Atypical Ganglion Cell Tumor of the Sciatic Nerve

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Context: Although herniation of a lumbosacral intervertebral disk is a major cause of sciatic distribution pain, relentlessly progressive symptoms or signs should alert one to the possibility of a tumor involving the nerve.

Objective: To describe the clinical, neurophysiological, and histological features of a pathologically unique tumor involving the sciatic nerve.

Setting: Tertiary referral university hospital.

Patient: A 36-year-old woman was seen with a 6-year history of increasingly severe symptoms in the distribution of the left sciatic nerve.

Results: Electromyography indicated a sciatic nerve lesion in the region of the greater sciatic notch. Magnetic resonance imaging demonstrated a tumor involving the left sciatic nerve in this area. Light microscopy, electron microscopy, and immunohistochemistry results confirmed the presence of an atypical ganglion cell tumor of the sciatic nerve that exhibited prognostically conflicting clinical and histological features.

Conclusions: To our knowledge, this is the first report of an atypical ganglion cell tumor affecting the sciatic nerve, and illustrates the value of detailed neurophysiological examination in localizing the site of peripheral nerve injury to facilitate focused neuroimaging when standard investigations are uninformative. Longer follow-up is required to determine the true biologic potential of this lesion.

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HERNIATION OF a lumbosacral intervertebral disk is a major cause of chronic or recurrent low back and sciatic distribution leg pain. Less common diagnoses should be considered when the clinical presentation is atypical. Cyclical sciatica, that varies in intensity in a catamenial pattern, can be caused by endometriosis affecting the nerve, whereas relentlessly progressive symptoms or signs in the affected limb should alert one to the possibility of a tumor or an arteriovenous malformation involving the sciatic nerve.

OBSERVATION

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REPORT OF A CASE

A 36-year-old woman had a 6-year history of increasingly severe left leg pain. She had initially reported intermittent aching pain in the left posterior thigh after waking. After a 2-year period, the pain radiated from the left buttock down the posterior aspect of the left leg to the ankle during the first 5 days of the patient’s menstrual cycle. Subsequently, she also experienced less severe symptoms during the remainder of the menstrual cycle. Four years after the onset of symptoms, the patient developed numbness and hyperesthesia over the left outer calf and foot, with intermittent shooting pains radiating from the sole of the foot to the left calf and thigh. The pain was exacerbated by prolonged sitting or exercise, unchanged by coughing or sneezing, and there was mild intermittent foot drop when the symptoms intensified. Laparoscopy around that time revealed a retroverted uterus, but no evidence of endometriosis.

The clinical features persisted until 2 months prior to presentation when the patient became pregnant. Her symptoms improved between the sixth and eighth week of gestation, but then, she developed a constant, severe, throbbing pain affecting the left buttock, calf, and foot, necessitating inpatient care and opiate analgesia. There was progressive wasting of the left glutal and calf muscles over the next 2 months, and by 20 weeks’ gestation, the patient walked with a complete left foot drop, avoiding all contact of the left foot with the ground. Clinical examination of the left lower limb revealed marked muscle wasting of the glutei, left tibialis anterior and gastrocnemius muscles, decreased muscle tone, and severe weakness of ankle and toe dorsiflexion and plantarflexion. The knee jerk was brisk but the ankle jerk was reduced. The left plantar response was not assessed because of hyperpathia, but the right plantar response was flexor. There was altered soft touch, pin prick, and temperature sensation, with allodynia and hyperpathia over the left L5 and S1 dermatomes. The remainder of the neurological examination was normal.

Pointense soft tissue mass at the greater sciatic notch, enveloping the proximal left sciatic nerve, and associated with gluteal muscle wasting; the lesion enhanced with gadolinium Gd 64 (Figure 1). A second series of magnetic resonance imaging scans 3 weeks later showed enlargement of the mass; therefore, a percutaneous needle biopsy under ultrasound guidance was performed. This showed a focally necrotic tumor of indeterminate origin and the patient proceeded to have an open diagnostic biopsy via a posterior approach. The roots of the sciatic nerve exited the greater sciatic notch in 4 separate bundles, emerging through the substance of the piriformis muscle before joining to form the sciatic nerve proper, 1 cm distal to the greater sciatic notch. The proximal 10 cm of the sciatic nerve proper was indurated, red-purple, and approximately 2 cm in diameter. The posterior femoral cutaneous nerve and the portion of the piriformis muscle in proximity to the sciatic nerve were also firm and thickened. The sciatic nerve was decompressed at the sciatic notch and multiple biopsy specimens were obtained.

Light microscopic examination revealed nodules of atypical ganglion cells in a background infiltrate of mononuclear round and spindle cells; Schwann cells were not seen (Figure 2A). The tumor cells had moderately pleomorphic nuclei, prominent nucleoli, and abundant acidophilic cytoplasm with extensive vacuolar alteration. Mitotic figures were not present, but focal areas of necrosis, perineural infiltration, and muscle invasion were identified. Results of immunocytochemistry studies showed that the tumor cells were positive for neuronal markers such as PGP 9.5, chromogranin, synaptophysin, and neuron-specific enolase. Glial (glial fibrillary acid protein), epithelial (CAM 5.2, AE 1, AE 3), melanoma (HMB 45), and smooth muscle (smooth muscle actin, desmin) markers were negative. In addition, staining for progesterone receptors was positive, but estrogen receptor positivity was not identified. Electron microscopy confirmed that the tumor was of ganglion cell origin (Figure 2B).

On the basis of these findings, a diagnosis of an atypical ganglion cell tumor of the proximal portion of the sciatic nerve was made. Six weeks postoperatively, the severity of the patient’s pain had decreased, the numbness over the lateral foot and toes improved, but the clinical features were otherwise unchanged. The patient subsequently was delivered of a normal healthy infant. Three years postoperatively, she was ambulatory with no evidence of disease progression but declined further investigations.

This patient had an unusual clinical history of sciatic distribution pain secondary to a histologically unique tumor involving the proximal sciatic nerve. The case emphasises the value of detailed neurophysiological examination in localizing the site(s) of peripheral nerve injury, to facilitate focused neuroimaging when standard investigations are uninformative. It also demonstrates the importance of considering rarer causes of sciatica, especially tumors involving the nerve, when the clinical history is atypical. Tumors with a neoplastic ganglion cell
component include gangliocytomas and gangliogliomas in the central nervous system, and ganglioneuromas in the peripheral nervous system, although the latter occasionally occur within the central nervous system.10 Gangliocytomas are rare tumors composed of neoplastic neurons with a ganglion cell phenotype in a background stroma of nonneoplastic astrocytes, whereas gangliogliomas contain an admixture of both atypical ganglion cells and neoplastic glia. Ganglioneuromas are characterized by atypical ganglion cells interspersed among sheaths of Schwann cells and a variable collagenous stroma that does not contain glial cells. This lesion is histologically unique in that it does not fulfill the diagnostic criteria for any of the typical ganglion cell tumors because glial cells and Schwann cells were absent,10 it was highly cellular, and there was an infiltrative growth pattern with areas of necrosis. The location of the tumor is also unusual. In a clinicopathologic study of 35 neurogenic tumors of the sciatic nerve, 21 (60%) were classified as neurofibrosarcomas, 7 (20%) as schwannomas, and 7 (20%) as neurofibromas, but no ganglion cell tumors were identified.4 Although it is uncertain whether the ganglion cells are of autonomic or dorsal root origin, one would not expect to find ganglion cells at this point along the course of the sciatic nerve. We postulate that the delayed union of the component roots of the sciatic nerve distal to the greater sciatic notch raises the possibility of a neuronal migration abnormality that could account for their peripheral location in this case. The initial catamenial variation in symptom intensity and subsequent enlargement of the tumor in pregnancy suggests a degree of hormonal sensitivity, and staining for progesterone receptors was positive. The role of progesterone in the patient’s catamenial symptom variability is unclear, because one would have predicted more pronounced symptoms during the second half of the menstrual cycle when progesterone levels are higher. However, the dramatic increase in symptoms during pregnancy may have been secondary to increased tumor vascularity associated with the vasodilatory effects of rising levels of progesterone.

The prognosis in this case is unknown. From a histological viewpoint, the lack of mitotic activity is reassuring, but the infiltrative growth pattern with multiple microscopic areas of necrosis may worsen the prognosis. Although the prolonged duration of symptoms for 6 years prior to presentation and the favorable clinical course following surgery suggest a benign clinical lesion, there was a dramatic clinical and radiological deterioration over a 3-week period during pregnancy. Longer follow-up is required to determine the true biologic potential of this lesion.

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