Mycobacterium Avium Complex Associated Cavitary Lung Disease In A Long-Term Haemodialysis Patient

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Citation

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Abstract

The compromised immunological state of dialysis patients has an effect of altering the immune response to almost every known pathogen when compared with the healthy population, giving atypical clinical findings. We report a rare case of a cavitary lung disease due to Mycobacterium avium complex in an HIV-negative non-neutropenic patient without preexisting underlying lung pathology. He was an end stage renal disease patient under dialysis for the past eight years and died following a rapidly progressive lung disease in a three months interval. In addition to the unusual clinico-radiological appearance, every treatment effort was unsuccessful due to a completely non-susceptible microorganism.

INTRODUCTION

The progressive deterioration of renal function is accompanied by a parallel decline in the immune status of the patient ([1]). Treatment by haemodialysis does not restore a normal immune response and sometimes may contribute to the suppression of the immune system ([2]). This is a clinically important situation because, even after controlling all modern parameters of adequacy of dialysis, infections remain one of the main causes of death in the haemodialysis population. Patients are anergic, highly susceptible to various infectious agents, and do not respond adequately to vaccinations especially with thymus-depended antigens. The abatement involves mainly the cell-mediated immune response. Clinically this is manifested by an enhanced susceptibility to mycobacterioses for which dialysis patients have a ten to fifteen times higher incidence than the healthy population ([3,4]).

CASE REPORT

Among the mycobacterioses diagnosed in our dialysis unit we describe a case of lung infection due to Mycobacterium Avium Complex (MAC). A 59 year old male was on regular haemodialysis for eight years due to chronic glomerulonephritis confirmed by kidney biopsy. His dialysis schedule was 4 hours per day, 3 times per week, with a C10 cuprophane filter. His Kt/V always exceeded 1.2 and he was in a generally satisfactory condition. During the last three months, he developed malaise, weakness, anorexia, weight loss (11 kg in 70 days), night sweats and other nonspecific symptoms. His lab tests and X-rays showed nothing at the 20th day. Blood cultures were negative for common pathogens. Two weeks later he developed an intermittent fever and a productive cough. Then the chest X-ray revealed 3 inhomogeneous nodular lesions in the upper right lobe with a rather smooth periphery. The linear tomography demonstrated that the lesions were cavitary, with thick regular walls and surrounded by a mild parenchymal inflammatory reaction (Figures 1a, 1b).

Figure 1

Figure 1a: This chest X-ray shows 3 inhomogeneous nodular lesions in the upper right lobe with a rather smooth periphery.

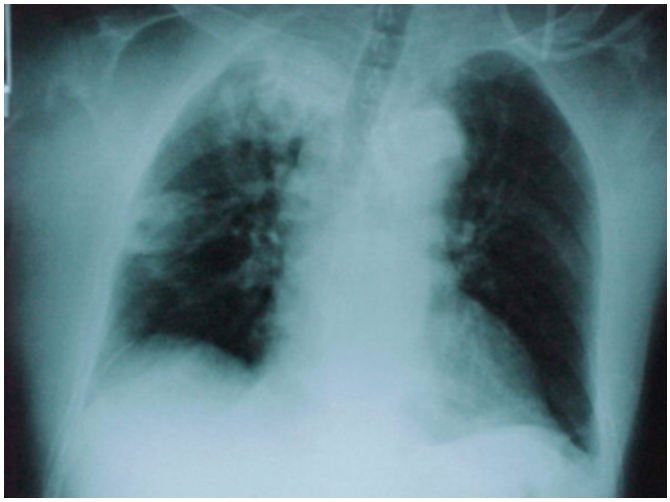
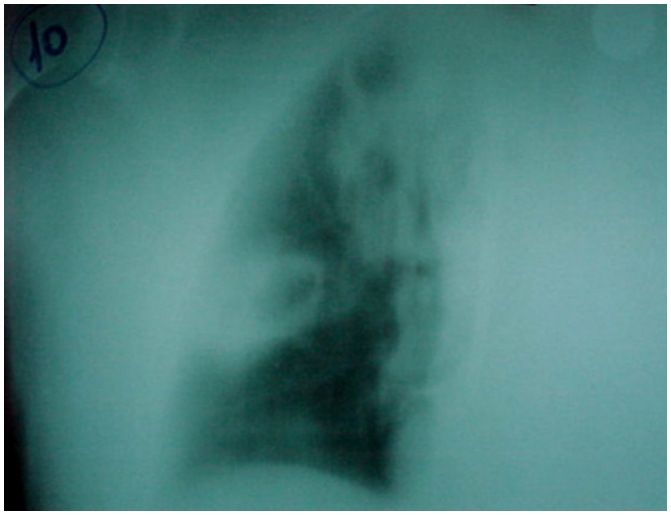


Figure 2

Figure 1b: Linear tomography during the same period demonstrating that the lesions were cavitary, with thick regular walls and surrounded by a mild parenchymal inflammatory reaction.



There were still no findings in his blood tests although a slight increase in his epoetin dose was necessary to keep his haemoglobin close to 12mg/dl. Repeated Gram and Zeihl-Neelsen stains, blood and sputum cultures for aerobic, anaerobic bacteria and fungi, as well as HAV, HBV, CMV, HSV1&2, EBV and HIV1&2 were all negative. A tuberculin test with 5 TU (PPD Merieux) was also negative (3mm). Because of the high incidence of tuberculosis in uremic patients and the suspicious clinical and radiological findings, a three anti-tuberculosis drug regime was commenced, i.e. isoniazid 300 mg daily, rifampicin 600 mg daily and pyrazinamide 25 mg/kg after each dialysis session. Bronchoscopy gave no evidence of pathology from the tracheo-bronchial tree.

Four weeks later acid-fast colony types were isolated in Löwenstein-Jensen medium cultures. The isolates were identified as Mycobacterium Avium Complex (MAC) with classical biochemical methods and clarithromycin 500 mg daily plus ethambutol 25mg/kg 3 hours before each dialysis were added to the therapy. The Zeihl-Neelsen stain of the broncho-alveolar lavage performed was also positive for acid-fast bacilli. Cultures of the new respiratory samples with a BACTEC TB 460-radiometric system produced a detectable growth after two weeks. The samples were tested with use of commercial DNA probes. The amplified Mycobacterium Tuberculosis Direct Test (AccuProbe) was negative, while the Mycobacterium Avium Complex identification test was positive.

The patient showed no response to treatment, deteriorated progressively and died following a cardiopulmonary arrest, during a haemodialysis session. The in vitro susceptibility test results showed a completely resistant microorganism to macrolides and to the entire first line antituberculus drugs.

DISCUSSION

Although MAC is the most common cause of pulmonary non-tuberculosis mycobacterial (NTMB) disease in the general population, in two extensive studies in ESRD patients it was never identified as the cause of a pulmonary infection. In the first study in Spain, 12 symptomatic cases with cultures positive for NTMB were identified out of 1,430 samples from ESRD patients, 4 with M. Fortuitum and 8 with M. Gordonii ([5]). In the second study a few outbreaks of infections with the atypical mycobacteria, Gondonii and Chelonei, were described in Canada, associated with contaminated water springs ([6]).

Recently Colby described a case of a MAC associated lung disease in a chronic haemodialysed patient. However, in that case report the lung disease was manifested by multiple bilateral small pulmonary nodules. The author supported the association of the infection with hot tub exposure ([7]). Von Reyn et al first correlated the colonization of the hot water system in an institution with a particular strain of MAC and the development of disseminated infection in HIV-infected patients exposed to those water springs ([8]). The source of the infection, in the case of our patient could not be traced. The possibility of a MAC nosocomial infection is scant and since then no other case of MAC associated infection was encountered in our dialysis unit. The progression of MAC disease is unpredictable in HIV-negative patients. Some patients maintain a stable picture for years, whereas others demonstrate a relatively rapid progression. Our case verifies the earlier observation of Rosenzweig that patients with extensive radiographic MAC infection and/or cavitations, are more likely not to respond sufficiently to treatment, compared to patients with non-cavitary localized disease.

In the case of MAC infection, in vitro susceptibility testing is not recommended as a routine as in the case of M. Tuberculosis infection. In the in-vitro tests designed for defining the susceptibility of M.Tuberculosis strains are using relatively low drug concentrations of isoniazid, rifampincin, streptomycin and ethambutol in which the strains of the complex are almost always resistant ([9],[10]). In our case, the clinician cannot apply this therapeutic criterion since three to six months are necessary for respond to

treatment with an unquestionable clinical and radiological improvement. When the disease does not respond to conservative therapy and is localized, surgery is an alternative, but as far as we could trace there is no experience in the dialysis population.

In our patient the disease presented with a typical manifestation with features similar to those of post-primary tuberculosis and radiological features indistinguishable from those of a cavitary tuberculosis disease ([11]). Pulmonary MAC infection has five distinct clinico-radiological manifestations: (a) classic infection with features similar to those of post-primary tuberculosis, (b) no classic infection with bronchiectasis and centrilobular nodules usually in the lingula and middle lobe of the lungs, (c) nodules in symptomatic patients, (d) infection in patients with achalasia that resembles aspiration pneumonia at radiography and (e) infection in the immuno-compromised host with findings in the chest radiograph similar to those of the primary tuberculosis ([12,13]). This particular presentation resembled the one met in MAC affected elderly white men with either a history of underlying lung disease, heavy cigarette smoking, or alcohol abuse ([14,15]) but none of the above predisposing factors were present in our patient. The manifestation of infection associated with such an opportunistic pathogen can be attributed only to the immunosuppression of the uremic environment ([16]), but they present with totally different clinico-radiological manifestations.

CONCLUSION

This patient's case is unique since for the first time a cavitary lung disease was associated with MAC infection in a chronic haemodialysis patient. The unusual radiographic appearance was accompanied by treatment failure and a rapidly deteriorating course because of a completely non-susceptible microorganism. It is a common belief, also verified in our case, that medical treatment of MAC pulmonary disease with resistance to macrolides, is usually frustrating and disappointing.

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