Malignant Peripheral Nerve Sheath Tumor of the Lumbar Spine

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Malignant peripheral nerve sheath tumors (MPNSTs) are rare in children. MPNSTs arise from peripheral nerves or show differentiation of nerve sheath elements, including Schwann cells, fibroblasts, and perineural cells. The term *malignant peripheral nerve sheath tumor* has replaced older terms, such as *malignant schwannoma, neurofibrosarcoma,* and *neurogenic sarcoma*. Incidence of MPNST ranges from 2% to 13%.[1] MPNSTs account for approximately 5% to 10% of all soft-tissue sarcomas.

Depending on its location and amount of nerve involvement, MPNST can present as a painful or painless mass. MPNSTs that arise from major nerves can cause sensory and motor symptoms, such as pain, paresthesia, and weakness. Most arise in association with major nerve trunks, such as the brachial or sacral plexus or sciatic nerve. Approximately 50% arise in the trunk, 30% in extremities, and 20% in the head and neck.[2] Compared with patients who do not have neurofibromastosis type 1 (NF-1), patients with NF-1 have a central distribution of primary tumors.[3] An association between MPNST and NF-1 has been well documented.[1-20] Patients with NF-1 and MPNST tend to be younger (28.7 years) than patients who have MPNST without NF-1 (39.7 years).[4] Prior radiation therapy has also been well documented as an important risk factor in development of MPNST.[3,7,8,16,18] Wong and colleagues[7] reported that, in 10% of their patients, radiation given for prior unspecified tumors induced MPNST.

MPNSTs often are difficult to diagnose and behave aggressively. Treatment includes wide surgical resection. Adjuvant therapy is advocated by some authors, though the results are mixed. Tumor size, patient age, tumor necrosis, and presence of neurofibromatosis can negatively affect survival. Despite appropriate treatment, recurrence is high and prognosis poor.

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We describe the case of a lumbar-spine MPNST that presented as chronic knee pain in a boy. The patient had many of the typical signs and symptoms of an intraspinal tumor, which facilitated appropriate diagnosis and treatment. Such signs and symptoms should be sought in children who present with neurogenic pain.

Case Report

A 6-year-old boy was brought in for a third opinion and evaluation of left knee pain. He complained of constant left posterior knee pain that often awoke him from sleep and caused him to cry in pain. The pain was not ameliorated with medication or local measures such as massage. The history revealed intermittent left buttock pain in addition to the left knee pain. In addition, the patient's mother reported that for months he would not bend over to tie his shoes or touch his toes, and his physical activity was now severely limited secondary to pain. On further detailed questioning, the mother reported a few recent instances of his having difficulty initiating urination. There were no other constitutional symptoms, such as weight changes, fevers, or night sweats.

> " 'Red flags' include severe pain, night pain, neurologic signs and symptoms, and pain that lasts more than 4 weeks.[21]"

The patient's medical and surgical histories were unremarkable. Family history was unremarkable. The patient had no allergies and was not taking any medications. He had reached normal developmental milestones, his immunizations were up-to-date, and he lived at home with both parents. Systems review was noncontributory, except those findings stated in the history of present illness. On physical examination, the patient was alert and oriented, in no acute distress, and cooperative. There were no gait abnormalities evident. On the Adams forward bending test, the patient had 20° of spine flexion, and his torso listed to the right. There was no tenderness to palpation of the spine, and no masses were felt. The Adams forward bending test showed no gross rotational deformity. Popliteal angles were 50° and 60° on the right and left, respectively. At the knee and ankle, there was hyporeflexia on the left compared with the right. Strength was decreased 4/5 on the left compared with

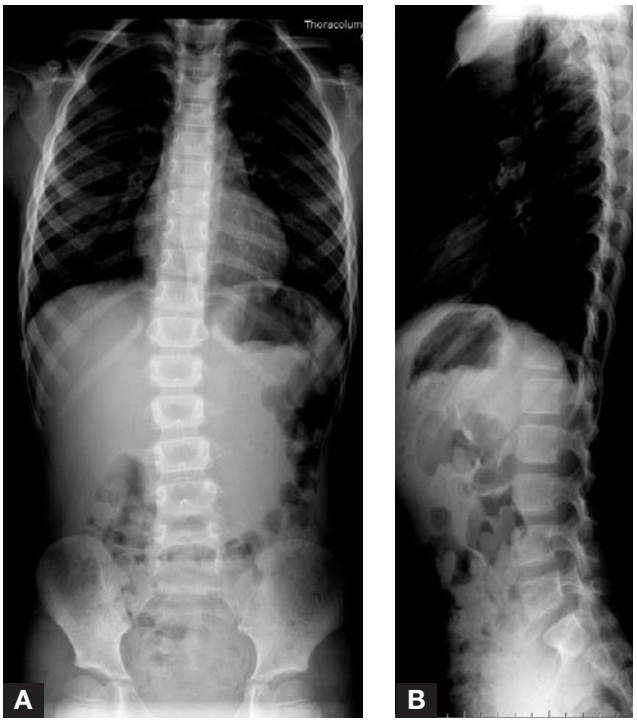

Figure 1. Anteroposterior (A) and lateral (B) radiographs of the spine.

the right lower extremities. Calf circumference measured 10 cm proximal to the medial malleoli was 22.5 cm on the right and 22.0 cm on the left. There were no evident sensory deficits and no clonus or Babinski sign. Umbilical reflexes were equal and symmetric.

The earlier radiographs and MRI scan of the left knee obtained in consultations with other physicians in the preceding 6 months were reviewed. There was no evidence of fracture, meniscal tear, or ligamentous injury. The whole-body bone scan did not demonstrate any focal abnormalities in tracer uptake, though lumbar scoliosis was evident. Given the abnormal findings on physical examination and the bone scan, spine radiographs were obtained. These radiographs showed a 13° right thoracolumbar curve without rotation or bony lesions (Figures 1A, 1B). An urgently obtained MRI scan showed a lumbar mass in the spinal canal extending out to the neural foramina (Figures 2A–2C). The patient was expeditiously referred for neurosurgical consultation.

Later that week, the patient underwent an L2–L5 laminectomy and intradural tumor removal. Histologic specimen revealed MPNST. The patient underwent chemotherapy. Since then, he has shown no evidence of residual disease or metastatic spread and now is on his fourth cycle of chemotherapy.

Discussion

The earliest symptom of a spinal cord tumor may be limb pain, leading to presentation at an orthopedist's office. Recognition of certain signs and symptoms may facilitate rapid diagnosis. By the time our patient was brought to us, he had already been seen by 2 other orthopedists. "Red

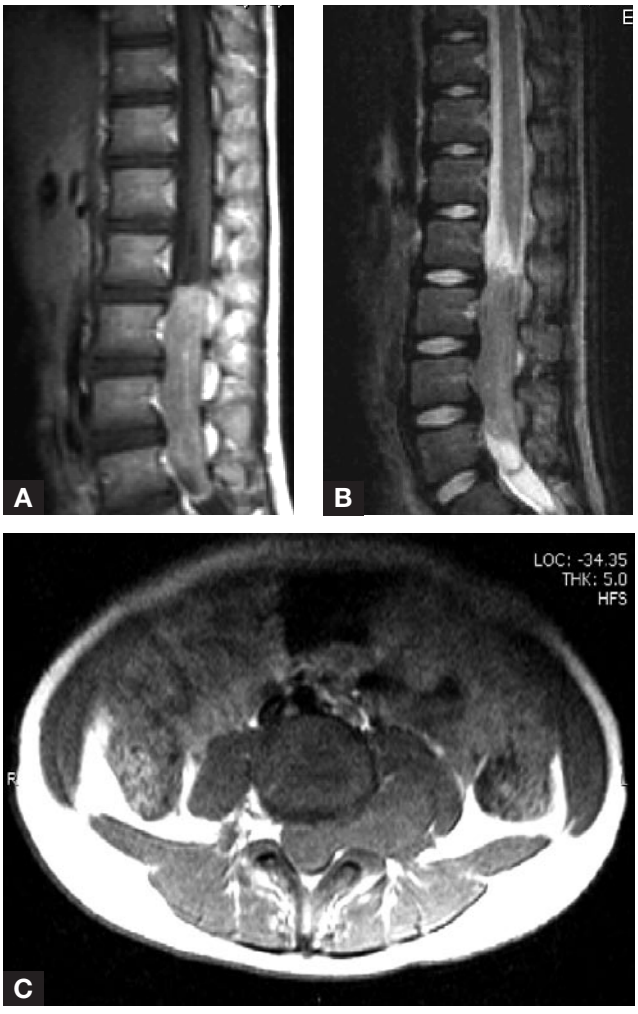

Figure 2. Magnetic resonance imaging of the spine: (A) T_1-weighted, (B) T_2-weighted sagittal, (C) T_1-weighted axial.

flags" include severe pain, night pain, neurologic signs and symptoms, and pain that lasts more than 4 weeks.[21] At time of presentation, our patient had many of the classic signs and symptoms of a spinal cord tumor: back stiffness, scoliosis without rotation, listing to the side during the Adams forward bending test, bladder symptoms, severe night pain, referred pain, hamstring tightness, weakness, and asymmetric deep tendon reflexes. Weakness, asymmetric reflexes, and night pain can often be effort-dependent and misrepresented in the adult population; however, in the pediatric population, they should be considered hallmarks of an organic disease process until proved otherwise. A thorough history and a complete physical examination are always recommended.

Careful questioning of parents and family members can help in identifying important facts, including bowel or bladder symptoms. In a well-trained child, development of incontinence, urgency, dribbling, or enuresis should raise suspicion. A child who complains of recurrent pain in a single location should be taken seriously and examined closely, as such pain is usually significant.[22] On physical examination, spine range of motion should be checked. According to Tachdjian and Matson,[22] musculoskeletal

deformity (including torticollis, scoliosis, and kyphosis) is often the first abnormality noted in patients with spinal tumors. Twenty-seven percent of their patients had scoliosis on presentation.[22] Range of motion is often diminished by space-occupying lesions in the spinal canal. In addition, deviation to the side on forward bending is highly suggestive of an intraspinal lesion. With idiopathic scoliosis, rotation is usually evident either on physical examination or radiographs. Our patient had a right thoracic curve without rotation, further leading to suspicion of spinal pathology. Hamstring tightness is commonly present in children with nerve compression in the lumbar spine. Weakness, sensory deficits, and reflex asymmetry are common as well. Motor weakness may be the commonest finding pointing to a spinal tumor.[22] In a young child, weakness may manifest as a limp or an inability to engage in action such as running or climbing.[22] Deep tendon reflexes are an important part of the neurologic examination, as their elicitation does not depend on cooperation and can easily be repeated.[22] Muscle atrophy, with resultant asymmetry in extremity diameter, may be seen in long-standing cases. Gait disturbances may also result from extremity weakness or pain.

In a review of 54 patients with MPNST, Baehring and colleagues[8] found that the most frequent initial symptom or sign was a painless mass. Meis and colleagues[13] found that 43 of 78 patients presented with a mass, followed by pain, and sensory or motor disturbances secondary to nerve compression (including weakness, muscle atrophy, spasticity, paraparesis, or radicular pain). Gnanalingham and colleagues[20] reported the case of a 59-year-old patient who presented with a 2-year history of midthoracic back pain radiating down both legs and who eventually was diagnosed with an intraosseous thoracic lesion causing cord compression. D'Silva and colleagues[19] reported on a patient who presented with persistent abdominal and back pain and who eventually was diagnosed with a psoas major muscle tumor.

Delay in diagnosis of this soft-tissue tumor is common. Patients with intraspinal tumors can have erroneous initial diagnoses, including poliomyelitis, spina bifida, appendicitis, cerebral palsy, muscular dystrophy, and Guillain-Barré syndrome.[22] Baehring and colleagues[8] found that median time from symptom onset to diagnosis was 5.5 months. Six of 17 cases were misdiagnosed as rotator cuff injury, disc herniation, or carpal tunnel syndrome. Lesions that affect the proximal parts of the peripheral nervous system can make it a more difficult diagnosis.

Radiographic imaging and electrophysiologic studies are helpful in the workup of MPNST cases, though findings do not allow differentiation from other tumors. As a result, a tissue diagnosis is necessary.

In the classic form of the tumor, the gross pathology shows distinct features, including a large fusiform, eccentric mass in a major nerve. Most of these tumors are deeply situated, and few arise in a superficial nerve. Mean diameter of these tumors is more than 5 cm. Their appearance is a fleshy, opaque surface with areas of secondary hemorrhage and necrosis.[5] Thickening of the nerve proximal and distal indicates tumor spread along the perineurium and the epineurium.

Microscopic and immunohistochemical analyses are critical in determining the correct diagnosis. Distinguishing schwannoma from MPNST is important because schwannoma has a benign course with rare malignant degeneration. In a retrospective review, Seppala and Haltia[6] found a favorable clinical outcome in cellular schwannoma compared with MPNST. Mitotic activity is high in both.

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Immunohistochemical analysis is useful in identifying nerve sheath differentiation. Nerve sheath tumors include S-100 antigen, Leu-7, myelin basic protein, and PGP 9.5.[1] Immunoreactivity for S-100 protein in 50% to 70% of MPNST cases, and p53 tumor suppression is also frequently seen in MPNST; however, there is no specific marker for MPNST.

Optimal treatment results are obtained with wide resection of the tumor. Resectability depends largely on location, as deep tumors require more extensive surgery and can be more difficult to reach. With tumor resection, sacrifice of the nerve root is often necessary. Studies have shown low risk for neurologic deficit after resection of a nerve sheath tumor bearing the nerve root.[10-12] Prognosis depends on several factors, the most commonly cited being age 5 to 7 years, tumor size 6 cm or more, central tumor location, and NF-1.[2-4,7,13]

Rates of local recurrence after wide resection have been reported to be 26% to 65% (median intervals, 5-32.2 months).[4,7,8,9,13] In addition, Meis and colleagues[13] reported that 50% of their 78 patients had metastases at 24 months. The most common sites of metastasis are lungs, bone, and pleura; other sites are liver, brain, and kidneys. Meis and colleagues reported lymph node involvement in 6 of 78 patients with metastasis. Their Kaplan-Meier analysis revealed median survival of 45 months.

Various adjuvant treatments have been used for MPNST—including chemotherapy, radiation therapy, intraoperative electron irradiation therapy, brachytherapy, and combination therapies—but results have been variable.[3,4,7-9] These treatments may be of benefit in metastatic disease or in salvaging treatment failures.

Conclusions

MPNST in children is seldom reported, and to our knowledge there are no articles on pediatric MPNST in the orthopedic literature. The present case report demonstrates the importance of a thorough history and complete physical examination in detecting a previously unidentified spinal cord tumor. This case points out the many important signs and symptoms that can aid the orthopedist in diagnosing spinal cord tumors, including MPNST. Such signs and symptoms include hamstring tightness; back stiffness, pain, or deformity; ongoing extremity pain, particularly night pain, despite negative radiologic workup; and history of neurologic signs or symptoms, including bowel or bladder complaints. A careful neurologic examination is warranted in children with these signs and symptoms. Early diagnosis and referral to a multidisciplinary team are important in ensuring the best prognosis in this young age group.

Authors' Disclosure Statement

The authors report no actual or potential conflict of interest in relation to this article.

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This paper will be judged for the Resident Writer's Award.