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CASE REPORT

Non-Hodgkin lymphoma of bone of the femur and humerus: a case report and review of the literature

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Abstract

Lymphoma of bone is a rare neoplasm composed of malignant lymphoid cells, producing a tumefactive lesion within bone. We report a 13-year-old male who presented with progressively increasing swellings at the right shoulder and right mid-thigh for one month. Radiological images revealed lytic destructive lesions associated with soft tissue masses in both sites and a pathological fracture on the right humerus. The patient had no significant medical history. Histological, immunohistochemical and fluorescent in-situ hybridization assessment of biopsies from the lesions confirmed the diagnosis of primary non-Hodgkin lymphoma of bone. Unfortunately, due to coronavirus disease 2019 outbreak, the patient was unable to follow-up treatment and died shortly after establishment of the diagnosis. Delay in diagnosis and treatment is of serious concern when it comes to improve the prognosis of patients with this disease.

INTRODUCTION

Primary non-Hodgkin lymphoma of bone is defined as a malignant lymphoid neoplasm producing at least one mass within bone without the involvement of extra-regional lymph nodes

and extra-nodal sites for at least 6 months. The presence however of regional lymph nodes in due course of the disease does not exclude the diagnosis [1]. The tumours are rare, comprising <1% of all non-Hodgkin lymphoma [2, 3]. Radiologically they have a wide variety of presentation, sometimes with a virtually

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Figure 1: A photograph showing swellings of the right shoulder (A), and right thigh (B) with surgical scars and suture marks in both following incision biopsies.

normal X-ray with a large soft tissue mass on magnetic resonance imaging (MRI) [4]. The histological diagnosis of these lymphomas may be a daunting task related to the rarity of its presentation, thus scrupulous immunohistochemical studies are essential for the definitive diagnosis [1–3]. Herein, we report the case of a 13-year-old male with a primary non-Hodgkin lymphoma of bone involving femur and humerus and a brief review of the literature.

CASE PRESENTATION

A 13-year-old boy was brought to our centre because of nearly simultaneously started swellings at the right shoulder and right mid-thigh with duration of 1 month. Each swelling was gradual in nature and progressively increased over time. The patient reported progressive weight loss and dizziness. His parents were peasants and his past medical history was unremarkable. Given the profession of the parents exposure to pesticides was considered, this could however not be documented.

On general examination, he was weak, pale, wasted and tachycardic with a pulse rate of 136 beats/minute. Blood pressure, respiratory rate and body temperature were within normal limits. On local examination, he had a firm round, non-tender, immobile swelling (11 × 5 cm) at the right shoulder (Fig. 1A). At the right mid-thigh, he had a circumferential fixed and non-tender (12 × 10cm), (Fig. 1B). Laboratory findings revealed the haemoglobin of 8.5 g/dl (11–15 g/dl), raised ESR of 28 mm/h (0–19 mm/1 h), normal leukocytes $6.13 \times 10^9/L$ (4.00–11.00)/l and AST: 40.60 (5–40)/l. Serum creatinine 93 (62–106 $\mu\text{mol/l}$), AST 40.60u/l (2.00–40.00 U/l), ALT 15.90 U/l (2.00–41.00 U/l). Other parameters including a bone marrow aspirate were essentially normal.

Conventional radiography of the right femur demonstrated a huge soft tissue swelling with diffuse permeative lesions in the mid and distal femoral shaft and medial cortical destruction (Fig. 2A). The right shoulder revealed large soft tissue swelling associated with a pathological fracture of the proximal humerus, (Fig. 2B). Chest X-ray and abdomino-pelvis ultrasound were normal i.e. no signs of metastasis seen. A diagnosis of sarcoma was suggested. Biopsies from the lesions were taken and the patient was discharged with a plan to start treatment in 2 weeks after establishing the histopathological diagnosis.

Histopathological findings of the two lesions highlighted a similar morphology showing diffuse proliferation of monotonous medium to large-sized atypical lymphocytic cell population (Fig. 3A and B). Using the limited immunohistochemical panel tests that were locally available, tumour cells were strongly positive for CD20 and CD45 (Fig. 4A and B), but negative with

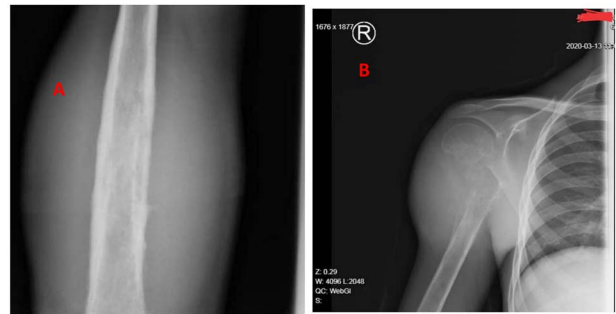


Figure 2: X-ray showing diffuse permeative lesion of mid and right distal femoral shaft associated with a large soft tissue mass (A), and right shoulder mass associated with proximal humeral destruction and a pathological fracture (B).

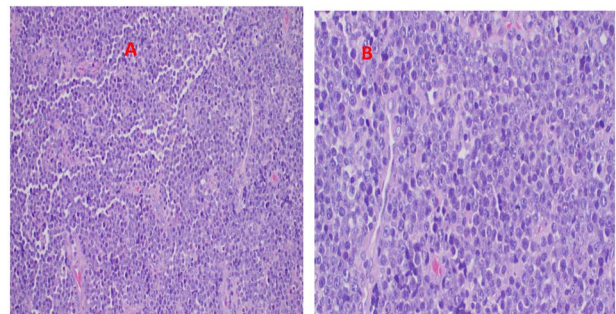


Figure 3: Histopathology of the right-shoulder mass showing diffuse lymphoid cellular proliferation, H&E, ×40 primary magnification (A), and femur mass demonstrating a diffuse atypical lymphoid cell population, H&E, ×100 primary magnification.

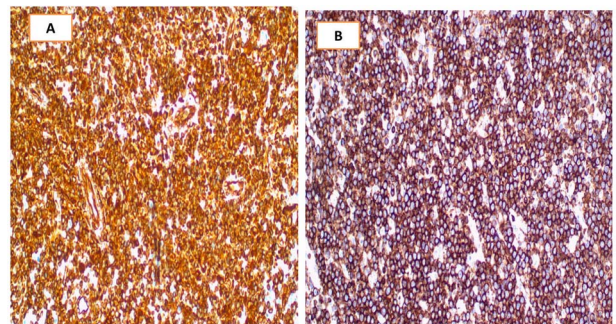


Figure 4: Strong immunopositivity of the tumour cells with CD45 IHC, ×40 primary magnification (A) and CD20 IHC ×60 primary magnification (B).

CD99 and cytokeratin 20. Diagnosis of a primary non-Hodgkin lymphoma of bone (DLBCL) with differential of Ewing sarcoma was made. Due to the rarity of the disease entity, tumour tissue blocks were shipped to Leiden University Medical Center, (Leiden, The Netherlands) for expert consultation. There, wider immunohistochemical panel tests and FISH for EWSR1 split, FUS split, BCOR split and CIC split were performed. All split-apart FISH showed the absence of split signals of tested genomic regions thus excluded the diagnosis of Ewing sarcoma and other small blue round cell tumor (SBRCT). Immunohistochemical staining were conclusive for the diagnosis of DLBCL (CD45+, CD20+ while CD99, Desmin, MYOD1, PAS negative). Due to the COVID-19 outbreak, the patient could not manage to turn back for oncological treatment. Unfortunately, he succumbed ~30 days post-hospital discharge.

DISCUSSION

Primary bone lymphoma is uncommon disease accounting for <5% of extranodal lymphoma and <1% of all non-Hodgkin lymphoma. Slight male preponderance has been documented and can occur at any age, with a mean age of 48 years [1–5]. The vast majority are B-cell lymphoma. Interestingly, these tumours can be mixed with reactive CD8+ T-cell infiltrates which can be confusing for recognizing it as a non-Hodgkin lymphoma of B-cell origin [6]. The density of the CD8+ T-cell infiltration and expression of BCL2 has proven to be of prognostic value [6]. At the tumour-genetic level, these lymphomas characteristically show a gain of chromosome 1q and amplification of 2p16.1 confirming their germinal centre-like phenotype and distinct makeup from other lymphomas [6].

Any skeletal bone can be involved; however, femur and humerus have been reported frequently [2, 3]; as it was the case in our patient. Similarly, patients with these tumors present with bone pain, palpable mass pathologic fracture or neurologic symptoms with spine involvement without B-symptoms [2–4]. The histological diagnosis of bone lymphoma may be very problematic especially in resources limited settings undoubtedly related to the rarity of its presentation. In their study, Heyning et al. [8], on array-based comparative genomic hybridization analysis, they reported recurrent chromosomal alterations in primary diffuse large B cell lymphoma [8]. The frequent radiological features include destructive lytic lesion with permeative margins associated with soft tissue mass [7, 9]. Differential diagnosis at the H&E level includes Ewing sarcoma and other SBRCT especially at the age of the current patient. However, it should be noted that Ewing sarcoma is very rare among patients with African ancestry probably as a result of genetic factors [10].

Treatment of primary bone lymphoma may include a combination of radiotherapy and chemotherapy, while in contrast to nodal diffuse B-cell lymphoma the nuclear factor-κB does not seem to be an attractive therapeutic target [7]. Surgery is indicated only when there is fracture [7]. Prognosis of the disease is relatively good with a 5-year-survival > 80% when treated with chemo-radiotherapy [3]. Factors associated with poor prognosis include advanced disease (>60 years) and site of mandible-/maxilla [9]. Our patient had poor outcome probably due to late presentation coupled with delayed treatment. Because of anxiety related to novel COVID-19 pandemic, the patient opted to stay at home postponing treatment. Delaying chemotherapy could lead to upstaging of the tumour while delaying palliative chemotherapy could lead to worsening of quality of life.

Primary bone lymphoma especially in African paediatric population is rare. Delay in diagnosis and treatment as it was the case in our patient is of concern when it comes to improve the prognosis of patients with this disease. Clinicians should have a suspicion of index for unusual cases and thus vigorously work-up including proper and timely diagnosis for optimal patient care.

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CONFLICT OF INTERESTS

The authors declared that no conflicting interests exist.

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None was received.

ETHICAL APPROVAL

The research meets ethical guidelines and adheres to the local legal requirements.

CONSENT

Agreement by the patient's parents was obtained prior to submission of the manuscript and noted in patient's chart.

GUARANTOR

Dr. Alex Mremi is the guarantor of this paper.

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