CASE STUDY

PERSISTENT PLEURAL EFFUSION IN AN HIV PATIENT TREATED FOR TUBERCULOSIS

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HISTORY ON FIRST PRESENTATION

A 31-year-old woman presented to the oncology clinic at Tygerberg Hospital in November 2003 with grade 3 dyspnoea and a dry cough for 2 weeks. She was known to be HIV-positive and had received 8 months' treatment at a primary health care facility for pulmonary tuberculosis. There was no other history of note.

On physical examination she had a performance status of 2, generalised lymphadenopathy, six small, raised Kaposi's sarcoma (KS) lesions on the right temporal area of the face, and a large perpendicular KS mass extending from the right tonsil and falling into the valleculae on breathing, causing obstruction of the airway (Fig. 1). Auscultation revealed diminished breath sounds and a large right-sided pleural effusion.

Laboratory studies revealed the following: haemoglobin 10.5 g/dl, white blood count 4.1 × 10^9/l, neutrophil count 2.0 × 10^9/l, lymphocyte count 1.62 × 10^9/l, and platelet count 208 × 10^9/l. The results of liver function tests and the serum creatinine, electrolyte, protein and uric acid levels were all within normal limits. The lactate dehydrogenase (LDH) level was 184 U/l (within the normal range). A CD4+ count at the onset of treatment was 324 cells/µl. A chest radiograph confirmed a large right-sided pleural effusion (Fig. 2).

Investigations on the pleural effusion revealed:

1. Chemistry: total protein 70 g/l, LDH 304 U/l (normal > 200 U/l) and adenosine desamidase (ADA) 82.7 U/l (> 30 U/l is suggestive of tuberculosis or malignancy).

2. Microscopy, culture and sensitivity tests were negative for tuberculosis.

3. Cytological examination confirmed a picture compatible with a non-Hodgkin's lymphoma (NHL) with the presence of CD30+ and CD45+ cells.

This picture was compatible with the diagnosis of a primary pleural effusion lymphoma (PEL).

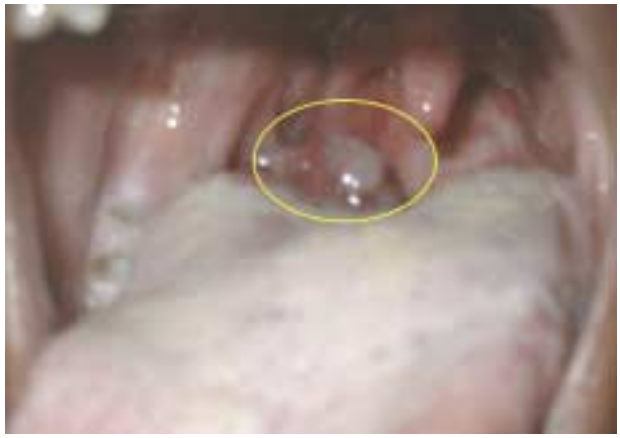
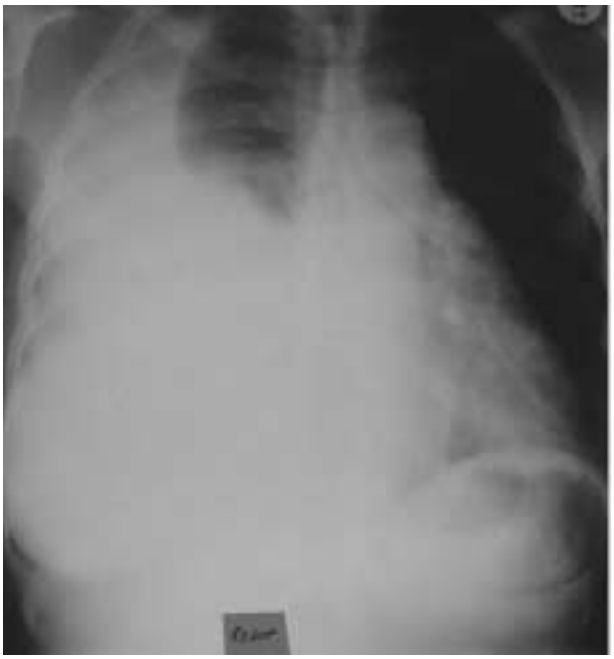


Fig.1, a and b. Kaposi's sarcoma lesion of the right tonsil and field marker for external beam radiation.

Staging for lymphoma was completed with the following examinations:

An abdominal ultrasound scan revealed bilateral inguinal lymph nodes. Histological examination of a lymph node



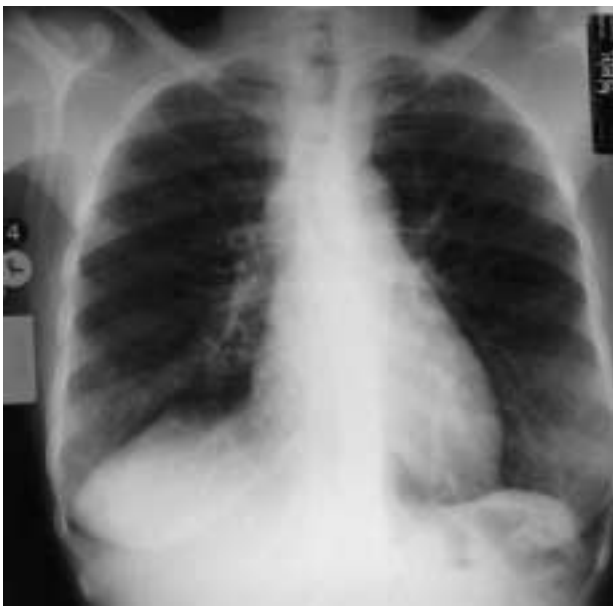


Fig. 2, a and b. Consecutive chest radiographs of pleural effusion lymphoma after 4 cycles of CHOP, showing a complete respsonse.

confirmed the diagnosis of KS (immunochemistry HHV-8 positive). Bone marrow aspiration and biopsy demonstrated no abnormalities. This case was considered to be a stage IaE (pleural effusion) NHL and KS T1, I0, S1 (poor risk) in a patient with WHO stage IV HIV disease.

TREATMENT AND RESPONSE

External beam irradiation (EBRT) with 60-cobalt, consisting of 4 Gray (Gy) × 5 fractions, was given to the oropharyngeal KS lesion to relieve the obstructive symptoms. The patient was then treated with the standard CHOP chemotherapeutic regimen consisting of cyclophosphamide 750 mg/m^2 on day 1, doxorubicin 50 mg/m^2 on day 1, vincristine 1.4 mg/m^2 on day 1, and prednisone 60 mg/day on days 1 - 5. Between January 2004 and April 2004, 6 courses of CHOP were given without significant toxicity apart from alopecia. The patient's general condition improved after the first course of chemotherapy for the NHL and EBRT to the KS, and sequential follow-up chest radiographs showed clearance of the pleural effusion after four courses of treatment. The first re-evaluation with chest radiograph was performed after the second course of chemotherapy. At the time, the pleural effusion was greatly reduced in size. The CD4+ count had decreased to 172 cells/µl by the end of treatment.

The patient thus presented with KS and PEL simultaneously, as late manifestations of her HIV disease. Chemotherapy for the lymphoma was well tolerated, probably because of the degree of immunosuppression (CD4+ count 162 cells/µl) at the commencement of therapy.

DISCUSSION

A rare type of NHL called primary lymphomatous effusion has been recognised as a separate entity based on distinctive biological features and the concomitant infection with the human herpesvirus 8 (HHV-8)/Kaposi's herpesvirus (KSHV). Because of the tropism of this entity for serous cavities it has been designated as a body cavity-based lymphoma (BCBL). In the USA, BCBL is also known as PEL.[1-3]

The majority of cases arise in the setting of HIV infection and most patients have been young to middle-aged men who have sex with men. Among patients with HIV the incidence of lymphoma is estimated to be between 1.6% and 8% per year.[3] In a recent publication by Simonelli *et al.*[4] only 4% of 277 AIDS/NHL patients were diagnosed with NHL. PEL also occurs in the absence of HIV infection, especially in areas with a high prevalence of HHV-8/KSHV infections. The HHV-8/KSHV is present within tumour cells, which often harbour the Epstein-Barr virus.[2,3]

The differential diagnosis of a pleural effusion in a HIV/AIDS patient should exclude tuberculosis, lymphoma, KS, hypoproteinaemia and bacterial and fungal infections.

Clinically PEL/BCBL gives rise to effusions without mass formation, although such masses have been reported. The most common sites of involvement are the pleural, pericardial and peritoneal cavities. Typically only one body cavity is involved. Other sites of involvement include the gastro-intestinal tract and extranodal tissues. Some patients have a pre-existing KS.[2,5] In most series the clinical outlook remains extremely unfavourable, with or without therapy, and a median survival of less than 6 months is reported.[1-5]

Our patient represents a typical case of PEL/BCBL with pleural effusion. The patient also had an associated KS. She responded well to EBRT for the oropharyngeal KS lesion, followed by CHOP chemotherapy for the PEL. Her facial KS lesions and lymphadenopathy also responded to the doxorubicin/vinca-alkaloid-containing CHOP regimen. She remains in complete remission for PEL after 4 months of follow-up.

At present, no recommendations can be made for treatment strategies for PEL/BCBL that differ from other AIDS/NHL treatments. However, a lesson from this case study is to be aware of other causes for a persistent pleural effusion in an HIV-positive patient.

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