Intramedullary neuroma of the cervicomedullary junction

Case report

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Following transection of a nerve in the PNS, proximal axons sprout in an attempt to reinnervate the distal nerve segment. When this process fails, a traumatic neuroma can form, becoming symptomatic as a painful nodule at varying intervals following the injury. When neuromas have also been described as intramedullary spinal cord lesions. These lesions have been identified as incidental autopsy findings in association with prior trauma and cervical spondylosis, multiple sclerosis, spinal tumors, and syringomyelia.

The authors report the case of a 50-year-old man who had been involved in a motor vehicle accident, during which his car was struck from behind as it was stationary at an intersection, more than 5 years before presentation. A workup for syncopal and presyncopal episodes involved magnetic resonance imaging that revealed a 1.1-cm lesion at the cervicomedullary junction (CMJ). The imaging features of the lesion raised the question of an ependymoma or subependymoma. The lesion was excised, and examination of the tissue demonstrated a neuroma with haphazardly arranged interlacing bundles of axons ensheathed by Schwann cells with interfascicular regions of reactive glial cells and Rosenthal fibers, consistent with those present after traumatic injury. This case may represent the first true traumatic intramedullary neuroma of the CMJ diagnosed in a living patient and treated surgically.

KEY WORDS • neuroma • cervicomedullary junction • trauma

Abbreviations used in this paper: CMJ = cervicomedullary junction; CNS = central nervous system; MR = magnetic resonance; MVA = motor vehicle accident; PNS = peripheral nervous system.

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intense to the medulla on T₁- and T₂-weighted MR images and was associated with a very small amount of surrounding T₂ prolongation suggestive of vasogenic edema or gliosis (Fig. 1A and B). The lesion appeared to be intramedullary, extending from the region of the central canal to the posterior pial surface of the cord where it produced a pronounced smooth posterior protrusion of the pial surface with obtuse margins (Fig. 1C and D). The possibility of an ependymoma or subependymoma was considered most likely. The patient’s symptoms were attributed to possible disruption or compression of brainstem circuits that mediate postural or baroreceptor reflexes, leading to sudden dysfunction of truncal and leg muscle tone. Resection of the lesion was the chosen therapy.

**Operation.** Intraoperatively the lesion appeared to be an exophytic mass resulting in lateral displacement of the fasciculus gracilis. The mass had a firm consistency distinct from the surrounding spinal cord. Gross-total removal of the lesion was performed circumferentially with an excellent plane of resection. There was slight diminished amplitude in the evoked potentials during the procedure, but both sides were ultimately spared in their waveform throughout the course of the operation.

**Histological Findings.** The use of tissue specimens was performed in accordance with our institutional review board policies. Histological evaluation of the lesion revealed a proliferation of interlacing large and small bundles of spindle cells with elongated nuclei consistent with Schwann cells. These fascicles were surrounded by diffuse foci of dense gliosis with abundant Rosenthal fibers (Fig. 2A and B). Within the fascicles was a striking axonal component that was readily revealed by immunostaining for neurofilament protein (Fig. 2C). The Schwann cells were highlighted by an immunostain for S100 protein (Fig. 2D). In some regions a dense population of axons was located concentrically around centrally located blood vessels. The close association of Schwann cells and axons in a pattern resembling peripheral nerve fascicles supported the diagnosis of a Schwann cell/axonal proliferation most consistent with a traumatic neuroma.

**Postoperative Course.** Following surgery, mild left-sided hypesthesia developed that gradually improved over time. In June 2005 postoperative MR imaging demonstrated minimal upper cervical spinal cord deformity at the CMJ, with minimal enhancement, probably representing postoperative granulation tissue. In September 2005 the patient presented again with symptoms similar to those present preoperatively. Repeated MR imaging has demonstrated no evidence of lesion recurrence.

**Discussion**

Neuromas are commonly encountered nonneoplastic proliferations of axons and Schwann cells resulting from transection of peripheral nerves that are located superficially or at visceral sites. Within the CNS, similar lesions are exceedingly rare and have been identified as both extramedullary lesions developing at cervical nerve roots and intramedullary lesions occurring within the brainstem and the spinal cord. Intramedullary neuromas have been described in several small case series; all were identified as incidental autopsy findings. To our knowledge, no intramedullary neuroma of the CMJ has been identified following resection in a living patient.
Clinical Presentation

Our patient experienced presyncopal and syncopal episodes of unclear origin. The imaging discovery of a 1.1-cm mass at the CMJ raised the possibility that this lesion was the cause of the patient’s symptoms. In retrospect, the mass may have been incidental because the patient has since presented with syncope in conjunction with bradycardia 9 months following the resection. The continued symptoms, however, have probably resulted from residual damage and gliosis within medullary circuits mediating the postural and baroreceptor reflexes, including the posteriorly located nucleus of the solitary tract. The lesion appears to have spared rostral regions of the lateral reticular formation of the medulla, the putative site of the human respiratory rhythm generator (that is, the pre-Botzinger complex). In addition, although the patient recalled that his episodes were associated with loss of consciousness, they may have actually represented drop attacks. These events can be due to sudden increases in pressure that compress the anterior brainstem and the basilar artery, ultimately leading to brainstem ischemia and loss of lower-extremity and truncal muscle tone.

The intramedullary neuromas described in the literature are associated with a history of traumatic injury, compression, or other brainstem and spinal cord lesions. In our case, one possible cause could be the MVA that occurred 5 years prior to the discovery of the CMJ mass. At the time of the MVA, the patient complained of bilateral neck and shoulder pain that radiated from the bottom of his neck to the back of his head, and muscle strain and spasm were diagnosed. Because imaging was not performed at that time, it is not possible to state definitively the time course or origin of the formation of this lesion. The history of trauma and the size of the lesion are consistent with other such reported posttraumatic lesions. Cases of similar smaller lesions have been described in the absence of known trauma, and hence it cannot be entirely excluded that this lesion preceded the MVA or was unrelated in cause.

Fig. 2. Photomicrographs showing paraffin-embedded sections of tissue obtained from the CMJ tumor. A and B: Disorganized fascicular proliferation of Schwann cells and axons with extensive reactive changes including abundant Rosenthal fibers. The close association of axons and Schwann cells, as well as the reactive changes, is consistent with the diagnosis of a neuroma. H & E. C: Immunostaining for neurofilament protein highlighting the haphazardly arranged fascicles of axons. D: Schwann cells adopting a vague plexiform pattern are strongly positive for S100 protein. Original magnifications × 100 (A and D), 400 (B), and 200 (C).
Cervicomedullary junction neuroma

Imaging Features

Gadolinium-enhanced MR imaging is the study of choice for evaluating intramedullary tumors because it clearly delineates the extent of the lesion and tumor margins and it can demonstrate associated peritumoral edema, syringohydromyelia, or additional lesions. Computed tomography may be useful for detecting calcification or osseous remodeling associated with lesions that extend into the neural foramina, which may favor the diagnosis of schwannoma. Although it is the preferred modality for evaluating intramedullary tumors, MR imaging is rarely diagnostic and a broad differential diagnosis must be considered. The general differential diagnosis of an enhancing intramedullary mass at the CMJ includes astrocytoma, ependymoma, hemangioblastoma, metastasis, and, less commonly, schwannoma and subependymoma. In the present case, the clinical history, extension of the lesion from the posterior aspect of the central canal, lesion shape, enhancement, and signal characteristics were thought to favor ependymoma or subependymoma.

Histological Features

The histologically based differential diagnosis for this lesion would include schwannoma because of the abundant Schwann cell component of this lesion. Although also exceedingly rare, intramedullary schwannomas have been described. These CNS tumors, like their PNS counterparts, display the classic pattern of variability in cellularity between densely cellular Antoni A and loosely cellular Antoni B regions. Notably, schwannomas are commonly devoid of axons although some can exhibit a few sparse axonal fibers. In our case, in contrast, we observed a diffuse and abundant component of axons, which were ensheathed by Schwann cells. This Schwann cell/axonal proliferation was arranged haphazardly in bundles and microfascicles, as are classically seen in PNS neoplasms. In addition, the regional variability seen in schwannomas was not present. Overall, these features supported the interpretation of the lesion as a neuroma rather than as a Schwann cell neoplasm.

Origin of CNS Neuromas

A complete discussion of the origin of these CNS lesions occurred at a 1964 annual meeting of the American Association of Neuropathologists, in which seven neuropathologists commented on their findings in reviewing 37 intramedullary neuromas of the spinal cord and brainstem, all identified at autopsy examination. This lesion was considered a regenerative phenomenon characterized by the sprouting of collateral structures from perivascular rootlets of both anterior and posterior nerve roots in response to an adjacent intraxial lesion such as a traumatic cyst, inflammation, or a neoplasm. In cases with no history of trauma, some authors have considered the possibility of errant axonal migration during embryogenesis, and this has been supported by the observation of aberrant peripheral nerve fibers in otherwise normal medullas and spinal cords. Moreover, it has been suggested that intramedullary neuromas may result from regenerative outgrowth of severed CNS axons as well as ingrowth of peripheral nerves. Support for the CNS and PNS origins of sprouting axons has come from experimental models of axonal injury in adult rats in which significant, albeit limited, amounts of axonal regenerative sprouting have been demonstrated following spinal cord injury due to transection, contusion, compression injuries, and ischemic injuries. These findings point to an inherent capacity of the CNS to repair itself and suggest important avenues of pathological and therapeutic investigation.

Conclusions

Neuromas are exceedingly rare lesions of the brainstem and spinal cord. With the increasing use of neuroimaging techniques in the evaluation of patients with neurological symptoms such lesions will be better recognized. The appropriate treatment of patients with intramedullary brainstem and spinal cord lesions and a history of traumatic injury will require the prudent integration of clinical and imaging data.

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