CASE REPORT

Paradoxical worsening of chest radiographs secondary to immune reconstitution syndrome (IRIS) in a patient with advanced HIV infection and *Rhodococcus* pneumonia

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SUMMARY

We present a rare case of post-antiretroviral therapy (ART) paradoxically worsening of radiological findings in a patient with advanced HIV-infection on treatment for *Rhodococcus pneumonia* who was misdiagnosed with pulmonary tuberculosis. Despite clinical improvement, serial chest radiographs showed deteriorations a month after starting ART. This was attributed to Immune Reconstitution Inflammatory Syndrome (IRIS) which spontaneously resolved without any treatment.

INTRODUCTION

Early detection and management of opportunistic respiratory infections such pulmonary tuberculosis (PTB) in patients with advanced HIV-infection is crucial in view of high mortality risk. *Rhodococcus equi* infection mimics PTB clinically and radiologically posing a diagnostic challenge.

We report a rare case of paradoxical worsening of radiological findings with initiation of antiretroviral therapy (ART) attributable to immune reconstitution inflammatory syndrome (IRIS) in a patient with advanced HIV-infection misdiagnosed with PTB but later diagnosed with *Rhodococcus* pneumonia. There has only been one other case reported.[1]

CASE PRESENTATION

A 38-year-old man presented with one-month of low-grade fever, productive cough with yellowish sputum and weight loss of 10kg, associated with poor appetite. At presentation his temperature was 37.5°C with oxygen saturation of 95% at room air. There was oral thrush. Bronchial breathing was heard on the right upper and mid-zones.

Sputum smears were negative for tuberculosis. Combo test was reactive for HIV-1. His CD4 count was 9cells/mm^3. Chest radiograph showed ill-defined opacities with cavitation at the right upper zone (Figure 1a). Based on the symptoms and the chest radiograph appearance he was provisionally diagnosed as advanced HIV with smear-negative PTB and commenced on standard anti-TB regimen.

He was later discharged and planned for a bronchoscopy in two weeks later. His fever and cough however persisted but his anti-TB therapy had to be stopped due to elevated serum alanine aminotransaminase level of 220U/L. His chest radiograph showed right upper zone opacity that had enlarged to mid zone (Figure 1b) and as a result intravenous ceftazidime 2gm TDS was initiated for presumed hospital-acquired pneumonia.

Bronchoalveolar lavage analysis was negative for tuberculosis. *Rhodococcus sp*. sensitive to cotrimoxazole, ciprofloxacin, ceftriaxone, azithromycin and cefepime was isolated from blood culture. He was treated with intravenous azithromycin 250mg OD and intravenous ciprofloxacin 400mg BD. Fever resolved within 24-hours and he was discharged after two weeks with oral forms of the antibiotics. Although he was scheduled for a review at 2-week, he presented only after 4-week. His cough had resolved with no fever recurrence. However, the chest radiograph showed persistent right upper lobe opacities and cavities (Figure 2a). ART consisting of tenofovir fumarate, emtricitabine and efavirenz was initiated for HIV infection at this review.

He missed his scheduled review at two weeks and again presented 29 days later but despite that, he was adherent to both ART and antibiotics. He was asymptomatic and had gained 11kg in weight. However, his chest radiograph showed worsening of consolidation with partial right upper lobe collapse (Figure 2b). The antibiotics and ART were continued. He remained well and chest radiograph at 3-month showed complete resolution of lung cavitatory lesions (Figure 2c).

DISCUSSION

Rhodococcus sp. is an aerobic gram-positive coccobacillus found in soil, water and guts of foals (baby horses). Inhalational exposure or ingestion of contaminated material are major routes of human infection. Exposure to foal should be elicited in history taking although it may not be present.[1] Several species are pathogenic to humans but most human infections are caused by *R.equi*. Up to 90% of patients with R.equi infection are immunocompromised with more than half of them having HIV infection and CD4 count of <200cells/mm^3.[2]

The lungs are the most common site of infection caused by *Rhodococcus sp* with 50-75% predilection for the upper lobes often with concomitant cavitation, mimicking PTB. Other

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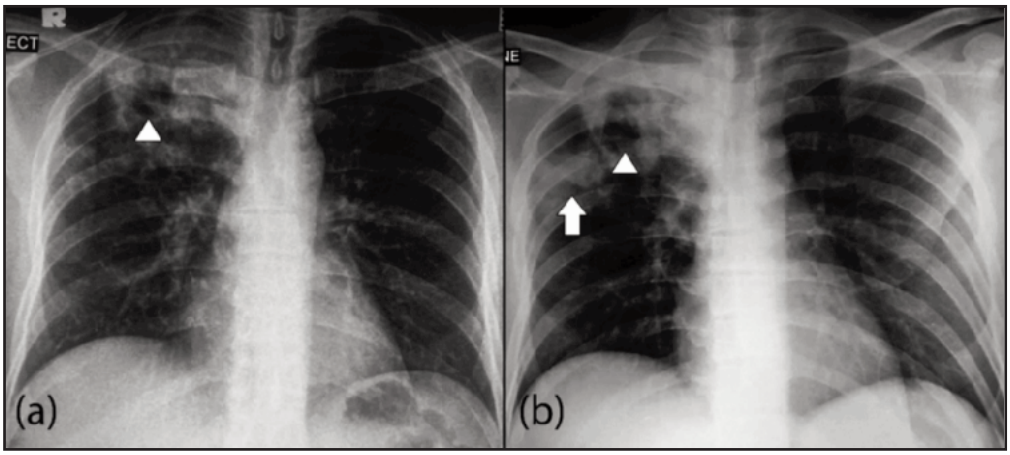

Fig. 1: (a) Chest radiograph at initial presentation showed ill-defined air space opacities with a small cavity (arrowhead) at right upper zone. (b) Chest radiograph 2-weeks later showed increased opacity surrounding the cavity (arrowhead) and at the middle zone of the right lung (arrow).

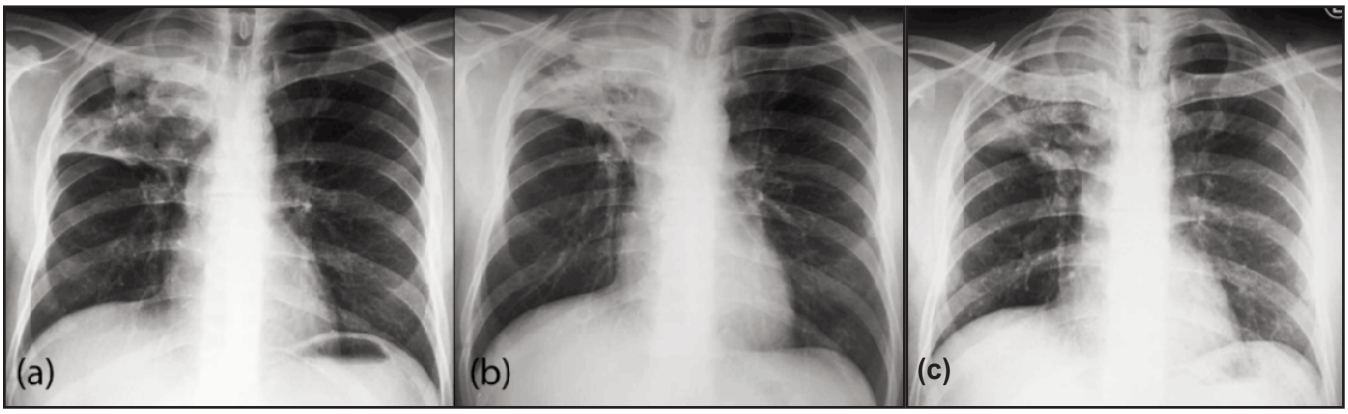

Fig. 2: Follow-up chest radiographs at (a) 5-weeks and (b) 2-months after ART showed worsening right upper lobe consolidations and cavitation. Partial right upper lobe collapse seen as evidenced by elevation of the right transverse fissure and right hilar structures in (b). (c): Chest radiograph 3 months after antibiotics showed resolving right upper lobe consolidation with no evidence of cavity.

radiological features include nodular lung opacities, pleural and pericardial effusions, empyema, and mediastinal lymphadenopathy.[3] Radiological differential diagnoses include tuberculosis, fungal infections, lymphoma or primary bronchogenic carcinoma.[3] Extra-pulmonary manifestations due to haematogenous spread include uveitis, osteomyelitis, septic arthritis and abdominal abscess.

Combination therapy with two or three drugs is the mainstay therapy due to concerns regarding emerging resistance, especially among immunocompromised patients. Quinolone combined with macrolide and/or rifampicin which have high intracellular concentrations are recommended as *Rhodococcus* tend to be intracellular within macrophages.[4]

This patient was treated with intravenous ciprofloxacin combined with azithromycin. Rifampicin was not used due concerns over possible drug-resistance as it was part of his anti-TB regimen. Recommended duration of therapy is at least two months with the ultimate duration guided by radiological improvement. Patients with persistent clinical or radiographic evidence of infection require longer duration of antibiotic therapy. This patient received 4-months of oral azithromycin and ciprofloxacin before switching to secondary prophylaxis with oral azithromycin 250mg OD and levofloxacin 750mg OD until his CD4 is >200cells/mm^3 with ART.

Immune reconstitution inflammatory syndrome (IRIS) is an exaggerated inflammatory reaction from immune system recovery following treatment with ART. There are two manifestations of IRIS. 'Unmasking IRIS' is the flare-up of previously undiagnosed infection while 'paradoxical IRIS' is the worsening of previously treated infection.[5]

The median time for development of IRIS after ART initiation is about 33 days.[5] This patient developed paradoxical worsening of chest radiograph findings 29 days after initiation of ART although he remained well compared to 21 days in another similar case.[1] The worsening radiological findings are attributed to IRIS. Risk factors for the IRIS include low baseline CD4 count, high viral load, rapid increase in CD4 count, rapid decline of viral load, and presence of opportunistic infections. Initiating ART was a difficult

decision in this patient in view of persistent lung lesions [Figure 2(a)] despite improvement in his general wellbeing four weeks into the treatment for *Rhodococcus*. Early ART provides immune recovery needed to get over the infection but presents a real risk of IRIS, particularly in patients with very low CD4 count and opportunistic infection.

The consensus in the management of IRIS is not to discontinue medications including ART if the patient is asymptomatic. In most cases, IRIS is self-limiting. Where there are severe or prolonged symptoms affecting quality of life or organ function, corticosteroids may be indicated. At 3 months post-ART initiation the patient remained asymptomatic with complete resolution of cavitatory lung lesions on chest radiograph (Figure 3).

CONCLUSION

This case demonstrated that *Rhodococcus* pneumonia in patients with advanced HIV infection may be misdiagnosed as PTB due to similar chest radiographic findings. *Rhodococcus* infection should be suspected in patients with advanced HIV infection presenting with an upper lobe cavitary pneumonia who respond poorly to conventional antibiotic therapy. The infection is often successfully treated with a regimen containing antibiotics with intracellular activities administered orally, and always in combination with ART. The possibility of paradoxical IRIS manifesting clinically or radiologically should be taken into consideration.

REFERENCES

1. Lattur M, Marco D, García Gasalla M, Arribas Escobar V, Soleto Roncero MJ, Bassa Malondra A. [Rhodoccocus equi pulmonary infection in a HIV-infected patient and radiological worsening following treatment: Case report.] An Med Interna 2008; 25: 370-1.
2. Capdevila JA, Bujan S, Gavalda J, Pahissa A. Rhodococcus equi pneumonia in patients infected with human immunodeficiency virus. Report of 2 cases and review of literature. Scan J Infect Dis 1997; 29(6): 535-41.
3. Muntaner L, Leyes M, Payeras A, Herrea M, Gutierrez A. Radiologic features of Rhodococcus equi pneumonia in AIDS. Eur J Radiol 1997; 24(1): 66-70.
4. Yamshchikov AV, Schuetz A, Lyon GM. Rhodococcus equi infection. Lancet Infect Dis 2010; 10(5): 350-9.
5. Haddow LJ, Easterbrook PJ, Mosam A, Khanyile NG, Parboosing R, Moodley P, et al. Defining immune reconstitution inflammatory syndrome: evaluation of expert opinion versus 2 case definitions in a South African cohort. Clin Infect Dis 2009; 49: 1424-32.