Rare disease

A rare entity of primary extranodal diffuse large B cell lymphoma of the lower limb calf in an HIV-infected young adult on highly active antiretroviral therapy

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Summary

Primary cutaneous and skeletal muscle lymphomas are particularly rare phenomena in HIV sero-positive patients. The authors report a case of primary extranodal malignant diffuse large B cell lymphoma of the left gastrocnemius in a 21-year-old young adult who presented to the Infectious Diseases Institute, Kampala, Uganda having been on antiretroviral therapy for 2 years. The patient is still undergoing chemotherapy.

BACKGROUND

Diffuse large B cell lymphomas (DLBCLs) in HIV-seropositive persons can either involve the lymph nodes or an extranodal site.¹ The commonest extranodal site is the brain accounting for 15–30% of HIV-associated non-Hodgkin's lymphomas (NHLs).¹ Other extranodal sites include the gastrointestinal tract, the liver, the lungs, in the skin as testicular lymphomas, the bone marrow and rarely in the female genital tract.^{1 2} To the best of our knowledge, primary cutaneous and skeletal muscle DLBCLs in HIV-seropositive persons are extremely rare, with only three cases being reported in literature.^{3–5} The case we present in this report is an extremely rare case of primary extranodal DLBCL arising from the left gastrocnemius in an HIV-seropositive adolescent on highly active antiretroviral therapy (HAART) with metastatic involvement of the left tibialis anterior, left hypogastrium and right lower back.

CASE PRESENTATION

A 21-year-old young adult presented with a 5-month history of a painful left nodular gastrocnemius mass with additional nodular masses involving the left tibialis anterior (figure 1), left hypogastrium and right lower back. He had reported the primary lesion as being the nodular masses involving the left gastrocnemius with secondary cutaneous involvement of the left hypogastrium and right lower back. There were associated symptoms of intermittent low-grade evening fevers, drenching night sweats, weight loss and loss of appetite. He had no prior history of lymphoma. He had been on HAART – tenofovir, lamivudine and nevirapine since September 2009 and reported 100% adherence. He had initially presented to the Infectious Diseases Institute in 2009 with WHO stage II disease – with a history of recurrent upper respiratory tract infections and weight loss <10% of body weight and a nadir CD4 count of 45 cells/ml.

General examination revealed an ill-looking young man with no clinical evidence of anemia, jaundice or lymphadenopathy. Physical examination showed a 10×8 cm left

nodular gastrocnemius mass with additional nodal masses measuring 6×3 cm involving the left tibialis anterior, 4×3 cm mass involving the left hypogastrium and a 6×4 cm mass involving the right lower back. Dermatological examination revealed multiple firm cutaneous nodules over the left gastrocnemius and tibialis anterior regions which were neither pulsatile nor cystic. The smaller solid masses located at the left hypogastrium and the right lower back were erythematous in appearance with associated skin ulceration. His vital signs were as follows: blood pressure 110/70 mm Hg, pulse rate 98 beats/min, respiratory rate 12 breaths/min and body temperature 35.4°C. Precordial, respiratory and abdominal examinations were unremarkable.

INVESTIGATIONS

Laboratory studies revealed a white blood cell count of 5900/mm³ and an elevated erythrocyte sedimentation rate of 128 mm/h (0–15 mm/h). Renal function tests, liver function tests, serum cryptococcal antigen, hepatitis B surface antigen and antibody titres and *Treponema pallidum* haemagglutination assay were normal. CD4+ counts were 158 cells/ml (9%). The viral load was undetectable (<400 copies/ml).

The plain radiograph of the left leg showed soft tissue swelling involving the anterior and posterior aspect of the leg with no tibia or fibula involvement. The chest radiograph and abdominal CT scan were unremarkable. The CT scan of the left lower limb revealed a solid mass with a diameter of 6.5 cm arising from the skeletal muscle, involving the proximal two thirds of the left leg with no adjacent osseous involvement.

Histopathology of an excision biopsy which was conducted under local anesthesia of the left lower limb mass revealed a DLBCL (figures 2). Bone marrow aspiration and biopsy demonstrated no evidence of infiltration by lymphoma. Cerebrospinal fluid examination was negative for lymphoma infiltration. Immunocytochemical staining and immunophenotypic studies of the tumour could not be done due to the high costs involved.

Figure 1 Left gastrocnemius swelling and nodular swelling involving the left tibialis anterior. Also visible is the biopsy site on the medial aspect.

DIFFERENTIAL DIAGNOSIS

- Rhabdomyosarcoma
- Osteosarcoma.

TREATMENT

The patient was then referred to the national oncology institute for the management of DLBCL. Following the prechemotherapy investigation, the patient was commenced on the conventional chemotherapy regimen of cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP) in combination with radiotherapy. Continual adherence to cotrimoxazole and HAART is continually being emphasised.

OUTCOME AND FOLLOW-UP

The patient has so far completed three cycles of CHOP having commenced in November last year with excellent results. There was complete and partial resolution of the soft tissue secondary involvements to the left hypogastrium and right lower back, respectively. There has also been partial reduction in the left gastrocnemius and left tibialis anterior nodular masses. He is still undergoing chemotherapy which will be followed by radiotherapy.

DISCUSSION

HIV infection causes severe impairment of the immune system particularly to the CD4 lymphocytes which significantly increases the risk of developing lymphomas. Extra-

nodal HIV-associated NHLs generally involve regions which are regarded to as lymph node rich regions particularly the head, neck, gastrointestinal tract, liver, small bowel, lungs, stomach, in the skin as testicular lymphomas, the bone marrow and rarely in the female genital tract.^{1 2 6}

We have presented a rare entity of primary DLBCL localised in the skeletal muscle of the left gastrocnemius with subsequent metastasis to the left tibialis anterior muscle and cutaneous involvement of the left hypogastrium and right lower back with no bone involvement in an HIV seropositive young adult. Extranodal NHL of the soft tissue or skeletal muscle is extremely rare affecting only 0.1% of cases.^{7 8} Because of the rarity of the disease, we reviewed the current medical literature for primary HIV-associated soft tissue and skeletal muscle DLBCL. We found only three documented cases of primary HIV-associated DLBCLs of the soft tissues and skeletal muscles particularly the shoulder, muscles of mastication and the breast.³⁻⁵

DLBCLs are an aggressive form of NHLs. They morphologically show a diffuse spectrum of peripheral B-blasts, centroblasts or immunoblasts as was seen in our patient⁹ (figure 2). The standard treatment for DLBCL is combination chemo- and immunotherapy which consists of rituximab, doxorubicin, cyclophosphamide, vincristine and prednisone (R-CHOP) and radiotherapy.¹⁰ The patient however, showed remarkable improvement following three cycles of CHOP. He was unable to access rituximab due to financial constraints. He is scheduled though to receive radiotherapy after completion of chemotherapy.

Figure 2 Sheets of lymphoid cells. There is pleomorphism in cellular and nuclear size and shape. Majority of the cells are medium sized and have ample volume of amphophilic cytoplasm. Their nuclei are round, non-cleaved with vesicular chromatin and multiple nucleoli (centroblastic). Other cells with single central prominent nucleoli are also seen (immunoblastic). Large sized with multi-lobated nuclei are also seen (H&E stain; magnification, x40).

The documented DLBCL cases were aged 34 years, 52 years and 40 years, respectively.^{3–5} Our case of a 21-year-old young adult however, is the youngest documented case of primary DLBCL of the skeletal muscles. No other cases of HIV-associated DLBCL of the lower limb muscles in HIV patients with dimensions compared with the one reported in this report have ever been described in the literature. The other aspect we found unique about this case was the development of DLBCL in the muscle of an HIV sero-positive patient who had been on HAART for 2 years and was virologically suppressed.

Learning points

- ▶ Primary skeletal muscle lymphomas are rare.
- ▶ This case reported an extremely rare entity of DLBCL originating from the left gastrocnemius muscle and subsequently metastasising to the left tibialis anterior muscle, with cutaneous involvement of the left hypogastrium and right lower back in an HIV infected young adult.
- ▶ It therefore is important for clinicians to consider a differential diagnosis of primary DLBCL in HIV sero-positive persons with suspicious nodular masses.

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Competing interests None.

Patient consent Obtained.

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