

# Diffuse large B-cell lymphoma presenting as a sacral tumor

## Report of two cases

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Primary lymphomas of the sacrum are rare tumors, reported only in a few cases in the literature. The authors describe two patients with diffuse large B-cell lymphomas presenting as a sacral tumor.

In the first case a 52-year-old man presented with progressive back pain, bilateral radicular pain, and saddle block anesthesia secondary to a lytic, expansile soft-tissue mass. The mass arose from the sacrum and eroded through the right S-1 to S-4 foramina and extended into the epidural space of the spinal canal. On magnetic resonance imaging, the sacral mass enhanced homogeneously with Gd. In the second case a 64-year-old man presented with left-sided radicular pain, paresthesias, and progressive weakness due to a lytic soft-tissue mass in the left sacral ala extending into the left L-5 and S-1 foramina. Metastatic workup in each patient demonstrated unremarkable findings. In both cases, an open biopsy procedure was performed after nondiagnostic examination of needle biopsy samples. Histopathological examination showed evidence consistent with diffuse large B-cell lymphoma in both patients. In the first case the disease was classified as Stage IAE, and the patient subsequently underwent four cycles of cyclophosphamide/doxorubicin/vincristine/prednisone (CHOP)- and rituximab-based chemotherapy followed by consolidation radiotherapy. In the second case the disease was also classified as Stage IAE, and the patient underwent CHOP-based chemotherapy and consolidation radiotherapy. In both cases radiography demonstrated a decrease in size of the sacral lymphomas.

The authors review the clinical, radiological, and histological features of sacral lymphomas. Lymphoma should be considered in the differential diagnosis of sacral tumors.

**KEY WORDS** • non-Hodgkin lymphoma • sacrum • spinal tumor

Neoplasms of the sacrum are relatively uncommon, representing 1 to 2% of all musculoskeletal tumors.<sup>2</sup> They can be classified as primary or metastatic lesions, the former being either benign or malignant. The most common malignancy of the sacrum is metastatic disease, whereas the most common primary sacral tumor is chordoma. Other sacral malignant lesions include Ewing sarcoma, myeloma, osteosarcoma, neurofibrosarcoma, angiosarcoma, chondrosarcoma, and rarely lymphoma. Referred pain in the leg or buttock is the typical presenting symptom of sacral tumors. Neurological signs are rarely seen, and their manifestation is often late. We describe two rare cases in which diffuse large B-cell lymphomas presented as primary malignant sacral tumors.

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*Abbreviations used in this paper:* CHOP = cyclophosphamide/doxorubicin/vincristine/prednisone; CT = computerized tomography; MR = magnetic resonance.

## CASE REPORTS

### Case 1

**History.** This 52-year-old man presented with a 3-week history of increasing back pain radiating down his right leg and testicle. The pain eventually progressed to both buttocks and legs with numbness and tingling in the buttocks, posterior thighs, and perineal region. He also experienced subjective urinary retention but not bowel incontinence. He denied experiencing fevers, chills, night sweats, or weight loss. An MR imaging study of his lumbar spine performed 1 year before presentation was unremarkable. His family history was significant; one brother died at age 59 years of lymphoma.

**Examination.** The patient was ambulatory and had full lower-extremity motor strength. He had decreased sensation to pinprick in the S-1, S-2, and S-3 regions bilaterally. Areflexia was present in both knees and ankles. Toes

were downgoing bilaterally, and clonus was absent. His rectal tone was normal and a bulbocavernosus reflex was present. Examination of a postvoid residual sample revealed 240 ml of urine. The serum lactate dehydrogenase level was found to be slightly elevated at 679.

Lumbosacral CT scanning revealed a large lytic sacral mass centered at S-2 extending to the upper coccyx with areas of destructive change (Fig. 1 *upper left* and *right*). An associated presacral mass was also present. Osseous remodeling and scalloping with enlargement of the right S2–3 and S3–4 neural foramina observed on CT scans. The mass extended into the epidural space compressing the distal thecal sac. Magnetic resonance imaging demonstrated a large, enhancing, destructive expansile mass in the right distal sacrum, extending from S-2 to the upper coccyx (Fig. 1 *lower left*).

**Operation and Pathological Examination.** Two fluoroscopic biopsy procedures were attempted, but the results were nondiagnostic. The patient subsequently underwent a right S2–3 sacral laminectomy and exploration of the sacral canal for a biopsy and partial resection of the sacral mass. Pathological examination showed large atypical B cells consistent with a diffuse large B-cell lymphoma (Fig. 2). Immunohistochemical analysis showed CD-20 (B-cell marker) and Bcl-6 (germinal center marker). The MIB-1 staining was positive in approximately 70% of the large atypical B cells.

**Postoperative Course and Follow Up.** A CT scan of the patient’s chest, abdomen, and pelvis revealed no adenopathy or metastatic disease. Members of the oncology service examined a bone marrow biopsy sample, which was negative. His disease was classified as Stage IAE (Ann Arbor Classification<sup>3</sup> [Table 1]) with localized disease. He subsequently underwent six cycles of CHOP- and rituximab-based chemotherapy and radiotherapy. An MR image of the pelvis obtained at 4 months posttreatment revealed a significant decrease in size of the sacral mass (Fig. 1 *lower right*). The presacral and epidural components of the tumor were no longer present. The tumor remained present within the right sacral ala and the right S1–2, S2–3, and S3–4 neural foramina. At 9 months MR imaging demonstrated stable residual disease without evidence of recurrence. Clinically, he remained neurologically intact.

**Case 2**

**History.** This 64-year-old man presented with a several-month history of left sacroiliac pain that radiated into his left leg. This progressed to increasing pain, numbness, and weakness. He also noted a mass in his lumbar region that had been increasing in size. He had difficulty ambulating and used a cane for assistance because of the extreme severity of his pain. He denied experiencing fevers, chills, night sweats, or weight loss. A melanoma was re-



Fig. 1. Case 1. Neuroimaging studies. *Upper Left* and *Right*: Coronal (*left*) and sagittal (*right*) lumbosacral CT scans revealing a large, lytic sacral mass centered at S-2 and extending to the upper coccyx with areas of destructive change and enlargement of the right S2–3 and S3–4 neural foramina. An associated presacral mass is also present. *Lower Left*: Axial Gd-enhanced MR imaging demonstrating the enhancing mass extending into the epidural space and compressing the distal thecal sac. *Lower Right*: Postoperative Gd-enhanced MR image of the pelvis obtained at 4 months after chemo- and radiotherapy, revealing a significant decrease in size of the sacral mass with resolution of the epidural compression.

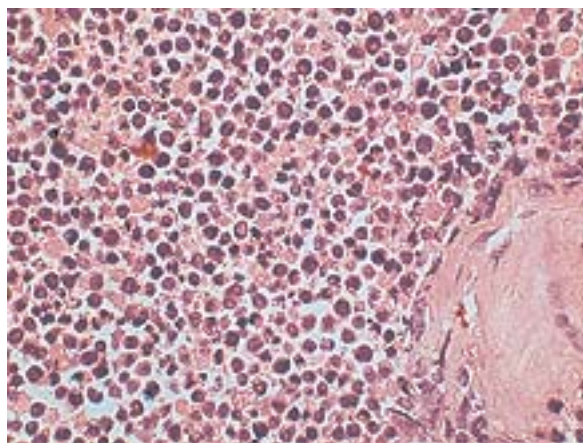


Fig. 2. Case 1. Photomicrograph showing small, round blue cells. Additional immunohistochemical studies were positive for CD-20 and Bcl-6, which were consistent with a diffuse large B-cell lymphoma (data not shown). H & E, original magnification  $\times 400$ .

moved from his left cheek 5 years prior. His family history was significant for breast, prostate, and skin cancer.

**Examination.** The patient had no palpable lymphadenopathy. He exhibited tenderness when the sacrum and left hip were palpated. There was significant limitation of internal and external rotation of the left hip due to joint pain and stiffness. A palpable mass was present in the left sacral region. Motor testing revealed Grade 4/5 strength in the left hip flexors, quadriceps, and hamstrings. He had decreased sensation to pinprick in the left S-1 distribution. His reflexes were normal and his toes were downgoing.

A CT scan revealed a  $6.8 \times 3.9$ -cm lytic soft-tissue mass centered around the left sacral ala with involvement anterior and posterior to the left ilium that extended to the left S-1 sacral foramina and to the left iliopsoas and iliacus (Fig. 3 upper and center). Post myelography CT scanning demonstrated no evidence of thecal compression or proximal nerve root impingement. Computerized tomography scans of his chest, abdomen, and pelvis revealed no evidence of metastatic disease or adenopathy.

**Operation and Pathological Examination.** Examination of a fine-needle aspiration biopsy specimen was nondiagnostic. Open-core biopsy procedures were then performed and diagnostic tissue obtained. Pathological examination showed a diffuse infiltrate of intermediate-to-large atypical B-lymphoid cells with a proliferation index of 70%, consistent with a diffuse large B-cell lymphoma. Immunoperoxidase studies showed positivity for CD20 (B-cell marker) and nuclear expression of Bcl-6 (marker of germinal center derivation).

**Postoperative Course.** Members of the oncology service examined a bone marrow biopsy sample, which was negative. Based on these results, his disease was classified as a Stage IAE with localized disease. The patient subsequently underwent three cycles of CHOP-based chemotherapy, which was followed by radiotherapy. At 3 months, the patient was ambulating without assistance, but exhibited a slight limp. The soft-tissue mass in the left sacrum was no longer palpable. A CT scan obtained at 13

months postoperatively revealed a significant decrease in size of the left sacral mass (Fig. 3 lower).

## DISCUSSION

Sacral tumors constitute a wide range of pathological entities including primary, metastatic, benign, and malignant conditions.<sup>1,2,9-11</sup> In a series of 160 sacral tumors, 82% were primary and 18% secondary.<sup>2</sup> The distribution of primary tumors was equal between benign (25%), low-grade (26%), and high-grade malignant tumors (30%).

Giant cell tumors are the most common benign tumors of the sacrum. They are usually located in the sacral wing and tend to expand toward the sacral canal and sacroiliac joints. Other benign tumors include osteoid osteomas, osteoblastomas, aneurysmal bone cysts, neurilemmomas, and ependymomas. Chordomas are the most common low-grade malignant tumors as well as the most common primary tumors of the sacrum. Other low-grade malignant tumors include chondrosarcomas, desmoplastic fibromas, teratomas, and low-grade osteosarcomas. Among high-grade malignant tumors, metastatic carcinomas are the most frequent. Ewing sarcomas, osteosarcomas, plasmacytomas, and lymphomas comprise the remainder of high-grade malignant sacral neoplasms. Clinical presentation depends on the anatomical location, the direction of spread, and the biological behavior of the tumor.

Primary lymphoma of bone occurs in fewer than 5% of cases of non-Hodgkin lymphoma and, histologically, is almost always diffuse large B-cell lymphoma. The most common sites of bone involvement are the femur, pelvis, and vertebral column. Although diffuse large B-cell lymphoma is the most frequent type of non-Hodgkin lymphoma, representing 40% of all new cases of lymphoma, the incidence of primary sacral lymphoma is unknown. Diffuse large B-cell lymphomas are highly invasive in nature and can cause local compression of neighboring structures with destruction of bone. Although bone marrow involvement is present in only 10 to 20% of patients initially, its detection is important because of its strong correlation with later spread to the central nervous system. Similar to other sacral lesions, referred pain in the leg or

TABLE 1  
Summary of clinical stages of non-Hodgkin lymphomas according to the Ann Arbor classification\*

Stage	Distribution of Disease
I	involvement of a single lymph node region (I) or a single extralymphatic organ or site (IE)
II	involvement of $\geq 2$ lymph node regions ipsilateral to diaphragm alone (II) or w/ involvement of limited contiguous extralymphatic organ or tissue (IIIE)
III	involvement of lymph node regions on both sides of the diaphragm (III), which may include the spleen (IIIS) &/or limited contiguous extralymphatic organ or site (IIIE, IIIES)
IV	multiple or disseminated foci of involvement of $\geq 1$ extralymphatic organs or tissues w/ or w/o lymphatic involvement

\* All stages are further divided on the basis of the absence (A) or presence (B) of the following systemic symptoms: significant fever, night sweats, and/or unexplained weight loss of greater than 10% of normal body weight.



Fig. 3. Case 2. Neuroimaging studies. *Upper:* Postmyelography CT scan revealing destructive osseous changes caused by the left sacral mass. There is no evidence of thecal compression. *Center:* Axial CT scan of the pelvis demonstrating a 6.8 × 3.9-cm lytic soft-tissue mass centered around the left sacral ala with involvement anterior and posterior to the left ilium that extends to the left S-1 sacral foramina and to the left iliopsoas and iliacus. *Lower:* Postoperative CT scan obtained at 13 months after chemo- and radiotherapy, demonstrating a significant decrease in size of the left sacral mass.

buttock is the usual presenting symptom because of nerve root irritation. The duration of symptoms at the time of diagnosis varies, depending on the aggressiveness of the lesion. Patients often have an antalgic posture of the hip in external rotation, which becomes more pronounced on flexion. Pain, secondary to bone and/or nerve root involvement, can be a source of significant discomfort. Neu-

rological signs are rarely seen and often manifest late. Rectal examination often reveals a palpable anterior soft-tissue mass because sacral tumors have a tendency to grow into the presacral space.

The Ann Arbor staging system developed for Hodgkin disease has also been used in staging non-Hodgkin lymphomas (Table 1).<sup>3</sup> The staging system focuses on the number of tumor sites (nodal and extranodal), location, and the presence/absence of systemic symptoms. Both patients presented in this report suffered focal extranodal disease with the absence of systemic symptoms (Stage IAE).

Percutaneous biopsy sampling of sacral lesions is a reasonable first line diagnostic tool. Fine-needle aspiration biopsy sampling performed using CT scanning, fluoroscopic, or ultrasonographic guidance has been reported to be successful. Gupta, et al.,<sup>7</sup> reported a diagnostic rate of 93% in their series of 29 patients with lytic spinal lesions. The series included three patients with sacral lesions (metastatic carcinoma and plasmacytoma). Because there is a 7% rate of false-negative findings, a negative biopsy result should prompt a repeated biopsy procedure, preferably using a core or trephine tool. In Case 2, examination of the initial fine-needle biopsy specimen was nondiagnostic, and a subsequent open-core biopsy procedure was required. An open surgical biopsy procedure may be required in a small number of patients in whom examination of a preoperative specimen yielded inconclusive results, as was demonstrated in Case 1.

The CHOP-based chemotherapy regimen has been the standard of care for the treatment of diffuse large B-cell lymphoma. It induces a complete response in 40 to 50% of patients, with 3-year event-free and overall survival rates of 30% and 35 to 40%, respectively. Abnormal serum LDH level, poor Ann Arbor staging grade and Zubrod performance status, extranodal involvement, and advanced age are poor prognosticators.<sup>12</sup> The authors of a prospective study demonstrated a complete response rate of 99% and an overall survival rate of 85% in patients with limited-stage disease (no systemic symptoms, Ann Arbor Stage I or II) treated with three cycles of CHOP-based chemotherapy followed by field radiotherapy.<sup>6</sup> Rituximab (Rituxan), a chimeric monoclonal antibody against the CD20 B-cell antigen, has therapeutic activity in diffuse large B-cell lymphoma.<sup>4,8</sup> Recently, the authors of a randomized study demonstrated an increase in the complete response rate and disease-free and overall survival rate in elderly patients with diffuse large B-cell lymphoma who underwent both rituximab- and CHOP-based chemotherapy compared with those in whom CHOP chemotherapy alone was performed.<sup>5</sup> The addition of rituximab to CHOP chemotherapy significantly reduced the risk of treatment failure and death. The two patients in our report received slightly different chemotherapy regimens because in each case a separate oncologist prescribed the chemotherapy. The patient in Case 2 underwent three cycles of CHOP chemotherapy followed by radiotherapy, which is currently the standard of care. At our institution, some oncologists have added rituximab to the CHOP regimen in some elderly patients (as in our Case 1) because an increased survival benefit has been shown. Future studies will determine whether the addition of rituximab to CHOP chemotherapy will become the standard of care.

## Sacral lymphoma

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