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Case Reports

Atypical presentation of Hodgkin lymphoma with predominant osseous involvement in a 10-year-old child

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ABSTRACT

Hodgkin lymphoma (HL) in pediatric patients typically presents with mediastinal and supradiaphragmatic lymphadenopathy. Predominant skeletal involvement at diagnosis is exceptionally rare and represents a significant diagnostic challenge. We present the case of a 10-year-old child with a 6-month history of progressive weight loss, right hip pain, and gait disturbance. Initial imaging suggested non-malignant orthopedic conditions, but further studies revealed multifocal osteolytic bone lesions. A bone biopsy ultimately confirmed classical Hodgkin lymphoma. A Positron Emission Tomography/Computed Tomography (PET/CT) scan demonstrated intensely hypermetabolic osseous lesions with only minimal, disproportionately mild, nodal disease. Based on the Lugano classification, the patient was classified as Ann Arbor stage IV. The patient exhibited rapid clinical improvement following the initiation of OEPA (Vincristine, Doxorubicin, Etoposide, Prednisone) induction chemotherapy. This case underscores the importance of including lymphoproliferative disorders in the differential diagnosis of unexplained multifocal osteolytic lesions in children and highlights the critical role of timely tissue biopsy.

Keywords: Bone, chemotherapy, child, extralymphatic, Hodgkin lymphoma

Introduction

Hodgkin lymphoma (HL) is the most common hematologic malignancy in adolescents and young adults, accounting for approximately 3-5% of all pediatric cancers (1). The disease typically presents supradiaphragmatic lymphadenopathy, with mediastinal involvement observed in 60-90% of cases at diagnosis (1,2). Extranodal involvement, affecting sites such as the liver, spleen, or lungs, occurs in 10-15% of advanced cases (3).

While bone marrow infiltration can be seen in 2-5% of patients, the skeletal involvement at presentation accounts for only 0.1–15% of cases, Such an atypical presentation poses substantial diagnostic challenges, as initial radiological findings often mimic other conditions like metastatic bone disease, osteomyelitis, or Langerhans cell histiocytosis (LCH) (4,5). Definitive diagnosis invariably requires histopathological confirmation of CD30+ Hodgkin and Reed-Sternberg cells (1).

We present an atypical case of pediatric Hodgkin lymphoma characterized by predominant multifocal skeletal involvement and minimal nodal disease, emphasizing the necessity of a broad differential diagnosis and early bone biopsy in children presenting with multifocal osteolytic lesions.

Case Report

A 10-year-old male presented with a six-month history of progressive constitutional symptoms and right hip pain. The clinical course was characterized by an estimated weight loss of 10 kg, nocturnal diaphoresis, and a functional gait disturbance. His past medical history was unremarkable. On physical examination, the child showed signs of malnutrition and generalized asthenia. The musculoskeletal exam revealed restricted mobility of the right hip and an antalgic gait. Small, non-tender submandibular lymph nodes (approximately 1.0–1.5 cm) were palpable bilaterally; however, no other significant lymphadenopathy was noted.

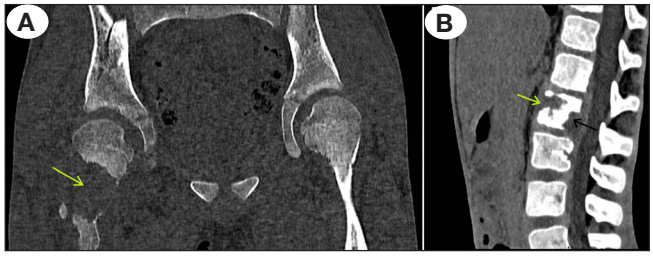

Figure 1: CT of the right hip demonstrating an anterior para-osseous osteolytic mass at the upper extremity of the right femur, associated with other mixed osteolytic and osteocondensing vertebral lesions at L1 and L2.

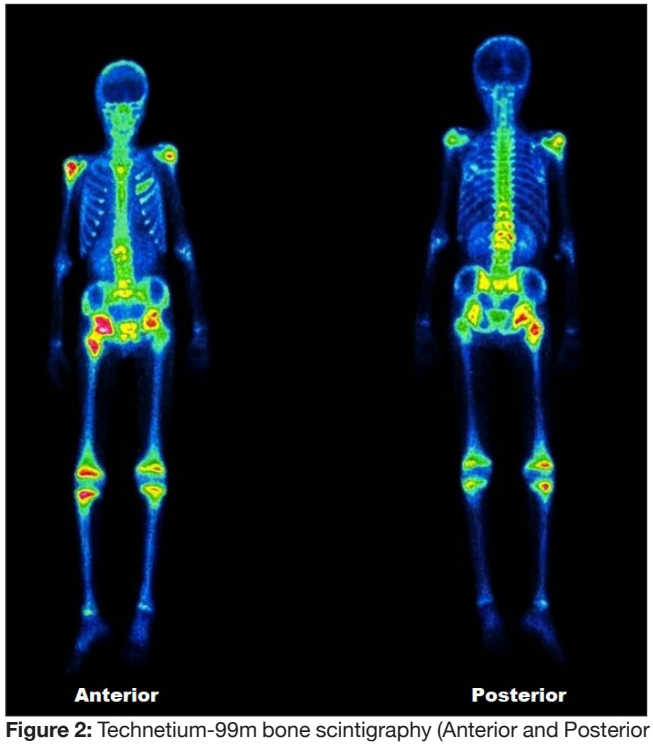

Figure 2: Technetium-99m bone scintigraphy (Anterior and Posterior views) showing multiple sites of pathological hyperfixation in the axial and peripheral skeleton.

Laboratory investigations showed a mild normocytic anemia (Hemoglobin: 10.4 g/dL) and an elevated erythrocyte sedimentation rate (40 mm/h). Biochemical analysis revealed reduced serum iron (15.23 µg/dL) and hypoalbuminemia (24.5 g/L). Lactate dehydrogenase (LDH) and calcium levels were within normal limits.

The diagnostic workup began with imaging of the right hip. Ultrasound and plain radiography were initially interpreted as a slipped capital femoral epiphysis (SCFE) with a grade 1 slip and an avulsion of the lesser trochanter. However, given the systemic symptoms, further investigation was pursued. A computed tomography (CT) scan of the hip revealed an anterior para-osseous osteolytic mass at the upper extremity of the right femur, along with mixed osteolytic and sclerotic lesions in the L1 and L2 vertebrae (Figure 1). Subsequently, a Technetium-99m bone scintigraphy confirmed multiple sites of pathological hyperfixation in the bilateral femoral heads, lumbar vertebrae, and anterior costal arches (Figure 2).

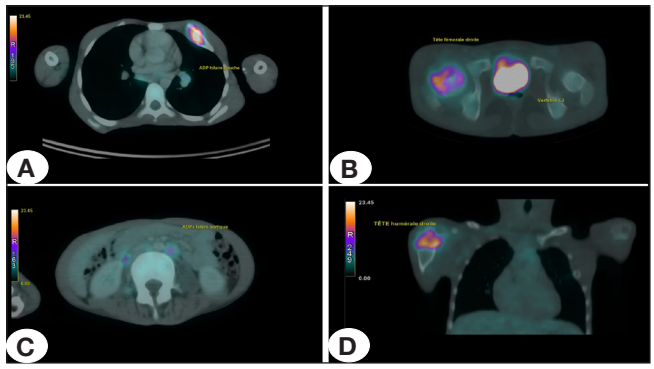

Figure 3: PET/CT images (Coronal and Transaxial) displaying intensely hypermetabolic osteolytic lesions in the right femoral head and L1 vertebral body.

For definitive staging, an 18F-FDG Positron Emission Tomography (PET/CT) scan was performed. This confirmed disseminated disease, demonstrating intensely hypermetabolic osteolytic lesions in the right humeral head, right femoral epiphysis, L1 vertebral body, and left third rib (Figure 3). The scan revealed only minimal mediastinal and retroperitoneal lymphadenopathy (largest node 15 mm), which was disproportionately mild compared to the extensive skeletal burden. No hepatic or splenic involvement was detected. A subsequent bone marrow biopsy was performed and showed no evidence of lymphoma involvement. According to the Lugano classification, the findings corresponded to Ann Arbor Stage IV disease (8,9).

An ultrasound-guided core biopsy of the right femoral neck lesion was performed. Histopathological examination revealed a cellular infiltrate containing small lymphocytes, histiocytes, and scattered multinucleated giant cells (Figure 4A). Immunohistochemical analysis identified large neoplastic cells with a CD30+ (Figure 4B), CD15- (Figure 4D), CD20-, CD3-, and weak PAX5+ (Figure 4C) immunophenotype.The available tissue was consumed for these initial diagnostic panels; consequently, additional markers, including EBER in situ hybridization and CD45 immunohistochemistry, were not performed.

The patient was treated according to the EuroNet-PHL-C1 protocol for Stage IV disease. He received two cycles of OEPA induction chemotherapy (Vincristine, Doxorubicin, Etoposide, Prednisone). One month following treatment initiation, the patient showed significant clinical improvement, including pain reduction, improved ambulation, and weight gain.

Follow-up and Outcome

An interim PET/CT scan was performed after the two OEPA cycles to assess treatment response. The scan demonstrated a robust morpho-metabolic response. However, the response was classified as incomplete due to residual bone lesions exhibiting FDG uptake levels marginally above the liver background (Deauville Score of 4), the patient proceeded with consolidation therapy consisting of 4 cycles of COPDAC (Cyclophosphamide, Prednisone, Vincristine, Doxorubicin, Dacarbazine) (Figure 5).

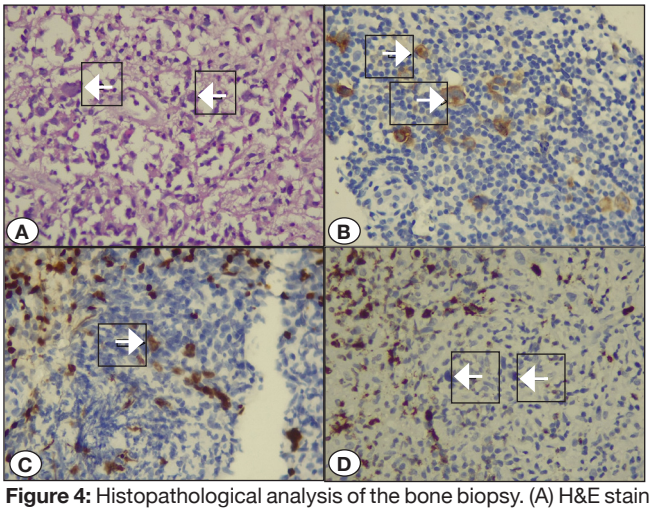

Figure 4: Histopathological analysis of the bone biopsy. (A) H&E stain (400x) showing classic Reed-Sternberg cells within an inflammatory milieu. Immunohistochemistry demonstrates that the neoplastic cells are strongly positive for (B) CD30, weakly positive for (C) PAX5, and negative for (D) CD15, confirming classical Hodgkin lymphoma.

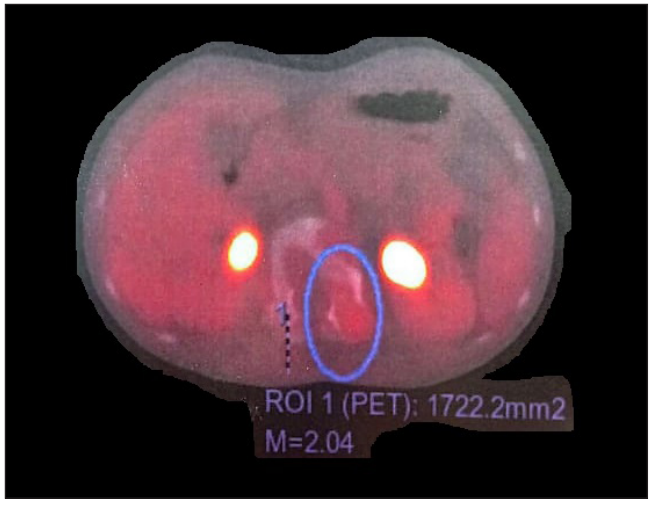

Figure 5: Evaluation revealed a robust morpho-metabolic response. However, the response was classified as incomplete due to residual bone lesions exhibiting FDG uptake levels marginally above the liver background (consistent with a Deauville Score of 4).

Discussion

This case illustrates a highly atypical presentation of pediatric Hodgkin lymphoma, defined by predominant destructive skeletal involvement with minimal nodal disease. This presentation contrasts sharply with the typical pattern of bulky lymphadenopathy. The discordance between the minimal nodal disease and extensive osseous destruction is a salient feature of this case, distinguishing it from typical advanced-stage HL. Due to the overwhelming discordance between the extensive, destructive cortical bone lesions and the minimal nodal burden detected only on PET/CT, this case is best classified as Primary Osseous Hodgkin Lymphoma (POHL). While primary nodal HL with secondary skeletal dissemination is more common, the presentation of multifocal destructive bone lesions as the herald symptom with disproportionately mild lymphadenopathy justifies the POHL designation.

The differential diagnosis for multifocal osteolytic lesions in this age group is broad, including metastatic neuroblastoma, Ewing sarcoma, osteomyelitis, and Langerhans cell histiocytosis (LCH) (4,5). The immunophenotype (CD30+, CD15-, PAX5+) and negative staining for CD1a, S100 expression on biopsy definitively excluded this diagnosis. The exact mechanism of primary osseous involvement in HL remains unclear but may involve retrograde lymphatic spread or hematogenous dissemination.

The diagnosis of classical HL in bone biopsies is often challenging due to sample size constraints and decalcification artifacts. While CD45 and EBER were not assessed in this case due to tissue exhaustion, the diagnosis was supported by pathognomonic Reed-Sternberg cell morphology in a typical inflammatory milieu, combined with a CD30+/weak PAX5+/CD20-/CD3- profile. Although CD15 was negative, this is observed in approximately 15% of classical HL cases and does not preclude the diagnosis when other markers are consistent (9).

Furthermore, while EBER is a valuable tool for identifying EBV-associated HL, particularly common in the pediatric population, the diagnosis of HL remains primarily a morphologic and immunophenotypic one. In the context of POHL, where tissue is scarce, the exclusion of more common mimics through the available panel was prioritized (10).

Prognostically, Stage IV HL has historically carried a guarded prognosis. However, modern risk-adapted protocols like EuroNet-PHL-C1, which use interim PET/CT to guide therapy intensity, have significantly improved outcomes (6, 7). Our patient's rapid clinical and metabolic response to induction chemotherapy is encouraging and aligns with reported outcomes from this regimen.

Conclusion

In conclusion, this case reinforces that Hodgkin lymphoma must be considered in the differential diagnosis of pediatric bone lesions, even in the absence of significant lymphadenopathy. A thorough, multidisciplinary diagnostic approach, centered on timely tissue biopsy, is essential for accurate diagnosis and effective management.

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