Vertical transmission of Kaposi's sarcoma

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Abstract

AIDS related Kaposi's sarcoma is commonly seen in homosexual men, only occasionally in men and women with heterosexually acquired HIV, and extremely rarely in children. The case of an HIV infected mother and her vertically infected child who both developed visceral Kaposi's sarcoma is reported. It is proposed that the putative Kaposi's sarcoma agent may also be transmitted vertically.

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Kaposi's sarcoma is the most common HIV related cancer in adults, occurring almost exclusively in homosexual men. In the United States, Kaposi's sarcoma has been reported in only 0·6% of children with AIDS (21/3439).[1] In Europe, of 5129 children with AIDS[2] there have only been 6 (0·12%) reported cases of Kaposi's sarcoma[3] and all of these have occurred in children infected with HIV postnatally through blood transfusions. We now report a case in an HIV infected mother and her vertically infected child. To our knowledge this is the first report of Kaposi's sarcoma and HIV in both mother and child.

Case report 1: mother

A 32 year old black woman from Zambia who had been in the United Kingdom for one year presented in 1991 with a 10 day history of fever and shingles (fig 1). In 1985 she had received a blood transfusion in Zambia. She had never injected drugs.

Examination revealed generalised lymphadenopathy, oral candida, and healing cutaneous herpes zoster. A small pigmented nodule was noted on her left shoulder.

Investigations confirmed that she was HIV-1 antibody positive with a CD4 count of 180 cells/mm^3 (15% of total lymphocyte count). A full blood count, serum biochemistry, and chest radiograph were all normal.

Four weeks later she developed further pigmented nodules on her left shoulder and arm, and on her hard palate. A skin biopsy confirmed the clinical impression of Kaposi's sarcoma, her AIDS defining diagnosis. She was started on zidovudine, with cotrimoxazole for prophylaxis against *Pneumocystis carinii* pneumonia.

Eight months later she represented with a five day history of dyspnoea on exertion and while supine, and a cough productive of scanty white sputum. She had also developed further cutaneous Kaposi's sarcoma and two hard submandibular lymph nodes. A chest radiograph showed diffuse interstitial infiltrates in the mid and lower zones bilaterally. A computerised tomography (CT) scan revealed extensive reticulonodular changes in the apical segments of both lower lobes.

At fibreoptic bronchoscopy multiple endobronchial lesions of Kaposi's sarcoma were seen. Cytological and microbiological

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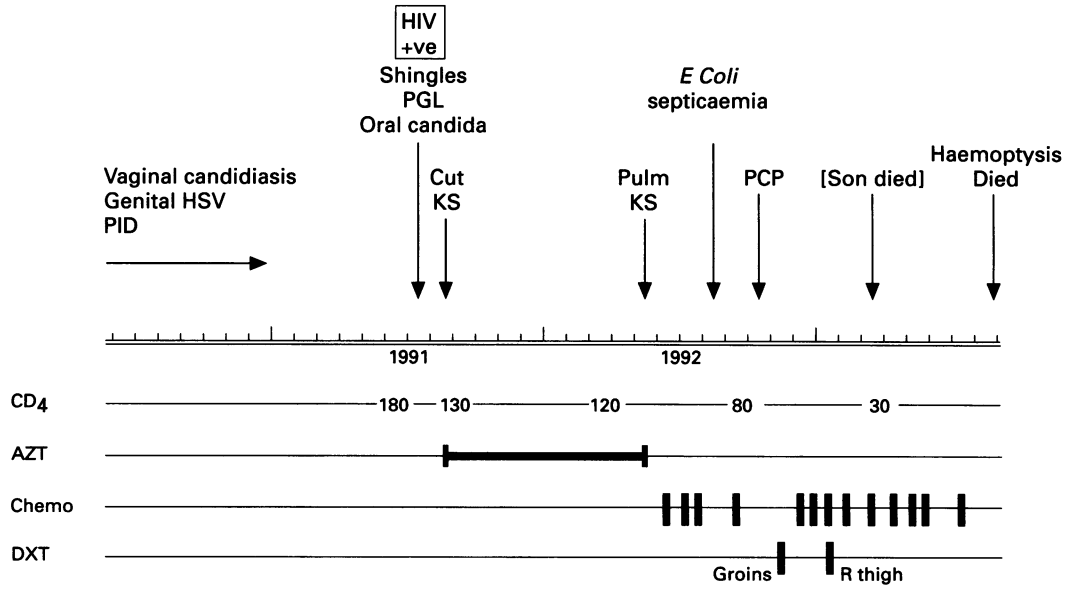

Figure 1 Case report 1. Clinical course of mother. CD4=CD4 cells/mm^3; AZT=zidovudine; Chemo=chemotherapy; DXT=radiotherapy; HSV=Herpes simplex virus; PID=pelvic inflammatory disease; PGL=polyglandular lymphadenopathy; Cut=cutaneous; Pulm=pulmonary.

examination of bronchoalveolar lavage fluid specimens were negative.

Her dyspnoea was attributed to pulmonary Kaposi's sarcoma. Systemic chemotherapy with three weekly cycles of intravenous vincristine and intravenous bleomycin and doxorubicin resulted in rapid resolution of her symptoms.

After 10 months of chemotherapy she was switched to liposomal doxorubicin because of hair loss. She also received radiotherapy to her inguinal region when infiltration of lymph nodes with Kaposi's sarcoma resulted in painful lymphoedema of her legs.

Two years after her initial AIDS diagnosis she was admitted to hospital with headaches and fever. Blood, sputum, and urine cultures and a serum cryptococcal antigen test were negative. A cranial CT scan was normal and examination of the cerebrospinal fluid (CSF) gave negative results. Her chest radiograph was unchanged. During the course of investigation she collapsed with a massive haemoptysis, had a cardiac arrest and died. A request for a necropsy was refused.

Case report 2: child

The mother's only son was born in Zambia in 1986. He was breast fed for 10 months and remained well for four years. He came to the United Kingdom in 1991. A month later he developed dyspnoea, recurrent ear and chest infections, and weight loss (fig 2).

Examination revealed generalised lymphadenopathy, hepatomegaly, and evidence of chronic respiratory disease with chest deformity.

Investigations confirmed that he was HIV-1 antibody positive. A chest radiograph showed diffuse reticulonodular shadowing with overlying patchy consolidation which was thought to represent lymphocytic interstitial pneumonitis with secondary chest infections.

During the following two weeks his chest symptoms deteriorated despite treatment with high dose cotrimoxazole for presumed *Pneumocystis carinii* pneumonia and with broad spectrum antibiotics for other respiratory pathogens. He was transferred to Great Ormond Street Hospital for Children in January 1992, when he was extremely ill and oxygen dependent. He had gross lymphadenopathy including large segmental and para-aortic lymph nodes (as demonstrated on an ultrasound scan of his abdomen). His CD4 count was 40 cells/mm^3 (7% total lymphocyte count). Bronchoscopy and lavage showed no evidence of *Pneumocystis carinii* or *Mycobacterium tuberculosis*. Cotrimoxazole was continued and steroids were added.

Biopsy of a submental lymph node showed classic histopathological changes of Kaposi's sarcoma.

After three weeks' high dose cotrimoxazole his respiratory symptoms had improved but his chest radiograph remained grossly abnormal. A thoracic CT scan showed bilateral extensive parenchymal consolidation with small pleural effusions. Kaposi's sarcoma was suspected; however, an open lung biopsy failed to show this and instead was consistent with lymphocytic interstitial pneumonitis; there was no evidence of infection with other pathogens. Despite the failure to confirm pulmonary Kaposi's sarcoma histologically a clinical diagnosis of visceral Kaposi's sarcoma was made.

He was treated with seven cycles of vincristine and bleomycin. He was also started on zidovudine and continued low dose cotrimoxazole. He tolerated the chemotherapy well and made a good clinical response with resolution of his lymphadenopathy. However, during his eight cycles of chemotherapy he developed respiratory problems which were thought to be bleomycin related and his treatment was stopped.

Two weeks later he developed bronchoscopically confirmed *Pneumocystis carinii* pneumonia, which was successfully treated with intravenous cotrimoxazole.

Five weeks later he again developed acute respiratory distress secondary to large bilateral pleural effusions. Ultrasound examination showed nodular lesions of the visceral pleura and new para-aortic lymph nodes. At

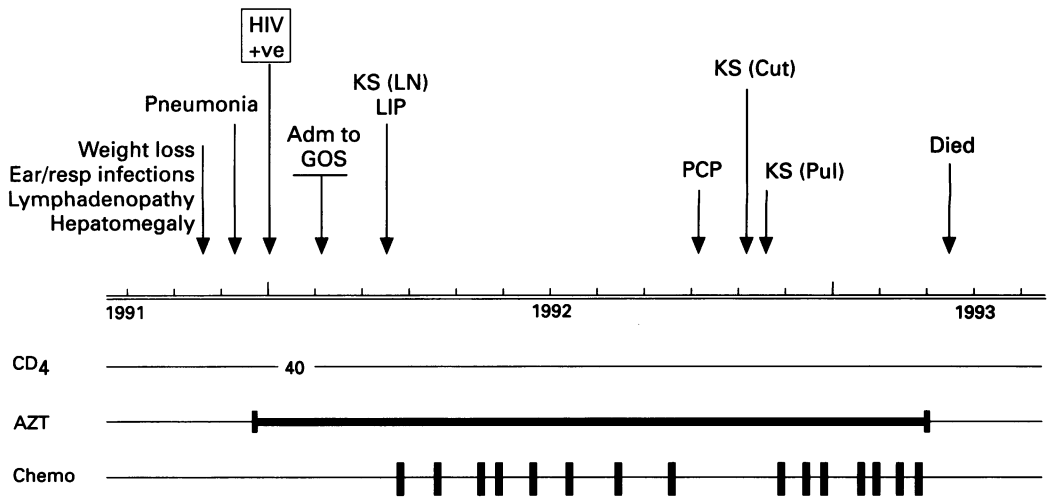

Figure 2 Case report 2. Clinical course of child. CD$_4$=CD4 cells/mm^3; AZT=zidovudine; Chemo=chemotherapy; DXT=radiotherapy; GOS=Great Ormond Street Hospital for Children; LN=lymph nodes; Cut=cutaneous; Pulm=pulmonary.

bronchoscopy endobronchial Kaposi's sarcoma lesions were seen; staining and culture of bronchoalveolar lavage fluid was negative for infection. Bilateral chest drains were inserted, which drained a blood stained exudate (protein 54 g/l) but no malignant cells were found. Coincidentally he developed histologically confirmed cutaneous nodules of Kaposi's sarcoma.

He was restarted on chemotherapy with liposomal daunorubicin. His pleural effusions resolved and for a short time his clinical condition improved sufficiently to enable him to resume a more normal life. However after three months of liposomal daunorubicin, which he tolerated well with no haematological toxicity, his Kaposi's sarcoma showed signs of progression with new cutaneous nodules and respiratory deterioration. When he developed loculated pleural effusions in association with cor pulmonale, active treatment was withdrawn.

He died one week later, 18 months after the initial diagnosis of Kaposi's sarcoma. A necropsy request was refused.

Discussion

This is the first reported case of HIV related Kaposi's sarcoma occurring in both a mother and child. It is also the first reported case of Kaposi's sarcoma in a vertically HIV infected child in the United Kingdom and in Europe.

Kaposi's sarcoma is rarely seen in HIV infected children; only 33 cases have been reported worldwide.[3] Approximately half of these cases (17/30 evaluable cases) were infected with HIV perinatally. None of the mothers was reported to have Kaposi's sarcoma, although they were all of Haitian or African origin, where the background incidence of HIV related Kaposi's sarcoma is reported to be high.[4]

Both mother and child developed a systemic aggressive form of Kaposi's sarcoma with predominant lymph node and visceral disease, but little of the cutaneous involvement more typical of HIV related disease. This is consistent with a recent review of Kaposi's sarcoma in Zambian children, which showed a fivefold rise in paediatric Kaposi's sarcoma cases from zero to 5·9 cases/million paediatric cases/year between 1981 and 1991.[5]

The nature of Kaposi's sarcoma in Zambian children has changed recently; over 80% are HIV related and the disease is occurring at a younger age, with a peak incidence between 1 and 2 years. The sexes are more equally effected (M/F=1·76/1). The disease generally takes the lymphadenopathic form, affecting the lymph nodes and viscera, and has an average 13 month survival.

The epidemiology of Kaposi's sarcoma strongly suggests a transmissible agent. Among patients with AIDS, Kaposi's sarcoma occurs approximately 10 times more often in homosexual and bisexual men than in other HIV transmission groups.[1]

Our mother-child pair lends support to the concept of vertical transmission in addition to sexual transmission of the Kaposi's sarcoma agent. It is already known that HIV facilitates the transmission of other viruses such as hepatitis C. Alternatively both mother and child may have been exposed to the same putative agent, as suggested by the observed clustering of Kaposi's sarcoma in African households.

Many putative Kaposi's sarcoma agents have been suggested, including CMV, amyl nitrite, and an HPV-16 related DNA virus. More recently a new DNA sequence similar to a human herpes virus has been identified in AIDS associated Kaposi's sarcoma lesions.[6] Chang *et al* in New York isolated this putative virus from 93% of Kaposi's sarcoma lesions in AIDS patients (25/27) and from 15% of tissue specimens from AIDS patients without Kaposi's sarcoma (6/39). The herpes-like sequences could not be detected in 90 HIV negative control patients. We are currently attempting to detect this sequence in Kaposi's sarcoma tissue taken from our mother and child pair.

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