Symptomatic hamartoma of the spinal cord associated with neurofibromatosis type 1

Case report

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The authors present a case in which a symptomatic hamartoma was found in the spinal cord of a patient with neurofibromatosis type 1 (NF-1). This 52-year-old woman presented with painful urinary incontinence. Magnetic resonance (MR) imaging revealed an intramedullary lesion within the lower thoracic spinal cord and conus medullaris, which was surgically removed. Pathological investigation showed a hamartomatous lesion consisting of glial cells, ganglion cells, abundant disoriented axons, and thin-walled vessels. This case provides a pathological correlate to the hamartomatous lesions demonstrated on MR imaging in patients with NF-1 and illustrates that these benign lesions may become symptomatic and require neurosurgical intervention.

KEY WORDS • neurofibromatosis type 1 • hamartoma • spinal cord

Neurofibromatosis type 1 (NF-1), also known as von Recklinghausen’s disease, is the most common of the neurocutaneous syndromes with an incidence of one in 3000 live births. Neurofibromatosis-1 has an autosomal dominant pattern of inheritance that is linked to a defect on chromosome 17, with approximately 50% of cases arising as new somatic mutations. Central nervous system lesions associated with NF-1 include optic nerve gliomas and parenchymal astrocytomas. Since the introduction of magnetic resonance (MR) imaging, incidental lesions with uncertain pathological characteristics have been a frequent finding in the brain and spinal cord of patients with NF-1. These lesions appear isointense on T1-weighted images and hyperintense on T2-weighted images and display no mass effect or contrast enhancement. They are typically asymptomatic. The proposed nature of these lesions has included low-grade tumors, heterotopias, foci of abnormal myelination, or hamartomas. We present the case of a patient with NF-1 who harbored a symptomatic, pathologically verified hamartoma of the spinal cord.

Case Report

History. This 52-year-old woman with NF-1 presented with a long history of low-back and right leg pain. The pain radiated down the posterolateral aspect of the leg into the calf and had been progressively increasing in severity. In the year before she underwent surgery, she began to experience intermittent episodes of urinary incontinence associated with sharp pain in her back and leg. She also complained of nocturia and urgency and stress incontinence that occurred when she coughed or sneezed. Her bowel function was normal and she noted no weakness or sensory abnormalities in her legs. She had no family history of neurofibromatosis.

Examination. On physical examination the patient exhibited typical features of NF-1 with multiple subcutaneous nodules and café-au-lait spots (Fig. 1). She had good range of motion in her back with no obvious deformities or local tenderness. Straight leg raising was normal at 90° bilaterally. Motor power and sensory examination yielded normal results. Her right knee deep tendon reflex was decreased and her right ankle deep tendon reflex was absent. Plantar reflexes were flexor on the left side and equivocal on the right.

Magnetic resonance imaging revealed an intramedullary mass in the thoracolumbar spinal cord and conus medullaris (Fig. 2), which appeared hyperintense on T2-weighted images (Fig. 3) and isointense on T1-weighted images (Fig. 4 left) and which displayed slight peripheral enhancement following contrast administration (Fig. 4 right).

Operation. At surgery, a laminotomy was performed from T-11 to L-1, exposing the dura in the region of the terminal spinal cord and conus. When the dura was opened, the conus appeared swollen with large surface...
veins, but no gross abnormalities. A midline myelotomy was performed and a firm reddish-colored mass was identified 2 to 3 mm below the surface of the spinal cord. The lesion had a fairly distinct interface with adjacent neural tissue around part of its circumference but was less distinct and tended to blend with the spinal cord in other regions. A conservative, subtotal removal was undertaken and the excised tissue was sent to the laboratory for pathological examination. Somatosensory evoked potentials were monitored intraoperatively and showed no changes during the operative procedure.

Pathological Findings. The pathological specimen consisted of several small fragments of soft, reddish tissue measuring approximately $4 \times 5$ mm in aggregate. Microscopic examination revealed numerous thin-walled vessels forming a network (Fig. 5). Interdigitated with the vascular network were disoriented axonal profiles, ganglion cells (Fig. 6 upper), and glial processes (Fig. 7). One binucleate ganglion cell was identified. None of the ganglion cells displayed neoplastic or anaplastic elements, thus excluding the diagnosis of ganglioglioma. No mitoses were identified. Immunostaining for Ki-67, a marker of mitotic activity, provided negative results, except for a rare intravascular or perivascular (reactive) nonneuronal cell. The densely positive Bielschowsky’s stains (Fig. 6 lower) almost certainly colored many unidentified nonaxonal profiles as well as axons. Immunostains for neurofilaments were less densely positive and correlated poorly with the Bielschowsky’s stain–positive profiles. Luxol fast-blue stains revealed occasional thinly myelinated processes. Electron microscopic examination confirmed the presence of occasional aberrant myelinated axonal profiles (Fig. 8 upper) as well as glial processes and occasional processes with dense-core vesicles (Fig. 8 lower),
supporting the presence of a differentiated ganglion cell component. In summary, the features of this lesion were malformative rather than neoplastic, being most consistent with a vascular and glioneural hamartoma.

**Postoperative Course.** In the immediate postoperative period, the patient’s bladder function worsened and she required intermittent catheterization. She experienced severe leg spasms, which improved in response to a course of baclofen. By the 3rd postoperative day, she was voiding spontaneously, and she was discharged home on the 6th day after surgery. At the 6-week follow-up examination, the patient’s bladder function had returned to normal and her back and leg pain were greatly improved. At the 2-year follow-up review, the patient’s neurological function remained stable. She had no leg pain and her bladder function was normal. The patient had returned to her full-time employment without limitation. Magnetic resonance imaging performed 3 months, 1 year, and 2 years after surgery demonstrated no changes in the size or signal characteristics of the residual mass.

**Discussion**

Lesions of the brain and spinal cord are frequently identified by using MR imaging in patients with NF-1.\(^6,10,11\) These lesions are typically asymptomatic and their pathological substrate remains obscure. In the brain, foci of increased signal intensity on T2-weighted MR images are frequently demonstrated in the cerebellum, pons, midbrain, internal capsule, and basal ganglia, with a reported prevalence of 53%\(^6\) and 79%\(^10\) in patients with NF-1. In our patient, T2-weighted MR imaging of the brain revealed two small symmetrical foci as hyperintense areas in the anterior midbrain; these are probably hamartomatous lesions. The MR studies that have been performed to define the natural history of these lesions suggest that the lesions are benign and tend to decrease in size or resolve with the advancing age of the patient, being rarely seen in individuals older than 20 years of age.\(^1,10\) Pathological specimens have rarely been examined because these lesions are asymptomatic. Zimmerman and colleagues\(^11\) have reported on the features of five lesions that were identified by MR imaging and obtained from two patients at autopsy. These lesions consisted of atypical glial infiltrates with bizarre hyperchromatic nuclei, foci of microcalcification associated with perivascular gliosis, and spongy changes in adjacent white matter. The authors have suggested that the lesions were malformative rather than neoplastic in nature.

Magnetic resonance imaging of the spinal cord in patients with NF-1 has demonstrated lesions similar to those found in the brain, which are hyperintense on T2-weighted images with no mass effect and no contrast
These lesions are typically asymptomatic and are also thought to represent glial hamartomas. Authors of previous reports have suggested that the hamartomas associated with NF-1 consist primarily of neural crest–derived neurons, glial cells, and Schwann cells in addition to fibroblasts, vascular endothelial cells, and mast cells, resulting in atypical glial cell nests, subependymal glial nodules, and ependymal ectopias. Rubinstein has provided the most comprehensive pathological study of central nervous system lesions in patients with NF-1. The spectrum of lesions found at autopsy includes subependymal gliofibrillary nodules along the ventricular system and aqueduct, hyperplastic meningoencephalic gliosis in the pons and cerebellum, and micronodular foci of capillary and endothelial proliferation. He suggested that the distinction from low-grade neoplasms was difficult in some situations but concluded that some of these abnormal foci of glial proliferation were probably hamartomas and that the range of tissue involved was not derived solely from the neural crest. There have been no pathological reports of hamartomatous lesions obtained from the spinal cord in patients with NF-1.

Conclusions

In the present case, the lesion produced symptoms consisting of back and leg pain that the patient had experienced for several years. In the year before she underwent surgery, the patient began to experience urinary inconti-
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ence associated with a sharp pain in the back and legs. Magnetic resonance imaging revealed an intramedullary lesion in the lower spinal cord and conus medullaris, which appeared isointense on T1-weighted images and hyperintense on T2-weighted images and which demonstrated a small peripheral rim of contrast enhancement. This lesion was believed to represent a low-grade neoplasm and was incompletely resected. Pathological examination of the surgical specimen revealed a hamartomatous lesion composed of ganglion cells, glial cells, abundant disoriented axons, and thin-walled vessels. To our knowledge, this case represents the first pathological description of a symptomatic hamartoma of the spinal cord in a patient with NF-1.

References

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