Mycobacterium kansasii: its presentation, treatment and outcome in HIV infected patients

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Abstract

***Aim*—To report the clinical significance and treatment of *Mycobacterium kansasii* infection in the context of HIV disease.**

***Design/methods*—Retrospective case review of all isolates of *M kansasii* until June 1994.**

***Results*—Ten cases of *M kansasii* were isolated. All but one patient with this infection had clinical symptoms compatible with generalised infection. The majority had chest infections with the organism isolated on induced sputum but not routine sputum. All isolates were sensitive to ethambutol and nine of 10 to rifampicin. All isolates were resistant to isoniazid and pyrazinamide.**

***Conclusion*—*M kansasii* is a pathogen in HIV infected patients and should be treated when isolated. Treatment should be with rifampicin and ethambutol but not isoniazid, as has been recommended previously.**

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Atypical mycobacteria are widespread in the environment and cause both local and disseminated disease. Prior to the HIV epidemic, pulmonary disease due to *Mycobacterium kansasii* has been most commonly reported in the USA and Western Europe, particularly in those with pre-existing lung pathology.[1] When found disseminated *M kansasii* infection was often associated with pancytopenia and immunosuppressive therapy.[2] Contamination of clinical samples was well recognised, and led some authors to specify strict criteria before a diagnosis of *M kansasii* infection could be made.[3] However, the suggestion that *M kansasii* is virtually never a contaminant and that isolation from respiratory cultures is correlated with pulmonary disease has become more accepted with the advent of the HIV epidemic.[4 5]

With the rising prevalence of HIV infection there has been an increase in the number of reports of all the mycobacterial diseases, but the proportion of patients developing *M kansasii* infection remains small relative to those for *Mycobacterium tuberculosis* and *Mycobacterium avium* complex.[6 7]

Methods

A retrospective case review was undertaken on all HIV seropositive patients identified by the microbiology department as having *M kansasii* isolated from clinical specimens. AIDS was diagnosed according to the CDC classification in use at the time of study.[8]

Patients presenting to our unit with pyrexia routinely have blood cultures taken. In addition, if the CD4 count is less than 100 cells/mm^3, blood cultures for mycobacteria are performed using a BACTEC 13A radiometric system. Patients with diarrhoea are asked to provide at least three stool specimens, examination of which includes that for mycobacteria. If respiratory symptoms are present sputum samples are sent for microscopy and culture. If *Pneumocystis carinii* pneumonia is suspected an induced sputum is performed, which is always cultured for mycobacteria. All radiographs are reviewed independently by medical staff within the department of radiology.

When mycobacteria are isolated sensitivity testing is performed using both the resistance ratio[9] and radiometric[10] methods. In the resistance ratio method the minimum inhibitory concentration of the test strain is compared with the modal average results of several control strains using the same batch of medium. The radiometric method is similar in principle but the medium is liquid. This allows for a more rapid growth and for the detection to be automated.

Based on criteria used by Levine *et al*,[11] patients were defined as having definite pulmonary *M kansasii* infection if symptomatic for more than two weeks (fever, cough, dyspnoea), chest *x* ray changes suggestive of infiltration or cavitation, and two positive sputum cultures. Possible pulmonary *M kansasii* infection was diagnosed if only one culture was positive. Disseminated disease was defined as isolation of *M kansasii* from tissue other than lungs, skin, cervical or hilar lymph nodes.

Results

Ten cases of *M kansasii* were isolated between January 1992 and June 1994 (table 1). Only one case occurred in 1992 and one in 1993, the rest being diagnosed in 1994. No case of *M kansasii* was found prior to 1992. All but one patient experienced clinical symptoms compatible with generalised disease. Six had confirmed disseminated infection with positive blood cultures. The remaining four had positive induced sputum cultures, of which three could be defined as having definite pulmonary infection, and one had a diagnosis of possible infection.[11] In none of the six patients who had a positive induced sputum was *M kansasii* isolated on routine sputum examination, although at least two specimens

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Table 1 Clinical and micrbiological data of patients with Mycobacterium kansasii *infection*

Patient number	*Months since first AIDS diagnosis*	*CD4 count at time of* M kansasii *isolation (cells/mm³)*	*Presenting symptoms and signs*	*Concurrent opportunistic infections/tumours*	*Source of* M kansasii *isolate*	*Antimicrobial sensitivities*	*Treatment*	*Outcome from time of* M kansasii *isolation*
1	55	2 (1%)	Fever Malaise Abscess	Oral candida	Abscess Blood	Ethambutol Ciprofloxacin	Ethambutol Clarythromicin Ciprofloxacin	Died 4 months later
2	60	2 (1%)	Fever Malaise Cough Anaemia	Kaposi sarcoma CMV retinitis	Induced sputum (n = 2) Blood	Rifabutin/rifampicin Ethambutol Ciprofloxacin Clofazamine	Rifabutin Ethambutol Ciprofloxacin	Alive at 8 months; symptoms controlled; negative induced sputum and blood cultures at 2 months
3	48	14 (4%)	Fever Neurological	*Listeria* meningitis	Stool Blood	Rifabutin/rifampicin Ethambutol Ciprofloxacin	Rifabutin Ethambutol (stopped) Clarythromicin Clofazamine	Died 5 months later of overwhelming sepsis; negative blood cultures at 3 months
4	10	40 (8%)	Fever Malaise Cough Hepatosplenomegaly Anaemia	None	Induced sputum (n = 1) Stool Blood	Rifabutin/rifampicin Ethambutol Ciprofloxacin Clofazamine	Rifampicin Isoniazid Ethambutol	Alive at 5 months; control of symptoms
5	18	2 (1%)	Fever Malaise Cough Hepatomegaly Anaemia	*Pseudomonas* chest infection	Blood	Rifampicin Ethambutol	Rifabutin Ethambutol Clofazamine	Alive at 6 months; control of symptoms
6	17	1 (1%)	Fever Cough Anaemia	*P carinii* pneumonia	Blood	Rifampicin Ethambutol	Rifabutin Clofazamine Ethambutol (stopped)	Alive at 15 months; control of symptoms; negative induced sputum, BAL and blood cultures at 9 months
7	26	16 (4%)	Fever Malaise Cough/ dyspnoea Anorexia	None	Induced sputum (n = 2)	Rifampicin Ethambutol	Rifabutin Ethambutol Ciprofloxacin	Alive at 4 months; control of symptoms
8	24	18 (2%)	Fever Malaise Anaemia	CMV retinitis Lymphoma	Induced sputum (n = 1)	Rifabutin/rifampicin Ethambutol Clarythromicin Ciprofloxacin	Rifabutin Ethambutol Clarythromicin	Died at 1 month from associated lymphoma
9	2	10 (5%)	Chest pain Cough Malaise	Kaposi sarcoma	Induced sputum (n = 2)	Rifampicin Ethambutol	Rifabutin Ethambutol Ciprofloxacin	Alive at 19 months; intermittent positive induced sputum
10	0	96 (6%)	Fever Cough Anaemia	*P carinii* pneumonia	Induced sputum (n = 2)	Rifampicin Ethambutol Ciprofloxacin	Rifabutin Clarythromicin Ciprofloxacin	Alive at 1 month; control of symptoms

CMV = cytomegalovirus; BAL = bronchoaveolar lavage.

from each patient were sent to the laboratory for culture. At the time of *M kansasii* isolation, seven of 10 patients were receiving cotrimoxazole (960 mg od).

In the six cases where positive induced sputum cultures were obtained, pulmonary symptoms were present. However, only two of the chest radiographs were felt to be abnormal. Patient 4 had evidence of cavitation and fibrosis and patient 10 had bilateral alveolar shadowing but at the same time was infected with *P carinii*.

During the same study period 50 cases of *M avium* complex infection were diagnosed, as were 33 cases of *M tuberculosis* infection, of which 16 were extrapulmonary. The median CD4 at diagnosis of *M kansasii* was 17 (mean 20; range 2–96) which was comparable with that for *M avium* complex (mean 23; median 17; range 0–156), but significantly lower than that for *M tuberculosis* (mean 166; median 70; range 3–375).

Review of antimicrobial sensitivities (table 1) indicates that all isolates were sensitive to ethambutol and nine of 10 were sensitive to rifampicin. All were resistant to isoniazid and pyrazinamide. Six isolates were tested against ciprofloxacin and all were fully or partially sensitive.

All cases were treated initially with at least two drugs to which their *M kansasii* infection was sensitive. By April 1994 three of the 10 patients had died; *M kansasii* infection is felt to have contributed partially to two deaths, although both patients had multiple, advanced AIDS related illnesses. Patient 8 had treatment for *M kansasii* withdrawn after one week and died within one month of disseminated lymphoma. The remainder were alive one to 15 months after diagnosis.

Discussion

This report details a series of *M kansasii* disease associated with HIV infection in the

UK. Like infection with *M avium* complex, in this study *M kansasii* disease occurred in those with severe immunosuppression. Presentation was non-specific; fever and malaise were common, although specific symptoms were usual in patients with respiratory infection. In contrast with the experience of Levine *et al*[11] chest radiographs were often normal in patients with pulmonary disease. This lack of cavitation and fibrosis has been noted in other series[12–14] and presumably reflects the underlying level of immunosuppression.

In patients with AIDS, initial respiratory or gastrointestinal isolation of other atypical mycobacteriae is frequently followed by widespread dissemination of the infection.[15 16] Similarly, Levine *et al*[11] found that in HIV infected patients when *M kansasii* infection was left untreated, most cases resulted in progressive clinical deterioration, but if treatment of *M kansasii* infection was undertaken documented clinical improvement resulted. All of our patients received treatment. Patient 9 was poorly compliant with treatment and continued to be symptomatic and to produce positive isolates. The others achieved good control of symptoms and no further isolates of *M kansasii* were obtained. Thus, we would recommend that if *M kansasii* is isolated, treatment should be commenced. If further samples yield positive cultures of *M kansasii*, then treatment should be maintained indefinitely. If further samples fail to yield *M kansasii*, decisions concerning further investigation or treatment will depend upon the clinical picture and the initial response to treatment.

From the antimicrobial sensitivities presented, we would continue to recommend the initial use of rifampicin/rifabutin and ethambutol as first line treatments. All patients in this series had isoniazid resistant *M kansasii*, an observation seen partially or fully in a number of other reviews.[5 11 12] Thus, in contrast to the recommendations of the American Thoracic Society[17] it would seem sensible not to include isoniazid in a treatment regimen and that if use of a third drug is necessary, to consider one of the newer quinolones. Although only a limited number of isolates were tested against clofazamine (n = 2) and clarythromicin (n = 1), as a result of the favourable sensitivities obtained, these drugs could also be considered in patients intolerant or failing first line treatment.

In reviewing previously reported in vitro sensitivity of *M kansasii* to sulphur based drugs, sulphamethiazole has been recommended as a treatment option[18] and has proved efficacious in HIV infected patients not responding to other treatment.[19] However, in the dosage used in prophylactic treatment of *P carinii* pneumonia sulphamethiazole seems to offer little protection against the development of *M kansasii* infection.

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