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Case report

Balancing risk in a patient with primary bone histiocytic sarcoma during pregnancy: Case report and review of the literature

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ABSTRACT

Introduction and importance: Histiocytic sarcoma (HS) is a rare, aggressive malignant neoplasm of hematopoietic cell origin. Primary HS of the proximal humerus, without involvement of lymph nodes or bone marrow, or systemic features, is very rare.
Case presentation: We report a rare case of primary bony HS of the proximal humerus without bone marrow involvement in a healthy 33-year-old pregnant woman. She was successfully treated with surgical resection during pregnancy and radiotherapy post-delivery.
Clinical discussion: This is the first report of a patient with primary bony HS during pregnancy. This highlights the fact that although HS is a neoplasm of hemolymphoid cell lineage, it frequently arises in non-lymphoid organs.
Conclusion: This case emphasizes the importance of a multidisciplinary approach and the need for balancing treatment risk in a patient with primary bone HS during pregnancy.

1. Introduction

Histiocytic sarcoma (HS) is an extremely rare and high-grade neoplastic proliferation of hematopoietic cells with mature histocytic features [1]. The diagnosis of HS is clinically and histopathologically challenging. It is usually an aggressive malignancy and may present as a localized extranodal disease or as a disseminated disease associated with nonspecific systemic symptoms (fever, weight loss, anorexia, asthenia) [2]. Although several cases of HS have been described in the literature, primary involvement of the proximal humerus is exceedingly rare, especially during pregnancy. Here, we report a rare case of primary bony HS of the proximal humerus during pregnancy and highlight the multidisciplinary treatment approach provided at our tertiary university hospital. This work has been reported in line with the SCARE 2020 criteria [3].

2. Case presentation

A 33-year-old (G5 P3 A1) woman, with no medical history of note, presented to the orthopedic outpatient clinic at 19 weeks of gestation with complaints of severe progressive pain in the left shoulder for three months. Her symptoms started three months ago, when she first noticed dull aching pain in the left shoulder radiating to the lateral aspect of the arm. This was associated with progressive restriction of shoulder movement. The pain worsened with movement and at night. There were no focal neurological deficits, history of fever, weight loss, swelling, history of trauma, injury, or previous history of a similar problem. There was no family history of malignancy. Physical examination of the left shoulder revealed no palpable mass or deformity, but there was severe local tenderness around the proximal humerus. She had limited range of motion in all directions, with a normal distal neurovascular examination. There were no palpable lymph nodes or hepatosplenomegaly.

Initially, she had visited her local health center and was administered pain relief medication without any imaging. Her symptoms progressively worsened, and hence, she went to the emergency department where pain relief medication was given again without radiography as she was in the first trimester of pregnancy. The diagnosis was considered to be frozen shoulder.

At our clinic, a single anteroposterior radiograph of the left shoulder was obtained (Fig. 1). It showed an aggressive lytic lesion involving the medial aspect of the surgical and anatomical neck of the left proximal humerus with a wide zone of transition and cortical destruction. Thus,

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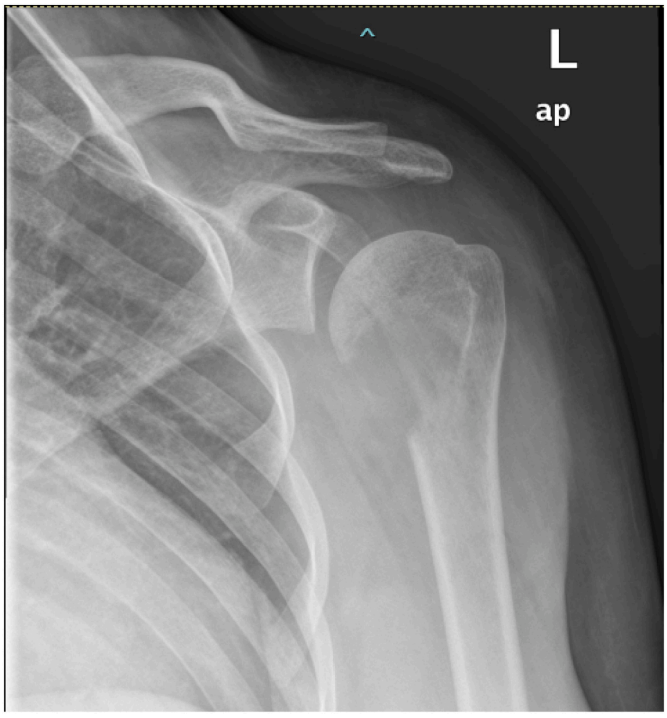

Fig. 1. Anteroposterior view of the left shoulder reveals an lytic lesion involving the medial aspect of the surgical and anatomical neck of the left humerus. It has wide zone of transition with cortical destruction.

the patient was admitted for further evaluation. All blood investigations were normal. Magnetic resonance imaging (MRI) scans of the left shoulder and humerus (Fig. 2) showed an aggressive large marrow-replacing lesion in the left proximal humerus measuring approximately 5.3 cm craniocaudally. The lesion extended from the anatomical neck to the proximal diaphysis of the humerus with multifocal areas of cortical destruction and peri-osseous soft tissue extension. The soft tissue component was seen along the medial aspect of the lesion, extending from the 9 o'clock to the 11 o'clock position. There were no skip lesions in the humerus. Non-contrast computerized tomography (CT) of the chest revealed no obvious chest metastatic lesions or any other significant abnormality. Under ultrasound guidance using local anesthesia, a True-Cut needle biopsy was performed.

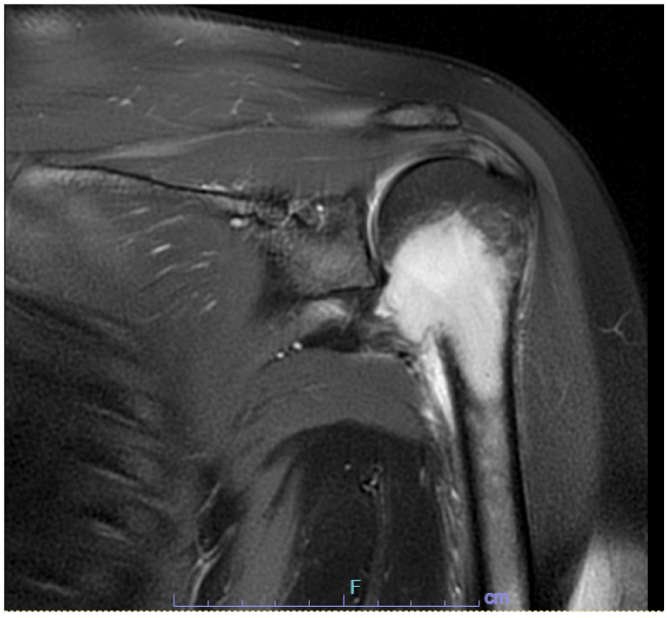

Fig. 2. Coronal T2-weighted MRI of left shoulder reveals a large marrow replacing lesion of the left proximal humerus. The lesion is extending from the anatomical neck of the humerus till the proximal diaphysis.

Histopathology showed linear tissue fragments with diffuse infiltrate composed of atypical cells with abundant eosinophilic cytoplasm, eccentric nuclei, and prominent nucleoli. Scattered multinucleated cells were also observed. There were mixed inflammatory cells composed of small lymphoid cells, plasma cells, and neutrophils. The atypical cells were positive for CD68, lysozyme, vimentin, and CD4. LCA was focally positive. The cells were negative for AE1/AE3, pan CK, CAM 5.2, HMB45, S100, Melan A, PLAP, CD3, CD20, CD30, CD1a, CD117, desmin, SMA, and CD34. The morphology and immunophenotype were those of HS.

Bone marrow trephine biopsies from the superior posterior iliac spine showed normocellular bone marrow and no evidence of abnormal infiltrates. A multidisciplinary team of orthopedists, hematologists, obstetricians, radiation oncologists, and radiologists determined that surgical excision would be the best option, considering her pregnancy and the localized lesion.

Hence, the patient underwent a wide surgical tumor resection of the left proximal humerus according to the modified Tikhoff-Linberg-type IA technique (intra-articular proximal humerus resection with partial deltoid resection), and insertion of a temporary cemented spacer due to unavailability of the tumor prosthesis. She was at 22 weeks of gestation at that stage, which was managed well by the high-risk obstetric team and all other investigations were normal. However, she was diagnosed with gestational diabetes at 20 weeks, which was controlled with insulin.

The patient was induced at 33 weeks and five days, resulting in spontaneous vaginal delivery of a live female infant (birth weight, 1.674 kg; Apgar scores at 1 and 5 min were 8 and 9, respectively). The baby was admitted to the neonatal unit for prematurity and discharged on day 11 in a stable condition. The mother was discharged 48 h post-delivery, with no complications. She was readmitted two weeks later for second-stage reconstruction surgery using the MUARS-Humerus inverse prosthesis (Fig. 3). The patient had an uneventful postoperative clinical course after the surgery and was discharged after three days. Two weeks after surgery, she received radiotherapy for the postoperative tumor bed of the left shoulder (45 Gy/25 sessions) using mixed photons (6MV + 15MV) for six weeks.

3. Discussion

HS is an extremely rare neoplasm of hematopoietic origin characterized by the proliferation of malignant cells with the morphological and immunohistochemical patterns of mature tissue histiocytes [1]. HS represents less than 1% of all hematopoietic malignancies and affects slightly more men than women, at an average age of 46 years [2].

Furthermore, HS is aggressive and usually presents at an advanced clinical stage with a rapidly progressive clinical course. The clinical presentation depends on the affected location, and localized pain, swelling, lymph node enlargement, or disseminated disease may be seen. Lymphadenopathy is common, and most cases present with extra-lymph nodal involvement, mostly in the skin, gastrointestinal tract, and soft tissue [4]. Disseminated disease is associated with systemic symptoms such as hyperthermia, weight loss, anorexia, and asthenia [4].

Radiologically, HS is quite challenging to diagnose, depending largely on the site of involvement. In bones, HS frequently presents as an infiltrative lesion with bony erosion, suggestive of more common metastatic lesions [5]. Differential diagnoses include metastatic lesions, primary bone malignancies, and chronic infections.

Histologically, several previous cases of HS have been incorrectly diagnosed as lymphomas, leukemia, or carcinomas. Definitive diagnosis is established by the anatomo-pathological study of the affected organ,

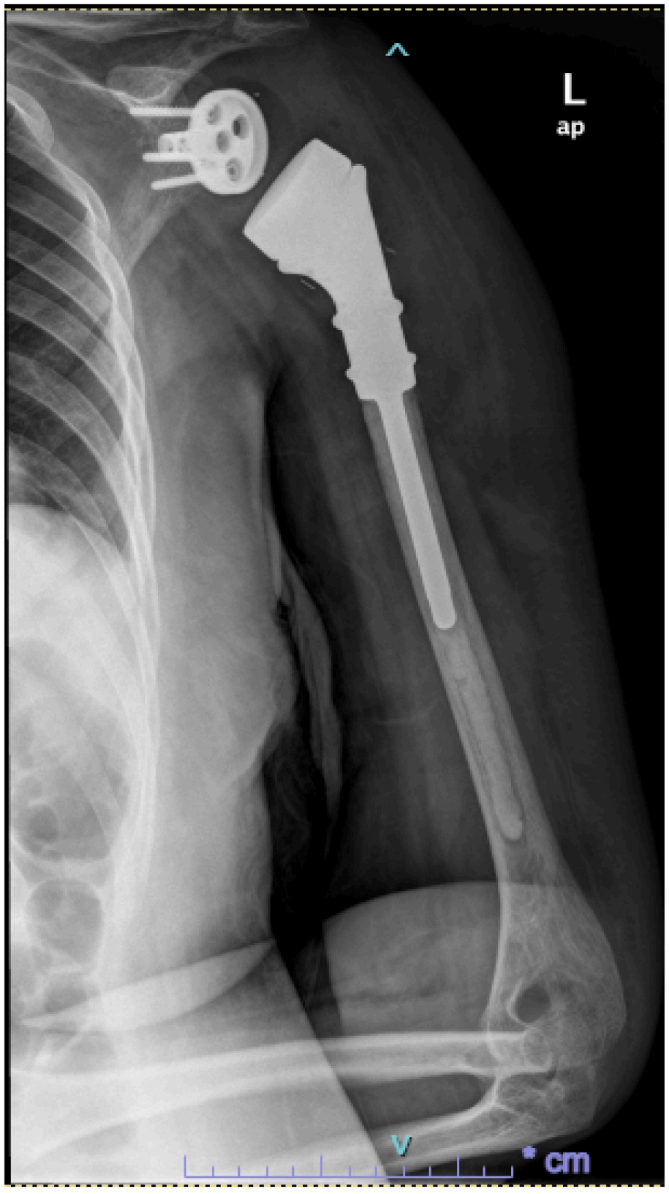

Fig. 3. AP view of left humerus. Post-surgical resection and reconstruction using MUARS-Humerus inverse prosthesis.

with immunophenotypic analysis and genetic studies[2]. The disease is characterized by histocytic proliferation, with positive expression of macrophage-associated antigen, CD68, and lysozyme, and negativity for CD1a, CD21, and CD35. Recently, CD163 has become a promising marker for histiocytic neoplasms. HS must be morphologically differentiated from malignant Langerhans cell histiocytosis, dendritic cell sarcomas, anaplastic large cell lymphomas, inflammatory pseudotumors, and other sarcomas [1,6].

In our case, the diagnosis of HS was established by an immunophenotypic study with markers similar to those found in the literature. The anatomo-pathological study identified large cells with irregularly shaped nucleui and nucleoli, with some showing binucleate forms and eosinophilic cytoplasm positive for CD68, CD163, and CD4 antigens, thereby proving histiocytic proliferation. Additionally, they were negative for CD1a and Langerin, which excluded the differential diagnoses of giant cell lymphoma and dendritic cell sarcoma.

Due to its rarity, no standard treatment has been developed for HS. In addition, the natural history of HS is mainly unknown and variable. Therapeutic choices are primarily based on the extent of disease, patient performance status, and the medical team's experience. Localized disease is best treated by surgical resection, with or without radiotherapy. On the other hand, treatment for advanced disease usually consists of systemic chemotherapy. Such treatments are based on a limited number of case reports [7] and are sometimes challenging during pregnancy.

The prognosis of HS is poor. Disease stage and tumor size are important prognostic indicators. This poor prognosis, especially in disseminated disease, results from the difficult systematization of a standard therapeutic protocol with good response. In such cases, most patients die from progressive disease in approximately two years. Localized disease has a favorable prognosis and is often associated with adjuvant methods (chemotherapy or radiotherapy) along with oncological surgical resection [7].

The incidence of malignancy during pregnancy is rare, with a reported incidence of 0.07% to 0.1% [8,9], and guidelines regarding clinical diagnostics and treatment of musculoskeletal tumors during pregnancy do not exist [10]. Misdiagnosis is also common. This is indicated by the fact that the period between the first consultation and correct diagnosis is significantly longer for pregnant patients, with an average delay of 4–6 months for diagnosis [11]. Thus, the delay in diagnosis in our patient was consistent with the literature. Although radiation exposure should be avoided whenever possible during pregnancy, especially in the first trimester, a single radiograph after the first trimester has negligible risk and can be performed safely. Other imaging modalities, such as ultrasound and MRI, are safe and can be performed at any stage of pregnancy [12]. Treatment of malignancy during pregnancy requires a multidisciplinary approach, with careful analysis and consideration of the necessity for and the extent to which treatment is acceptable for both the mother and fetus [13].

In this case, the treatment option was surgical resection (modified Tikhoff-Linberg-type IA technique) because the disease was localized in the proximal humerus without any systemic features. Limb-sparing inter-scapulothoracic resection (Tikhoff-Linberg surgery) is a surgical option for bony and soft tissue tumors of the proximal humerus and shoulder girdle. Classically, this procedure comprises the resection of the proximal third of the humerus and the extra-articular removal of the shoulder joint, the distal third of the clavicle, and the entire scapula and the adjacent soft tissue [14]. The selected patients must not have tumors in the thoracic wall or neurovascular bundle. The resection levels are variable and depend on the extension of the tumor [15].

4. Conclusion

In conclusion, this is the first reported case of primary HS with localized bone involvement during pregnancy. Considering the rare nature of the disease, we emphasize the need for a multidisciplinary approach for effective treatment. High clinical suspicion and pathological examination with specific immunohistochemical phenotyping are essential and play an important role in early diagnosis and prognosis.

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Ethical approval

I certify that this kind of manuscript does not require ethical approval by the Ethical Committee of our institution.

Consent

Written informed consent was obtained from the patient for

publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

Ayman Al-Amri: Writing the manuscript, corresponding author, and operating surgeon.

Murtadha Al-Khabori: Writing and reviewing the manuscript.

Nihal Al-Riyami: Writing and reviewing the manuscript.

Ibrahim Al Haddabi: Writing the manuscript.

Research registration

Not applicable.

Guarantor

Ayman Al-Amri.

Declaration of competing interest

None declared.

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