

Bronchopulmonary Kaposi's sarcoma in patients with AIDS

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Abstract

Background Kaposi's sarcoma is the most common secondary neoplasm to complicate HIV infection and may cause pulmonary disease.

Methods A prospective study was carried out in 140 consecutive patients who were HIV seropositive and required bronchoscopy for new respiratory symptoms of at least two weeks' duration, with either a chest radiographic abnormality or abnormality of pulmonary function. The patients were classified into those with single local endobronchial lesions of Kaposi's sarcoma or generalised widespread lesions. Before bronchoscopy all patients had routine simple pulmonary function tests and chest radiography.

Results Thirty nine (21%) patients had evidence of cutaneous Kaposi's sarcoma. Nineteen of the 39 were found to have endobronchial Kaposi's sarcoma lesions at bronchoscopy, but none of those who did not have cutaneous Kaposi's sarcoma. Respiratory symptoms of cough and breathlessness and radiographic abnormalities were attributed to Kaposi's sarcoma in this group, except in four patients who had concomitant pneumocystis pneumonia. Eight patients had local endobronchial Kaposi's sarcoma lesions and 11 had extensive lesions. Patients with extensive lesions had more widespread radiographic abnormalities; four of the patients with local endobronchial lesions had normal chest radiographs. All patients had reduced transfer factor for carbon monoxide and transfer coefficient, whereas patients with extensive endobronchial lesions also had reductions in forced expiratory volume in one second and forced vital capacity. Median survival (with palliative chemotherapy with vincristine and bleomycin) was only seven months. In three patients who needed further diagnostic bronchoscopy endobronchial lesions had regressed while they were having chemotherapy.

Conclusions This study suggests that endobronchial Kaposi's sarcoma is a relatively common finding in patients with AIDS and is particularly common in patients with cutaneous Kaposi's sarcoma who present with respiratory illness. Endobronchial Kaposi's sarcoma causes respiratory disease and abnormalities of pulmonary function. Pulmonary Kaposi's sarcoma should be considered as a pos-

sible cause for respiratory illness in any patient with cutaneous Kaposi's sarcoma.

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Kaposi's sarcoma is a common manifestation of the acquired immunodeficiency syndrome (AIDS). It occurs in up to a quarter of patients with AIDS, being particularly common in homosexual and bisexual men.¹ It usually presents with cutaneous lesions, with the gut and lymph nodes frequently affected. Kaposi's sarcoma may attack the lungs, pleura, and tracheobronchial tree, so it should be considered in the differential diagnosis of respiratory disease in patients who are HIV-1 seropositive. The true incidence of intrathoracic lesions in patients with Kaposi's sarcoma is difficult to assess. A postmortem study found pulmonary Kaposi's sarcoma in 47% of patients with cutaneous disease.² In clinical studies pulmonary Kaposi's sarcoma has been described in 3-13% of patients with AIDS overall,^{3,4} in 6-32% of patients with AIDS and cutaneous Kaposi's sarcoma,^{3,5,6} and in about 10% of patients with AIDS and respiratory symptoms.^{4,7} Difficulties in the diagnosis of pulmonary Kaposi's sarcoma arise because symptoms and chest radiographic appearances are non-specific, endobronchial lesions may not be present at bronchoscopy, and parenchymal lesions may be patchy and be missed at transbronchial biopsy. Non-invasive investigations do not distinguish pulmonary Kaposi's sarcoma from the other causes of pulmonary disease in AIDS.⁸ Endobronchial lesions have a distinctive red or purple appearance, however, when seen during fiberoptic bronchoscopy,^{2,9,10} and alveolar haemorrhage has been described in association with pulmonary Kaposi's sarcoma.⁷ In this paper we describe clinical features of patients with Kaposi's sarcoma in whom endobronchial lesions were seen at bronchoscopy in a consecutive series of patients with AIDS. The endobronchial appearances are categorised according to their extent and compared with the results of pulmonary function tests and radiographic changes.

Patients and methods

One hundred and forty consecutive homosexual or bisexual patients who were HIV-1 seropositive underwent diagnostic bronchoscopy for investigation of respiratory symptoms over the 17 months July 1988 to November 1989. Criteria for inclusion in this study were (a) known HIV seropositivity and

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(b) new respiratory symptoms of more than two weeks' duration (cough or breathlessness) and either chest radiographic abnormality or abnormality of pulmonary function. Some patients had received broad spectrum antibiotics before bronchoscopy. At bronchoscopy the tracheobronchial tree was carefully examined for the presence of Kaposi's sarcoma and the extent of the lesions were described as (1) local if lesions were confined to the wall of the trachea or affected a segmental bronchus of a single lobe or (2) extensive if they affected the tracheal wall and segmental bronchus of a single lobe or segmental bronchi of two or more lobes. Bronchoalveolar lavage with 180–240 ml of warm sterile saline was performed either from the lobe most affected by radiographic shadowing or, in those with diffuse radiographic abnormality, from the right middle lobe. Lavage fluid was examined macroscopically for evidence of alveolar haemorrhage (not confirmed by laboratory testing) and cytologically for the presence of *Pneumocystis carinii* and cultured for bacteria, mycobacteria, fungi, and viruses. The presence and duration of respiratory symptoms were recorded, and cutaneous or oral Kaposi's sarcoma was noted. All patients had a chest radiograph before bronchoscopy, which was reported blind by a radiologist (MM). The following pulmonary function tests were also performed before bronchoscopy: forced expiratory volume in one second (FEV₁), forced vital capacity (FVC; Vitalograph, Buckingham), peak expiratory flow (PEF), transfer factor (TLCO), and transfer coefficient (KCO) were measured by the single breath helium dilution method (P K Morgan, Chatham, Kent). Values for TLCO were corrected for haemoglobin and temperature, measurements being made between 9 and 11 am at the end of half an hour's rest after the patient arrived at the laboratory.

Statistical analyses were performed with Wilcoxon's signed pairs rank test.

Results

INITIAL FINDINGS

Bronchoscopy

Thirty nine of 140 (21%) consecutive HIV-1 seropositive patients who had diagnostic bronchoscopy for investigation of respiratory symptoms had cutaneous Kaposi's sarcoma. In 19 of these 39 patients endobronchial Kaposi's sarcoma was seen, but no lesions were seen in patients without cutaneous Kaposi's sarcoma. The age range of these 19 patients was 24–49 (median 35) years. Twelve were smokers and seven were non-smokers. In eight of these 19 endobronchial lesions were classified as local, the remaining 11 of the 19 being extensive. In two patients the lavage fluid had a distinct yellow-orange coloration suggesting alveolar haemorrhage. Oral Kaposi's sarcoma was present in 18 of the 19 patients with endobronchial Kaposi's sarcoma. In four of the 19 patients with endobronchial sarcoma *Pneumocystis carinii* pneumonia was diagnosed at bronchoscopy. In the 15 patients with no pathogens isolated at bronchoscopy symptoms and

radiological findings were attributed to Kaposi's sarcoma.

Symptoms

All 19 patients had cough and breathlessness. Two patients had anterior chest pain and one had haemoptysis. The overall duration of symptoms ranged from 2 to 20 (median 4) weeks. In patients with local endobronchial Kaposi's sarcoma, symptoms had lasted 2–12 (median 8) weeks and in patients with extensive Kaposi's sarcoma 2–20 (median 4) weeks (NS). The time from diagnosis of cutaneous Kaposi's sarcoma to discovery of endobronchial sarcoma at bronchoscopy ranged from 2 to 29 (median 12) months in those with local endobronchial Kaposi's sarcoma and from 3 to 19 (median 10) months in those with extensive endobronchial sarcoma (NS).

Lung function and radiographic findings

The peak flow, FEV₁, and FVC were normal in patients with local endobronchial Kaposi's sarcoma, but were reduced in patients with extensive disease ($p < 0.01$, < 0.05 , and < 0.05), whereas TLCO was reduced in both groups of patients, with lesser reductions in KCO (table). The lung function abnormalities were attributed to pulmonary Kaposi's sarcoma in the 15 patients where no other pathological findings emerged. The pneumocystis pneumonia found in the other four patients provides an additional source of lung function abnormality. Various abnormalities were seen on the chest radiograph. Four patients with local endobronchial lesions had a normal chest radiograph, whereas coarse, irregular bilateral shadows were seen only in patients with extensive endobronchial disease.

TREATMENT AND OUTCOME

All patients with endobronchial Kaposi's

Results of lung function tests and chest radiograph appearances in patients with endobronchial Kaposi's sarcoma

| | Kaposi's sarcoma | | |
|---|------------------|---------------------|------|
| | Local (n=8) | Extensive (n=11) | p |
| <i>Lung function (mean (SD)) % predicted</i> | | | |
| FEV ₁ | 92 (14) | 56 (26) | 0.05 |
| FVC | 89 (13) | 59 (29) | 0.05 |
| PEF | 102 (10) | 55 (28) | 0.01 |
| TLco | 51 (13) | 45 (7) | NS |
| Kco | 67 (15) | 84 (20) | NS |
| <i>Chest radiograph appearance (No of patients)</i> | | | |
| Normal | 4 | — | |
| Bilateral interstitial shadows | 2 | — | |
| Lobar consolidation | 1 | 1 | |
| Pleural effusion | — | 2 | |
| Microlithiasis* | 1 | — | |
| Coarse irregular bilateral shadows | — | 7 | |
| Hilar enlargement or perihilar infiltrate | — | 1 | |

*Intravenous drug user.

FEV₁—forced expiratory volume in one second; FVC—forced vital capacity; PEF—peak expiratory flow; TLCO—carbon monoxide transfer factor; KCO—transfer coefficient.

sarcoma received cytotoxic chemotherapy consisting of vincristine (2 mg) and bleomycin (10 mg/m²) administered intravenously at three weekly intervals. All the patients have now died. For the whole group survival was 1–16 (median 7) months for extensive disease, 1–14 (median 4) months, and for local disease, 1–16 (median 8) months. There was no significant difference in survival between those with local and with extensive disease.

REPEAT BRONCHOSCOPY

Three patients required a repeat bronchoscopy for new respiratory symptoms. All three had received chemotherapy before bronchoscopy. Two patients with localised endobronchial Kaposi's sarcoma had no visible lesions and one patient with extensive endobronchial lesions showed clear evidence of regression.

Discussion

In this study of 140 consecutive homosexual or bisexual patients with AIDS requiring diagnostic bronchoscopy endobronchial Kaposi's sarcoma was relatively common, being found in 14% of HIV positive patients overall and in 49% of patients who had cutaneous Kaposi's sarcoma. Comparison with other studies is affected both by the criteria used to establish a diagnosis of endobronchial or pulmonary Kaposi's sarcoma and by the varying incidence of Kaposi's sarcoma in different study populations. The reported incidence of pulmonary Kaposi's sarcoma in patients with Kaposi's sarcoma and respiratory symptoms ranges from 18% to 26%.^{5-7,11} In all the patients with endobronchial Kaposi's sarcoma symptoms and abnormalities on the chest radiograph are likely to be attributed to Kaposi's sarcoma, as in only four was an additional diagnosis (pneumocystis pneumonia) made. Bronchial biopsies were not done in this study as all patients had cutaneous lesions that had been biopsied to confirm the diagnosis of Kaposi's sarcoma before bronchoscopy. Additional histological confirmation of the characteristic endobronchial findings was regarded as unnecessary as well as carrying the potential hazard of bleeding. It is noteworthy that only one of the 19 patients with endobronchial Kaposi's sarcoma did not have oral Kaposi's sarcoma. If we exclude the four patients who also had pneumocystis pneumonia, in 15 of the 19 patients respiratory symptoms and radiographic abnormality were attributable to pulmonary Kaposi's sarcoma. No alternative diagnoses emerged over six weeks of follow up. All patients complained of cough and most complained of dyspnoea, but haemoptysis and chest pain were rare. The duration of symptoms varied considerably. There was also considerable variability in the time from diagnosis of cutaneous Kaposi's sarcoma to diagnosis of endobronchial Kaposi's sarcoma. A wide range of chest radiographic abnormalities was seen, the severity of which was related to the extent of endobronchial disease. Half of the patients with local endobronchial Kaposi's sarcoma had a normal chest radiograph, whereas over half

with extensive endobronchial Kaposi's sarcoma had widespread coarse irregular nodular shadows. In patients with local endobronchial Kaposi's sarcoma, spirometric values and peak flow were normal, as is generally the case in individuals infected with HIV with or without pulmonary complications.¹⁰ Substantial reductions in FEV₁ and FVC were, however, seen in patients with extensive endobronchial Kaposi's sarcoma, presumably reflecting the extensive airway lesions found at bronchoscopy. Transfer factor was substantially reduced in both groups, indicating that endobronchial lesions in Kaposi's sarcoma are probably only a crude marker for intrathoracic disease, where there may also be a substantial parenchymal component of disease, accounting for the abnormalities in transfer factor seen both in this and in previous studies.¹⁰ Analysis of studies that have reported on the premortem diagnosis of endobronchial Kaposi's sarcoma suggests that visual identification is the most sensitive diagnostic technique, endobronchial lesions being described in 44 of 60 (73%) bronchoscopies in patients subsequently diagnosed as having pulmonary Kaposi's sarcoma.^{3,5-7,19} Biopsy of endobronchial lesions at bronchoscopy has been reported as giving a histological diagnosis in 12 of 20 (60%) cases,^{5,7,12} transbronchial biopsy in 12 of 46 cases (26%),^{4,5,11} and open lung biopsy in 31 of 65 cases (48%).^{3-7,11}

This study shows that endobronchial Kaposi's sarcoma is a common bronchoscopic finding in patients with cutaneous Kaposi's sarcoma and that pulmonary Kaposi's sarcoma causes respiratory illness, chest radiographic abnormalities, and abnormal pulmonary function. Endobronchial Kaposi's sarcoma was not seen in patients without cutaneous Kaposi's sarcoma. The diagnosis should be carefully considered in patients with cutaneous Kaposi's sarcoma lesions, though the prognosis is poor.

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Adventitia

A rewarding combination

I am sure that variety provides stimulus and satisfaction in the practice of medicine. One of the most stimulating periods in my life was working with Dr John Gilson, under Professor Charles Fletcher, at the Medical Research Council Pneumoconiosis Research Unit. Tests of lung function were then non-existent, apart from measurement of vital capacity; so we had all the interest of developing them. But after seven years at that unit the frequent rain of South Wales depressed me, so I applied to go as senior lecturer in the new department of medicine in Jamaica, then British West Indies. "Do you think you are wise to leave the MRC?" was the only comment from Professor Witts, whom I knew from my days as his registrar at Oxford. Yes, indeed I was wise as that too provided exciting but different work. At first I rushed about as if I were in Britain and tried to pursue work in respiratory research. But that was really inappropriate to medicine in Jamaica, so I changed my research interest to diabetes because of its unusual clinical presentation there. Jamaican life held all sorts of fascination and I particularly enjoyed an expedition we organised from the university in Jamaica to climb mountains rising to 6000 m on the Colombian-Venezuelan border. My brief contact with the local Indians then made me long to learn more of their lives. But after a bit I began to feel unsettled, rather as if I were on a long holiday, even though I was working very hard at the new university hospital.

By then the Medical Research Council had employed Dr Kemp Fowler, an Australian

physicist, to design a mass spectrometer specifically for clinical respiratory work; so I had the chance of returning to Britain as director of an MRC respiratory research unit at the Royal Postgraduate Medical School in Hammersmith Hospital. What a change that was from Jamaica! It was immensely stimulating, with the brilliant weekly staff rounds created by Professor Sir John McMichael. Then, one dull grey day in Hammersmith, John McMichael said at lunch that he had been asked to give some lectures in Bogotá, Colombia, and did not wish to go himself. He asked if anyone might be interested. I readily volunteered, gave the lectures on respiratory medicine at the Juan de Dios Hospital, and after I had finished the lectures headed for the South American forests to canoe down the rivers with the local Indians, whom I had wanted to study since the previous climbing expedition. I was able to share their lives, learn to use a blowgun in the forest, and contribute some medical help as well as amateur dentistry.

From that time onwards I have somehow managed to combine sophisticated medicine in Britain with work in third world countries. This has meant working hard in London for a long stretch and then, about every other year, taking off a month or so to go on an expedition to some remote part of the world. It is a rewarding combination and I would fully recommend a spell of practising medicine in the developing world to any registrar despairing of an immediate consultant job here in Britain.

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