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Malignant Peripheral Nerve Sheath Tumor (MPNST) Involving the Sacrum

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Peripheral nerve sheath tumor (PNST) involving the sacrum occurs rarely, and malignant PNST is even rarer. These tumors are usually of considerable size at the time of diagnosis. We report on a 65-year-old woman with a rare malignant PNST in the sacral region who had complained of severe right hip pain and urinary and fecal incontinence for years. The lumbar magnetic resonance imagines showed a large pelvic mass. The tumor mass was completely removed through the posterior approach, and the pathological report showed this to be a highly aggressive malignant PNST, which usually has a poor prognosis. We discuss the therapeutic modalities and prognosis.

Key words: malignant peripheral nerve sheath tumor, sacrum

INTRODUCTION

Nerve sheath tumors that involve the sacrum are rare[1], and comprise only a small portion of the wide variety of lesions that occur in the sacral region[2,3]. Malignant peripheral nerve sheath tumors (MPNST) are extremely rare in this region, affecting 0.001% of the general clinic population[4]. MPNST are defined as any malignant tumor arising from or differentiating toward cells of the peripheral nerve sheath[5]. MPNST are high-grade malignant tumors[6] comprising 5-10% of soft tissue sarcomas[7]. The symptoms depend on the anatomical location of the lesion within the sacrum, its extension, and whether it compresses or invades neighboring structures, such as the sacral nerve roots or intrapelvic organs[8]. Herein, we reported on a patient with a rare MPNST involving the sacrum.

CASE REPORT

A 65-year-old woman suffered from severe electric-shocking pain over the right hip that radiated to the anterior and lateral aspect of the right lower leg for one month. She had experienced mild low back pain on and off during her fourth decade, and difficulty in defecation and urgency in urination developed one year before this admission. She had recurrent urinary tract infections and constipation during that period. An ovary cyst was found on the right side in a routine pelvic sonography. Exploratory laparotomy performed by a gynecologist at another hospital found a large presacral mass. No definite diagnosis was reported except for fibrosis. She had not sought any medical help for more than 10 years until she developed intractable pain over the right hip that radiated to the right lower leg.

No palpable mass over the abdomen or remarkable skin lesions over the trunk and extremities were noted on physical examination. The neurological examination disclosed decreased sensation at the L5 and S1 dermatomes, decreased deep tendon reflex, and bilateral weakness in dorsiflexion of the big toes and plantar flexion. The anal tone appeared flaccid and saddle anesthesia presented.

The plain radiograph demonstrated an osteolytic lesion associated with enlarged sacral foramina and remodeled sacrum bony structure (Fig. 1). MR imaging identified a large, intense, enhanced soft tissue mass involving the sacral body measuring 15.3×12.3×10 cm. The tumor extended posteriorly to the lumbar spinal canal and lamina (Fig. 2A) and protruded into the presacral and pelvic cavity, causing compression and displacement of the uterus and urinary bladder anteriorly, and the retrosigmoid colon left laterally (Fig. 2B). The sacral mass appeared as a U-shape on the sagittal MR imaging and contained internal areas of necrosis (or cysts). The large tumor was destroying the entire sacrum and only the distal coccyx remained.

A posterior approach was taken through a reverse U-shaped incision to avoid the risk of wound infection from the anus. After sacral laminectomy, the tumor was re-

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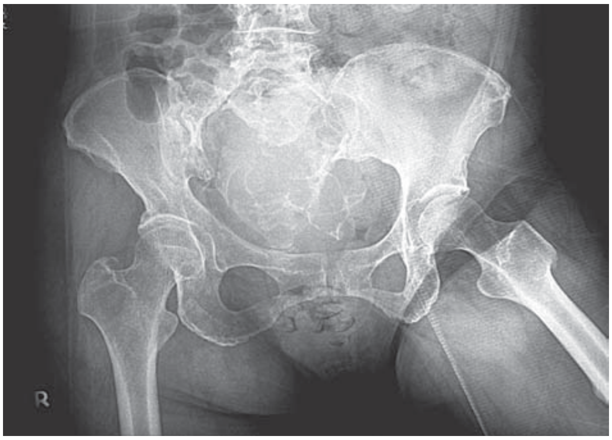

Fig. 1 An anterior–posterior plain radiograph of the pelvis demonstrating an osteolytic lesion enlarging the sacral foramina and remodeling the sacrum bony structure.

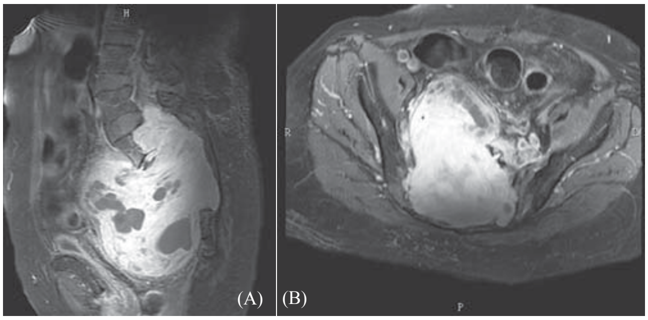

Fig. 2 (A) and (B) The T1-weighted MR imaging with contrast identified a large, intense, enhanced soft tissue mass involving the sacral body. The tumor extended posteriorly to the lumbar spinal canal and lamina, and protruded into the presacral and pelvic cavity, causing compression and displacement of the uterus and urinary bladder anteriorly, and the retrosigmoid colon to the left laterally.

moved meticulously, with special care taken to remove the intraspinal canal portion of the tumor to preserve as much of the nerve roots as possible. Near total resection of the intrapelvic portion of tumor was carried out. To preserve function and avoid the need for a colostomy, a small part of the tumor adhering to the rectum was left. The pathological report showed a neurofibroma with focal malignant change. Microscopically, the tumor grew in a fasciculated pattern of tightly packed hyperchromatic spindle cells with abundant, faintly eosinophilic cytoplasm in alternating loose and dense cellular areas (Fig. 3A). The tumor also showed mild pleomorphism, the presence of collagen by immunoreactivity to Masson stain, and a focally increased mitotic index (Fig. 3B). MPNST was diagnosed. The patient reported great relief of her right hip pain after the operation. She did not complain of urgency or frequency of urination anymore, but her anal tone remained flaccid, possibly because of long-term nerve injury. She walked normally without sensory or motor deficits. A course of radiotherapy with 4140 cGy in 23 fractions followed.

DISCUSSION

Almost two-thirds of MPNST arise from neurofibromas in patients with von Recklinghausen disease, or neurofibromatosis[4,9,10]. The neoplasm is usually noticed around the fourth decade of life, although it may appear earlier in patients who have von Recklinghausen disease[9,11]. The mean age of presentation of MPNST in patients with von Recklinghausen disease is 28.7 years compared with 39.7 years in patients free of this disease[12]. The estimated incidence of MPNST that develop in patients with von Recklinghausen disease is 2-5% compared with 0.001% in the general population[4]. Large- and medium-sized nerves are distinctly more prone to involvement than are small nerves. The most common sites are the buttock and thigh, the brachial plexus and upper arm, and the paraspinal region. The sciatic nerve is affected most frequently[6].

Because of the potential space in the presacral space, tumors in the presacral and sacral regions tend to grow to a considerable size before detection. The duration of symptoms before diagnosis ranged from one month to nine years (mean, 2.6 years) in one review[13]; the mean duration of symptoms is generally 1-7 years[1,13,14]. Clinical manifestations depend on the anatomical location of the lesion within the sacrum, the extent of the lesion, and whether it compresses or invades neighboring structures[8]. Histological type plays only a minor role in this issue. The most common initial symptoms of a sacral tumor are local pain because of its mass[14]. Neurological deficits develop as the nerve roots become increasingly compressed or even infiltrated by the tumor. The pain may radiate unilaterally or bilaterally into the buttocks, posterior thigh or leg, external genitalia, and perineum[15]. The natural neurological history of an expanding sacral lesion is characterized by a single but usually multiradicular sensory deficit, and at a later stage, motor deficit; involving eventually the bladder, bowel, and sexual dysfunction[8,15]. A digital rectal examination is one of the most important physical examinations in patients with a suspected sacral mass[8]. The mass is often palpable and may help the physician narrow the differential diagnosis[16].

A plain pelvic radiography provides an initial assessment. Features such as lytic lesions, distortion, expansion of the

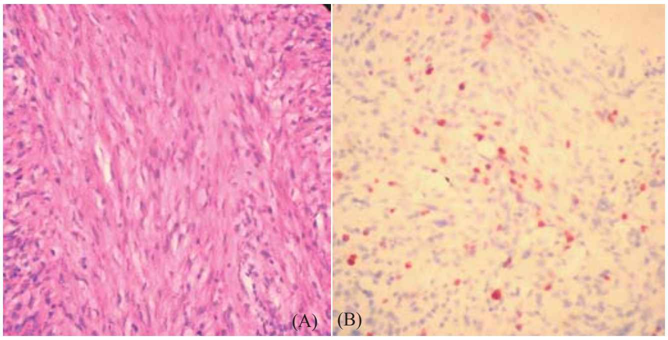

Fig. 3 (A) Hematoxylin and eosin stain of the tumor showing a fasciculated pattern of tight packed hyperchromatic spindle cells with abundant, faintly eosinophilic cytoplasm with alternating loose and dense cellular areas. (B) The Ki-67 stain showed a focal increased mitotic index.

normal sacral anatomy, enlargement of the sacral neural foramina, and abnormal calcifications are present in almost all patients. Computed tomography can help characterize the lesion further and assess its relationship with other pelvic structures. It provides the surgeon with details about bone involvement, especially when the tumor causes erosion of both the anterior and posterior sacral borders as well as expansion of the sacrum[16]. Peripheral nerve sheath tumors have several characteristic features on MR imaging, such as a fusiform shape, entering and exiting tails representing the host nerve[17,18], typically eccentrical placement, the split-fat sign[19], the target sign[17], and the fasicular sign. However, the enormous size, secondary bone involvement, and potential space in the sacral area cause sacral or presacral peripheral nerve sheath tumors to have different features on MR imaging. Sacral nerve sheath tumors are large, eccentric, well-defined heterogeneous, enhancing masses[1,3]. Degenerative changes, such as cystic formation, hemorrhage, necrosis, and calcification[1], are known as "ancient changes" in the histological literature[20]. These features are common in schwannomas but rare in neurofibromas. In addition, only 30% of neurofibromas have a pseudocapsule, which is often visible in schwannonmas[3]. Large size (> 5 cm), heterogeneity, satellite lesion, and lack of pseudocapsule are more suggestive of MPNST, but they could also be present in benign tumors. Further biopsy is needed to differentiate these tumors.

According to the history and physical examination, our patient did not have von Recklinghausen disease. The disease has a 20-year latency from the initial onset of symptoms to definite diagnosis. At the time of admission, the tumor had grown to a large size and had caused neurological deficits. Large size, heterogeneous enhancement, and lack of a pseudocapsule presented in the radiological studies and suggested that the tumor was malignant.

Plexiform neurofibromas, neurofibromas of major nerves, and clinical association with neurofibromatosis type I are considered precursor lesions to most MPNST[6]. MPNST occur rarely in the sacrum[4,21]. The hallmark features of MPNST include an association with von Recklinghausen disease[10], intrafascicular spread within or beyond the main tumor mass, and invasion of the surrounding tissue[1]. The use of immunohistochemical stains may also help to confirm the diagnosis. Markers such as S-100 protein, neurofilament, epithelial membrane antigen, and Leu-7 (CD57) are used frequently to assess neural differentiation of a neoplasm. In addition to the spindle cell pattern, MPNST may also display an epithelioid pattern, or even rarer, glandular MPNST[22], or include muscle in triton tumors[23,24]. In more unusual cases, cartilage, adipose tissue, and even bone are present[25]. Interestingly, there was cartilage within the tumor in our patient.

En bloc or radical resection is the treatment of choice. The main aim is to achieve surgical excision with negative margins and to control systemic spread with adjuvant treatment[5]. Unfortunately, the involvement of the critical neurovascular structures, intrapelvic organs, and the stability of sacroiliac structures limit the extent of excision[26]. The approaches to these tumors may be anterior or posterior, or a combination, depending on the amount of intrapelvic and intrasacral involvement[1]. Klimo et al. described a straightforward classification system to determine the best surgical approach.

Radiotherapy is generally avoided in the treatment of benign peripheral nerve sheath tumors because of the risk of malignant transformation[27-31]. However, postoperative radiation therapy reported in three patients with orbital MPNST produced a good response and nine-year survival[32,33]. A large MPNST of the proximal sciatic nerve in the thigh was removed subtotally from the sciatic nerve after administration of adjuvant radiation therapy[34]. Vauthey et al. used adjuvant radiotherapy in deep and high-grade MPNST of the extremities and achieved a local disease-free survival of 70% in three years[35].

Although one patient with MPNST of the sciatic nerve treated with high-dose chemotherapy demonstrated a complete response[7], the benefits of adjuvant chemotherapy remain controversial[36]. Adjuvant radiation or chemotherapy does not appear to affect survival[4,9]. Concurrent adjuvant therapy with radiation and chemotherapy should be suboptimally individualized[37].

Although the sacrum was destroyed by the tumor in our patient, the bilateral alar and the sacroiliac joints remained intact. Accordingly, we thought the lumbar-sacral junction was stable and no internal fixation was necessary. The tumor was subtotally removed because of its tight adhesion to the pelvic vital organs, and the patient was treated with a course of radiotherapy.

The five-year survival in patients with MPNST is around 33-39%[38,39]. Doorn and coworkers reported median disease-free survival of 14 months and median overall survival of 24 months[40]. Large tumor size[9,41], the presence of neurofibromatosis[41], and total resection[38] are the most important prognostic indicators[4]. Patients with von Recklinghausen disease and large, incompletely resected tumors have the most dismal prognosis[38,39], and none have survived more than 25 months. However, two studies show that von Recklinghausen disease has no significant effect on surviva[l9,40].

MPNST are highly aggressive neoplasms with a poor prognosis that occur rarely in the sacral or presacral region. These tumors usually have a long-term latency before the initial presentation. *En bloc* resection is the treatment of choice, but the involvement of surrounding critical structures and the tumor's enormous size limit the extent of resection. Adjuvant radiation therapy and chemotherapy may be of benefit in some patients whose tumors cannot be completely removed.

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