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CASE REPORT

Primary osseous sacral neuroblastoma in an adult

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Abstract
Neoplasms of the sacrum are rare. Given the non-specific imaging findings in sacral lesions, the imaging-based differential diagnosis is always difficult. This case is about an adult with primary sacral neuroblastoma and we have discussed imaging and histopathological findings of this rare tumor.

Keywords Sacrum · Neuroblastoma · Adult

Introduction

Neoplasms affecting the sacrum are rare [1]. Imaging-based differential diagnosis is challenging given the non-specific imaging characteristics of many sacral tumors [2]. Radiographs are limited for the detection and characterization of sacral lesions due to obscuration of the sacrum by overlying bowel gas and the complex anatomy of the bone [3]. Chordoma is by far the most common primary tumor of the sacrum and is usually cited as a leading imaging differential for midline sacral lesions [4]. We present an exceedingly rare neoplasm of the sacrum not previously reported in an adult in the English-language literature.

Case report

A 29-year-old man with no significant past medical history presented to the emergency department with 4 weeks of numbness in the right hip. He denied any recent trauma. Initial laboratories, including complete blood count, clotting profile, and metabolic panel were normal. A radiograph of the pelvis performed in the emergency department demonstrated a mixed sclerotic and lytic lesion with in the sacrum (Fig. 1). As the findings were suspicious for primary neoplasm or metastatic disease, an MRI of the pelvis was performed (Fig. 2). This demonstrated a marrow-replacing, destructive lesion involving the central sacrum from S1 through S4 with an associated anterior and posterior soft tissue mass extending into the central canal. The mass was isointense in signal to skeletal muscle on T1-weighted pulse sequences and had a lobulated appearance, with mild hyperintensity on water-sensitive sequences. Post-contrast images demonstrated mild, relatively uniform, contrast enhancement. This tumor extended into both sacral alae and obliterated the S1 through S3 neural foramina and nerve roots bilaterally. There was no extension into the sacroiliac joints and no pathologic fracture. There was no rectal involvement. Histopathology from an initial CT-guided percutaneous biopsy demonstrated extensive necrotic tissue. The patient underwent subsequent open biopsy of the sacral mass. Histopathology of the specimen demonstrated a small round blue cell tumor with abundant fibrillary background (Fig. 3), characteristic of neuroblastoma, without significant evidence of maturation. Immunohistochemical

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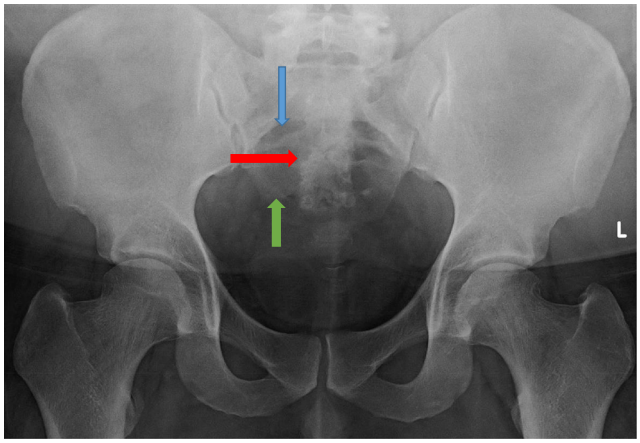

Fig. 1 Single anteroposterior view radiograph of the pelvis demonstrate mixed sclerotic and lytic lesion with in the sacrum. This mass demonstrates central sclerotic component (*red arrow*) with surrounding lytic component (*green arrow*). There is also distortion of the sacral arcuate lines (*blue arrow*)

stains were positive for chromogranin and synaptophysin and negative for CD99. The tumor was classified as a poorly differentiated neuroblastoma, low mitotic/karyorrhectic index (MKI). Following the biopsies, staging bone scintigraphy demonstrated marked radiotracer localization within the sacral body extending into the bilateral sacral ala, but no evidence of other osseous lesions. A subsequent I-123 metaiodobenzylguanidine (MIBG) scan (Fig. 4) demonstrated increased I-123 MIBG activity within the sacral lesion but no other foci of uptake to suggest metastasis or a remote primary tumor.

The patient received eight cycles of chemotherapy including carboplatin, etoposide, cyclophosphamide, doxorubicin, and cytoxan in varying combinations at different cycles. MIBG scan after four cycles of chemotherapy demonstrated a mild reduction in MIBG uptake and mild reduction in tumor size. The patient tolerated the chemotherapy and remains metastasis-free 8 months after the initial diagnosis. Radiation therapy is planned for local management of the sacral tumor.

Discussion

Neuroblastoma arises either from primitive sympathetic neural cells in the adrenal medulla or along the paraspinal sympathetic ganglia in the rest of the body [5]. Neuroblasts are derived from neural crest cells, which give rise to multiple important organs. Neuroblastic tumors are derived from the neuroectodermal cells of the peripheral neural crests that are routed to the adrenal medulla and sympathetic nervous system. The extramedullary cells typically disappear by 3 years of age. However, failure to involute may result in the malignant transformation of these neuroblasts into neuroblastoma when they are unresponsive to the normal differentiation or apoptotic signals [6].

Neuroblastoma is considered an exclusively pediatric malignancy, but cases in adults have been reported in the literature. Neuroblastoma is exceedingly rare among adults, with only one case per 10 million diagnosed per year [5]. Primary sacral neuroblastoma in an adult has been reported only once in non-English language literature to the best of our knowledge [7].

Given the rarity of this condition, the treatment strategies, staging and risk stratification have been developed by extrapolating pediatric data [8]. Overall survival among adult patients with neuroblastoma at 5 years is 36% as compared to 85% for infants [9]. Factors that dictate the survival outcomes are based upon International Neuroblastoma Risk

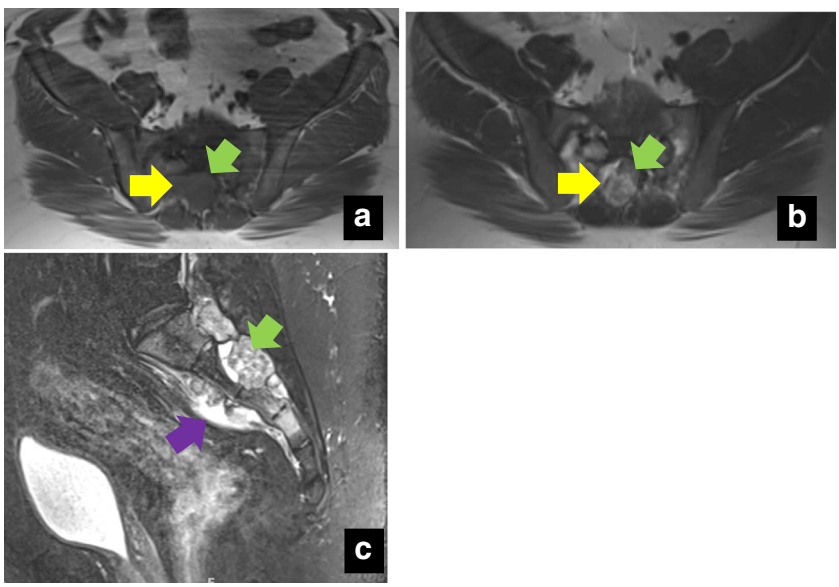

Fig. 2 Magnetic resonance imaging of the pelvis demonstrates marrow-replacing, destructive lesion involving the central sacrum from S1 through S4 (*yellow arrows*) with an associated anterior (*purple arrow*) and posterior soft tissue mass extending into the central canal (*green arrow*). The mass was isointense in signal to skeletal muscle on T1-weighted pulse sequences (**a**) and had a lobulated appearance, with mild hyperintensity on water-sensitive sequences (**b** and **c**)

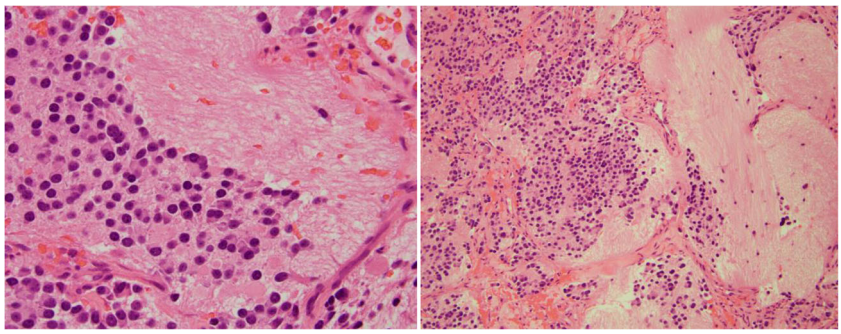

Fig. 3 Histopathology specimen from the sacral mass demonstrates small round blue cell tumor with abundant fibrillary background on this hematoxylin and eosin stain

Assessment system which employs age, stage, histology, tumor grade, MYCN oncogene status, chromosome 11q status, and DNA ploidy [10].

Survival rates among adults are comparable to children based on two large studies. Interestingly, adult patients who present with early stage disease have worse prognosis when compared to the children with similar stage disease, which may be due to the unfavorable histology in adult population and partly could be due to other comorbidities [5, 11]. Primary site of the disease in two large studies were different as shown in Table 1.

It has been shown that MYCN gene amplification often portends rapidly progressive disease and is a rare anomaly in adult-type neuroblastomas. A series of 40 adolescent and adult neuroblastomas cases from a large tertiary cancer center included only one patient with the MYCN gene amplification [11]. Our patient did not have MYCN gene amplification.

The leading consideration for a midline primary sacral bone tumor in an adult is chordoma [4]. Other typical etiologies in adults include metastasis, plasmacytoma, chondrosarcoma, and giant cell tumor. Also lymphomas and Ewing sarcomas involving the sacral nerves are other differential considerations [12]. Neuroblastoma arising in the sacrum is exceedingly rare in an adult, but retroperitoneal cases are on record [13]. Given its rarity, there are no specific imaging features available to suggest sacral neuroblastoma in the differential for a sacral mass, and hence tissue diagnosis based on histopathology is required for diagnosis.

This lesion was isointense to skeletal muscle on T1-weighted sequences and mildly hyperintense on water-sensitive sequences, with relatively uniform enhancement following contrast administration. Neuroblastomas have variable imaging appearances on MRI [14]. They tend to be isointense

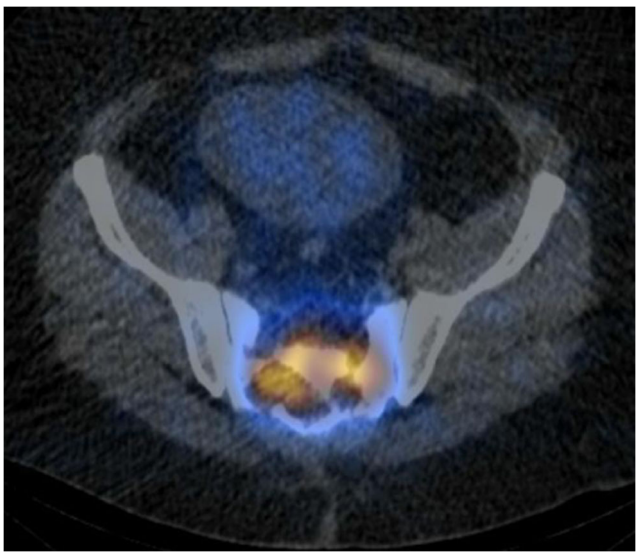

Fig. 4 I-123 metaiodobenzylguanidine (MIBG) scan SPECT/CT demonstrated increased I-123 MIBG activity within the sacral lesion. No other foci of abnormal uptake were seen elsewhere

Table 1 Number of adult patients with primary site of disease based upon data from two large United States based cancer centers

Primary site of disease	MD ANDERSON CANCER CENTER (1994–2012) [5] ($N = 118$)	MEMORIAL SLOAN KETTERING CANCER CENTER (1985–2001) [11] ($N = 30$)
Head and neck region	82	0
Thoracic cavity viscera	5	2
Abdominal cavity viscera or pelvis or thoracoabdominal	2	6
Soft tissue	9	0
Genitourinary tract including retroperitoneum	14	20
Central and peripheral nervous system	4	0
Musculoskeletal system	1	0
Metastatic cancer (involving 2 or more compartments)	1	0
Unclassified	0	2

Numbers in brackets represent the reference number cites in this paper for these studies

or hypointense to skeletal muscle on T1-weighted sequences and hyperintense on water-sensitive sequences. Contrast enhancement depends on the degree of internal hemorrhage or necrosis and can be homogeneous or heterogeneous [15]. MIBG scan is reported to be superior to FDG PET in detecting metastases [16]. This lesion was positive on MIBG scan with no evidence of distant metastases.

Neuroblastoma should be considered in the differential diagnosis of small round blue cell tumors. The histology can be favorable or unfavorable based upon the certain characteristics of the tumor cells including characterization of stroma and mitosis-karyorrhexis index according to International Neuroblastoma Pathologic Committee Classification (INPCC). Our patient had a poorly differentiated tumor and considered unfavorable histology (due to the patient's age). Neuroblastomas express CD56, synaptophysin, neurofilaments, chromogranin, and neuron-specific enolase while they are negative for CD99 and desmin among others [17].

There are no well-established treatment guidelines for adults with neuroblastoma. If the tumor is resectable, local control with surgery followed by radiation therapy may improve survival. High-dose cisplatin and etoposide alternating with vincristine, cyclophosphamide, and doxorubicin have been the mainstay of therapy in induction phases [18]. Myeloablative chemotherapy and stem cell transplant are the next set of treatment options in the consolidation phase [19]. For the treatment of minimal residual disease following stem cell transplant, evidence suggests that dinutuximab combined with GM-CSF and IL-2 given with isotretinoin can improve event-free survival [20].

Our patient was not a surgical candidate and is currently being treated with induction phase chemotherapy and will be followed by radiation therapy.

In conclusion, primary neuroblastoma of the sacrum is rare, and like neuroblastoma elsewhere, can have variable imaging features as well as clinical presentation. Imaging is useful to detect and stage aggressive sacral bone lesions and to guide biopsy, but tissue sampling with histopathologic and immunohistochemical analysis is essential to obtain the correct diagnosis.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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