A 40-year-old woman presented with a history of a painful left axillary mass that had progressively increased in size. She reported symptoms of night sweats and weight loss. Physical examination revealed a 17×13 cm left axillary nodal mass. Her left breast had the clinical appearance of mastitis. Abnormal laboratory studies revealed elevated serum uric acid (0.50 mmol/l, normal 0.15 - 0.35 mmol/l) and lactate dehydrogenase (1 009 U/l, normal 100 - 190 U/l) levels. An enzyme-linked immunosorbent assay was positive and the initial CD4+ count was 435 cells/μml. Microscopic examination of the lymph node mass confirmed a diffuse large B-cell lymphoma (DLBCL). Bone marrow aspiration and biopsy demonstrated no evidence of infiltration by lymphoma. Cerebrospinal fluid (CSF) examination was negative for lymphoma infiltration. Both the CSF cryptococcus Indian ink and latex tests were negative, but a positive Varicella zoster polymerase chain reaction (PCR) test was reported.

A mammogram was not feasible owing to painful ulceration of the breast mass. A computed tomography (CT) scan of the thorax and abdomen revealed a 5 cm lymphoid nodal mass in the left axilla and a 3.4 cm left supraclavicular lymph node. A gallium scan was consistent with uptake in an area overlying the left breast, anterior chest wall and markedly enlarged left axillary lymph nodes. Normal gallium biodistribution was seen in the rest of the body (Fig. 1). The case was considered to be a stage IIbAIDS-NHL.

The standard CHOP regimen consisting of cyclophosphamide 750 mg/m², doxorubicin 50 mg/m² and vincristine 1.4 mg/m² on day 1 and prednisone 60 mg/day on days 1 - 5 every 3 weeks was started. She completed 3 cycles without significant toxicity but then presented with clinical progression. The left axillary lymph node and breast mass had the appearance of breast cancer with erythema, oedema and nipple retraction. A solid mass was palpable within the breast with associated skin ulceration and multiple cutaneous nodules over the left infraclavicular region (Fig. 2).

However, an infection with varicella zoster virus (VZV) was clinically apparent along dermatome T11 and 5 weeks later she reported...
progressive bilateral lower limb pareses with associated weakening in bladder control. Magnetic resonance imaging (MRI) of the vertebral column showed degenerative changes with no focal spinal cord lesions. The patient defaulted and returned 8 weeks later reporting that the mass was more painful and larger with newly developed nodular cutaneous lesions of the left breast region. She was given a 4th cycle of CHOP and started concomitant antiretroviral therapy (lamivudine, stavudine and elavirenz). Four weeks later there was no visible change in the axillary and breast mass. The chemotherapeutic regimen was changed to second-line CMV (cyclophosphamide 750 mg/m², methotrexate 60 mg/m² and vincristine 1.2 mg/m²). A follow-up review revealed overt clinical progression, as there was an increase in both the size of the breast mass and the number of cutaneous lesions. A clinical oncology consult offered palliative radiotherapy, as she appeared resistant to first- and second-line chemotherapy.

The clinical dilemma was as follows: was this (i) a systemic NHL with extranodal involvement of the left breast; (ii) an overlooked primary breast lymphoma (PBL); or (iii) a misdiagnosed primary breast carcinoma? Before commencement of radiotherapy histological examination therefore again confirmed positivity for CD45 and CD20 lymphoma cells compatible with a DLBCL.

**RADIOThERAPY**

Palliative external beam radiotherapy (EBRT) with cobalt-60, consisting of 2 Gy × 18 fractions (36 Gy), was completed. The clinical target volume was determined by CT scan (Fig. 3). This included the left axillary nodal mass, the immediate lymphatic drainage, the left breast, the remaining left anterior chest wall and the left supra-clavicular region. Treatment was delivered using 8 MV photons with a 1 cm daily bolus.

**DISCUSSION**

NHL is the second most common AIDS-associated malignancy and the AIDS-defining diagnosis in an estimated 1.6 – 8% of HIV patients. PBL is rare, comprising 0.4 – 0.5% of all breast malignancies reported. Secondary breast lymphoma represents approximately 0.07%. When primary and secondary lymphoma cases are considered the most common sub-type is DLBCL (45 – 79%). Systemic AIDS-NHL treatment should include therapy for opportunistic infections (OIs) and the underlying HIV and involves modifications of conventional therapy.

There appears to be a survival advantage for patients receiving CHOP-ART therapy, suggesting that a decrease in OIs was responsible for reduction in morbidity. Based on a 15 – 20% central nervous system involvement at presentation, CNS prophylaxis is considered standard practice in AIDS-NHL. Series with chemotherapy reported a 50% complete response and a median survival of 18 months. An improved response rate does not significantly add to survival owing to relapse and death from AIDS progression.

Neurological manifestations of VZV have been described. Encephalitis due to VZV infection results from small-vessel vasculitis, presenting weeks after the original infection. An urgent MRI scan or myelography is required to exclude extrinsic cord compression due to bacterial abscess, tuberculous abscess or lymphoma. If these are excluded, CSF should be sent for VZV PCR.

The clinical and radiological features of PBL and carcinoma are similar, as both are diseases of middle age with a median onset in the 6th decade. Symptoms include pain, fever, sweating and weight loss. Contralateral involvement can be synchronous or metachronous up to 10 years after the primary lesion. Pathology remains the only way to differentiate between these malignancies, as treatment differs radically. Wiseman and Liao devised criteria to categorise breast lymphoma into primary and secondary forms. There is no standard treatment for PBL, and for small localised tumours adequate excision followed by radiotherapy may be effective. For widespread tumours with axillary involvement the addition of chemotherapy, surgery and radiotherapy may be required. The literature suggests that the Ann Arbor stage and histological subtype are significant factors for survival. Reported 5-year survival rates vary from 9% to 85%. PBLs have a better outcome than primary breast carcinomas.

Our patient presented with apparent systemic AIDS-NHL with extranodal involvement of her breast, but review of her clinical presentation and staging allows for reclassification as a PBL. Unfortunately she was lost to follow-up and attempts to contact her have failed. Close surveillance should be stressed, as contralateral involvement can appear up to 10 years after the primary lesion. The era of AIDS-related malignancies represents a challenge. There should be a heightened clinical suspicion for extranodal lymphoma in AIDS-NHL patients.

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**REFERENCES**