheroids and a moderate degree of iron deposition.
Postmortem cases of late adult onset (age > 50 y) Hallervorden–Spatz syndrome

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*Limited details given and the patient's specific pathology not described but was part of large postmortem series of Hallervorden–Spatz syndrome.

Deposition (fig 2 A and B). The iron deposition was most abundant extracellularly and was often perivascular (fig 2 C). It was also noted in astrocytes and more rarely in neurons. The striatum showed a moderate degree of neuronal loss and gliosis affecting chiefly the large neurons. Iron deposition was also noted, although less abundant than in the globus pallidus and in the same pattern of distribution. Severe neuronal loss was noted in the pars reticulata of the substantia nigra with a moderate degree of iron deposition and neuroaxonal spheroids (fig 2 D). The gracilis and cuneatus nuclei showed large numbers of neuroaxonal spheroids with no significant neuronal loss or pigment deposition. Sections of neocortex showed mild patchy neuronal loss and occasional spheroids. The substantia nigra pars compacta showed no significant neuronal loss and gliosis but a rare spheroid. Mild Alzheimer type changes were present (CERAD: neurofibrillary tangles 0, neuritic plaques sparse, and mild Alzheimer pathology). The pathological findings in our patient are deposition in the globus pallidus without the “eye of the tiger” sign or pronounced low signal in the globus pallidus without the additional inserted bright signal that has now.
been well documented in patients with Hallervorden-Spatz syndrome. In fact the abnormal low signal, designating excessive iron deposition, was restricted to the striatum despite the greater extent of pallidal involvement found at necropsy. This discrepancy may in part be due to the fact that the MRI was done early in the course of her disease.

It is difficult to explain the wide variability of clinical features that have been associated with the pathology of Hallervorden-Spatz syndrome. It is highly unlikely that our patient’s findings arose from the same pathophysiological mechanisms as typical paediatric cases. Hallervorden-Spatz syndrome is an umbrella term for a heterogeneous group of neurodegenerative disorders which will become antiquated as further research improves our understanding and classification.