Stereotactic pallidotomy in a child with Hallervorden–Spatz disease

Case report

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The authors present a case of Hallervorden–Spatz disease (HSD) in a 10-year-old boy treated with stereotactic pallidotomy for control of severe dystonia. Hallervorden–Spatz disease is a rare type of neuraxonal dystrophy that can be familial or sporadic. This is the first case of HSD reported in the literature in which a pallidotomy was performed. The patient had progressively worsening dystonias and spasms that prevented useful function of his entire right side and eventually threatened his respiratory ability. Pre- and postoperative magnetic resonance images are presented along with electrophysiological recordings made in the globus pallidus at the time of surgery. Functional improvement in the use of the patient’s limbs and relief from the painful dystonia were observed. Stereotactic pallidotomy should be considered as a potential treatment in the management of HSD.

KEY WORDS • Hallervorden–Spatz disease • neuraxonal dystrophy • dystonia • pallidotomy

Hallervorden–Spatz disease (HSD) is a rare neurological condition that affects children and adolescents with predominantly motor symptoms. It eventually leads to death during adolescence, the direct causes of which are other illnesses that take hold in the immobile, emaciated patient. Gait stiffness with atrophy of distal musculature followed by upper-extremity involvement is the most common presentation. Dystonias, painful muscle spasms, risus sardonicus, hyperreflexia, and anarthria are all commonly observed. Deterioration of mental function can be difficult to assess. Familial cases have been associated with pigment changes in the retina. Diagnosis is based on clinical symptoms and course of the disease, results of magnetic resonance (MR) imaging, and exclusion of other related diseases. A definitive diagnosis can only be made at autopsy. Pharmacological therapy has been used for symptomatic control of the dystonia and other movement problems, but provides limited benefit, particularly as the disease progresses. We present the case of a child with severe dystonias resistant to pharmacological therapy, who was successfully treated surgically with a pallidotomy. Although ethical issues have been raised over the continued use of the eponym for this disease, it will be used in the interest of consistency and clarity.

Case Report

History. This 10-year-old boy was referred to our institution for possible surgical treatment of severe dystonias. The child had been adopted. His biological mother, who was 36 years old at the time of his birth, suffered from cocaine and alcohol abuse. The boy was born prematurely at 35 weeks gestation; his birth weight was 2200 g and his Apgar scores were 6 and 9, respectively. At age 6 months the patient developed increased tone in all his extremities, with the left side worse than the right, and cerebral palsy was diagnosed. The child’s developmental milestones were delayed. He began to have respiratory problems that required intubation when he was 13 months of age. By the time he was 5 years old, he had dyskinesias, myoclonus, and choreoathetosis. The diagnosis of HSD was made when the patient was 6 years of age, based on clinical signs, MR imaging studies, and a lack of significant laboratory findings suggestive of other processes. The patient was treated with a wide variety of drugs for his movement disorders and spasticity, including levodopa–carbidopa, trihexyphenidyl hydrochloride, diazepam, phenobarbital, baclofen, carbamazepine, clonazepam, and vigabatrin, with little benefit. At times sedation with chlo-
Preoperative MR images were obtained from an outside hospital including T₁-weighted (obtained both before and after infusion of contrast agent), T₂-weighted, and proton density–weighted sequences. The T₂-weighted images revealed bilateral hypointense regions in the internal segment of the globus pallidus (Fig. 1). There were also small areas of hyperintense signal just anterior and medial to these areas. No other lesions or focal areas of abnormality were seen during the remainder of the examination.

**Operation.** The patient was sedated by using a propofol drip administered by the anesthesiologist with appropriate monitoring. A stereotactic frame (CRW stereotactic system; Radionics, Inc., Burlington, MA) was applied after administration of a local anesthetic agent. The patient was transferred to a 1.5-tesla MR imager (Signa; General Electric Medical Systems, Milwaukee, WI) to obtain the localizing images. A sagittal T₁-weighted sequence was performed to identify the midline; the anterior commissure (AC), and the posterior commissure (PC). Following this, 3-mm axial T₁- and T₂-weighted MR imaging through the AC–PC line was performed. Because the patient’s symptoms were markedly worse on the right side, a left-sided lesion was planned. A target in the globus pallidus was calculated 2 mm anterior to the midcommissural point, 3 mm below the AC–PC line and 20 mm left of the midline; the target was confirmed anatomically on both T₁- and T₂-weighted images. The coordinates from the fiducial markers were entered into a computer equipped with appropriate software (Radionics, Inc.) and the target coordinates were set on the stereotactic apparatus in the operating room. The patient was transferred to the operating room and his headframe was secured to the table. Local anesthesia and a propofol drip were used throughout the procedure. A single burr hole was made just behind the coronal suture and 2 cm lateral to the midline, and the dura was coagulated and opened. A total of three passes of the recording electrode to the region of the target were made, with the last two resulting in excellent recordings of pallidal cell activity down to 2 mm inferior to the target (Fig. 2). On the tract of the last pass, a radiofrequency lesion generator (Radionics, Inc.) was used first to coagulate the area of activity and no movement was seen in the contralateral extremities. Lesions were then made at that level and also 3 mm higher along the path, with the lesion generator set at 75° for 1 minute each. A second pair of lesions was made in the tract of the next-to-last pass, which was 3 mm farther anterior. The electrode was removed, the incision closed, and the headframe removed.

**Postoperative Course.** The patient spent 1 night in the intensive care unit for monitoring, followed by 1 day in the regular neurosurgical unit prior to hospital discharge. No complications or problems were encountered during his recovery. Improvement in his right-sided dystonia was evident immediately postoperatively with no change in his left-sided symptoms. Magnetic resonance imaging of the brain, which was performed on postoperative Day 1, showed good placement of the lesion (Fig. 3). Follow-up visits in the clinic and videotapes of the child obtained at home 4 and 13 days postoperatively demonstrated functional improvement in his right arm and elimination of his
painful dystonias on the right side. He was able to open a book and turn the pages, hold objects in his right hand, and use his right arm to prop himself up into a kneeling position, none of which he had been able to do for at least 2 years. The periods of respiratory distress caused by the severe muscle contractions remitted. Six months later the patient continues to be stable in this condition.

Discussion

Originally described by Hallervorden and Spatz in 1922, little progress has been made in the diagnosis or treatment of the disease. Dooling and colleagues3 looked at a group of 42 patients previously reported in the literature who fit the original description of the disease and outlined some characteristic clinical features as follows: 1) onset of disease after early childhood; 2) “extrapyramidal” motor symptoms including dystonia, muscle rigidity, choreoathetoid movements, and evidence of corticospinal dysfunction; 3) mental changes and dementia; and 4) a progressive course of the disease over several years with death in early adulthood. Although these characteristics represent most of the cases, early infantile and young adult onset varieties also exist.

An autosomal recessive inheritance pattern is often found in patients with HSD, but it can also occur sporadically. In this case the genetic background was unknown because the child was adopted. Recently the gene for this disorder was mapped to a region on chromosome 20p12.3–p13 by using data from a large consanguineous family.13 The primary defect is unknown, but is somehow related to brain iron metabolism because the major radiological and histopathological characteristics involve abnormal iron deposition in the basal ganglia. Iron can facilitate peroxidation, leading to cell death, and may also modulate dopaminergic neurotransmission.12 Computerized tomography scanning of the brain can demonstrate either hypodense or hyperdense regions in the medial portion of the pallidum, but is otherwise usually unremarkable.7,14 The results of MR imaging studies depend on the magnetic field strength, but consistent results are seen when using a 1.5-tesla machine. On T2-weighted images the common finding in all cases is a low signal intensity lesion with sharp borders in the pallidum, often with a smaller, more anteromedial high-signal lesion.19,10 This pattern has been called the “eye-of-the-tiger” sign by Sethi, et al.11 Correlation with autopsy studies shows that the low-signal area is a region of iron deposition and that the higher-signal area has less iron and more water content.7,10 Anecdotal reports of attempted iron chelation therapy with deferoxamine for extended periods show no benefit, even when the drug proved to be present in the cerebrospinal fluid.3,12

The usual histopathological findings of HSD at autopsy include deposits of iron-containing pigment in the globus pallidus and the pars reticularis of the substantia nigra. It is present in neurons, astrocytes, and microglia and is also free in the intercellular space surrounding blood vessels. This pigment has been shown to contain neuromelanin and lipofuscin in addition to iron. Axonal swelling or “spheroids” are the second common finding and can be present not only in the globus pallidus and substantia nigra, but also in the cerebral cortex and brainstem nuclei. Occasionally Lewy bodies or neurofibrillary tangles are

Fig. 2. Microelectrode recording of a single globus pallidus internus cell firing at a rate of 91 discharges/second obtained from the target area before lesioning. Of interest is the fact that this recording was made while the patient was in a state of light anesthesia induced by propofol.

Fig. 3. Axial T2-weighted nonenhanced MR image obtained 1 day postoperatively revealing the lesion made in the left globus pallidus internus.
found.6 There is one report of liver pigmentation and pituitary hypoplasia.16

Stereotactic pallidotomy has enjoyed a recent resurgence for the treatment of parkinsonian symptoms refractory to levodopa, but this is the first reported case in the literature in which it was used to control the dystonias seen in HSD. There is a single Japanese report of bilateral ventralis lateralis thalamotomies performed in a 10-year-old girl with HSD whose clinical presentation was similar to that of our patient.15 It is interesting to note that significant improvement in that case was seen only after multiple operations. The use of microelectrode-guided posteroverentral medial pallidotomy in patients with Parkinson’s disease has resulted in significant improvement in symptoms, at least at the 6- to 24-month follow-up examination.23 Contralateral tremor, rigidity, bradykinesia, and levodopa-induced dyskinesia have all been shown to respond to pallidotomy for up to 2 years and ipsilateral improvement of dyskinesia and bradykinesia occurred temporarily. It is not known how long the beneficial aspects of a pallidotomy will last, but younger patients seem to respond more fully.5

Most patients who undergo stereotactic procedures are awake or only slightly sedated so that their movements and response to electrode stimulation can be monitored. In this case, the patient was young, dystonic, and unable to cooperate; thus, induction of light general anesthesia was necessary. Electrical activity from the pallidal cells was easily found and monitored (Fig. 2), despite the fact that the patient was in a state of anesthesia induced by propofol.

Our patient had severe spasms and dystonias that not only affected his movement, but also his ability to breathe. Pharmacological therapy was not helpful except when he was heavily sedated. For this patient a stereotactic pallidotomy allowed him to obtain a functional recovery of the use of his right arm and relieved the dystonia and pain. He continues to do well 6 months postoperatively.

References

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