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Mycobacterium riyadhense as the opportunistic infection that lead to HIV diagnosis: A report of 2 cases and literature review

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ABSTRACT

Human immunodeficiency virus (HIV) infection usually presents with a wide range of manifestations. Although HIV patients are prone to pulmonary infections by opportunistic pathogens in the late stage of AIDS, manifesting the disease with pulmonary infections caused by *Mycobacterium riyadhense* (newly identified non-tuberculous mycobacteria) is extremely rare with only one case reported in the literature. We are describing two previously healthy patients who presented with *M. riyadhense* lung infection and were subsequently found to have HIV, illustrating the need for considering the possibility *M. riyadhense* lung infection as a presenting illness of HIV.

Introduction

Non-tuberculous mycobacteria (NTM) are generally rare but they are a common cause of infections in HIV infected patients, with pulmonary infections being the most common [1]. Although *Mycobacterium avium* complex remains the most common one, other species may cause infection, including *Mycobacterium riyadhense* (*M. riyadhense*), a newly recognized slow-growing, non-photochromogenic NTM. It was originally isolated in 2009 from a 19-year-old male in Riyadh, from where it got its name [2]. Few cases have been reported where *M. riyadhense* was found in HIV patients [3], or even more rarely, the presenting symptom of HIV infection [4]. We present two rare cases who presented with *M. riyadhense* pulmonary infection, as a presenting infection that lead to HIV diagnosis.

Patient 1

A 44-year-old female, with a known case of hypothyroidism presented to King Abdulaziz Medical City-Riyadh, on July, 2013 with one month history of productive cough with yellowish sputum, shortness of breath (SOB), and fever. She reported a significant history of weight loss, about 8 kg in the last month, otherwise her history was unremarkable. On physical examination, she was febrile with a temperature of 38.9 °C and a respiratory rate of 24 breaths per minute. Respiratory exam showed decreased breath sounds and bilateral coarse crepitations at both bases. Other exam was unremarkable. Her complete blood counts showed WBC of 9×10^9/L. Erythrocytes sedimentation rate (ESR) was 30 mm/h. Chest X-ray revealed right perihilar infiltration extending to the right upper lobe. No plural effusion. Chest CT with contrast showed diffuse back ground glass attenuation in both lung bases with focal segmental consolidation in the right upper lobe that contain small cavity (Fig. 1). Patient was admitted as a case of community acquired pneumonia and started on ceftriaxone and azithromycin. The next day she became hemodynamic unstable and hypoxic, so she was shifted to the Intensive Care Unit (ICU). Sputum for acid fast bacilli (AFB) was positive x3, but polymerase chain reaction (PCR) for mycobacterium TB (MTB) complex was negative. Final growth after 4 weeks was *Mycobacterium terrae* using conventional Bio-

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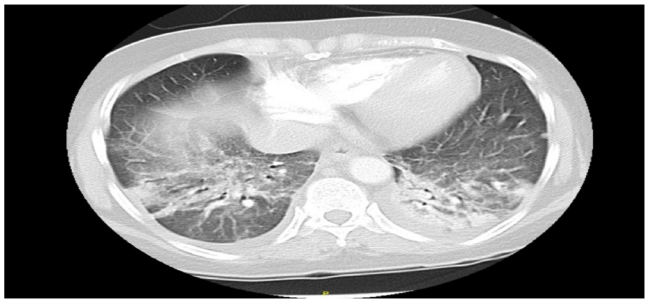

Fig. 1. Contrast-enhanced computed tomography showing diffuse back ground-glass attenuation in both lungs bases with focal segmental consolidation in the right upper lobe.

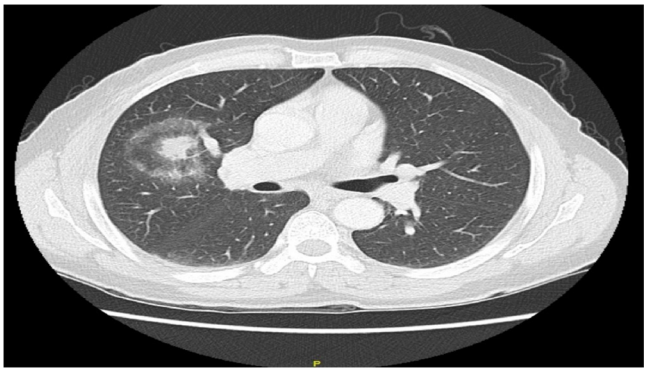

Fig. 2. A chest CT scan showing right upper lobe mass with hilar lymph node enlargement.

chemical Testing (Nitrate Reduction, Heat Catalase 68C, Tellurite Reduction, Urease Production, Tween 80 Hydrolysis, Arylsulfatase, Nacl Tolerance, MacConkey agar without Crystal Violet and Pigment Production) and INNOLiPA Test (a line probe assay based on reverse blot hybridization), and the specimen was sent for Bioscientia Reference Laboratory (Ingelheim, Germany) for genotypic testing, where it was identified as *M. riyadhense* which was susceptible to clarithromycin, ethambutol and rifampicin.

HIV screening using 4th generation enzyme-linked immunosorbent assay (ELISA) was positive and it was confirmed by a positive western blot test. The CD4 count was 29 cells/mcl and HIV viral load was 71,877 copies/ml. Since she presented with symptoms of fever, cough and weight loss, showed a radiologic evidence of pulmonary disease that was not due to TB, and had at least two sputum specimens positive for AFB thus satisfying the diagnostic criteria for NTM lung infections by the American Thoracic Society and Infectious Disease Society of America (ATS/IDSA) [5], she was started on azithromycin, ethambutol and moxifloxacin for NTM lung infection and 2 weeks later was started on combination of emtricitabine/tenofovir and efavirenz for HIV. She completed a course of 12 months of anti-mycobacterial therapy after which she showed complete resolution of her chest infection both clinically and radiologically, and her HIV infection was controlled with suppressed viral load and improved CD4 count.

Patient 2

A 51-year-old Saudi male, heavy smoker, known case of DM, HTN presented to King Abdulaziz Medical City-Riyadh, on Sep, 2015 with 3 months' history of productive cough with yellowish sputum, positive history of SOB, fever, weight loss, night sweats, and loss of appetite. One month prior to his presentation, he was admitted as a case of pneumonia. He received a course of piperacillin/tazobactam and azithromycin for 5 days and was discharged on amoxicillin/clavulanate for 5 days. His symptoms improved a bit but relapsed when he stopped his antibiotics. This time, chest CT showed right upper lobe mass with hilar lymph node enlargement (Fig. 2). Sputum AFB and culture were negative twice. On initial examination, patient looked ill, and in respiratory distress. Temperature was 39.2 °C, and respiratory rate of 23 breath/min. Respiratory exam revealed decreased breath sounds with crepitation on the right upper zone. Examination otherwise was unremarkable. His ESR was 95 mm/h. HIV screening using 4th generation enzyme-linked immunosorbent assay (ELISA) was positive and it was confirmed by a positive western blot test. CD4 count was 3.00 cells/mcl and viral load of 715,462 copies/ml. Repeated chest CT showed new bilateral diffuse opacification of both lungs, relatively sparing the bases, suspicious for infection. Patient underwent bronchoscopy and bronchoalveolar lavage was taken from right and left lung which was positive for Pneumocystis jiorvecii pneumonia (PJP), but negative for AFB and malignant cells. He was treated with high dose trimethoprim-sulfamethoxazole and adjunctive prednisone for PJP then followed by antiretroviral therapy (ART) with dolutegravir and emtricitabine/tenofovir 2 weeks later. One month later, he had a recurrence of the same respiratory symptoms despite that PJP was cured clinically and radiologically. Sputum AFB was positive this time and PCR for MTB complex was negative. Chest CT showed mediastinal adenopathy with localized tree in bud and ground glass attenuations. Using the same biochemical testing and INNOLiPA test in case one, the NTM was identified as *Mycobacterium smegmatis* few weeks later. It was also sent for genotypic testing by Bioscentia where it was identified as *M. riyadhense* which was susceptible to clarithromycin and rifampicin. The diagnosis of NTM lung infection was made based on the ATS/IDSA criteria [5], and he was started on moxifloxacin and clarithromycin for 10 months with clinical and radiological cure.

Discussion

Over 170 species of NTM exist and more are being identified as molecular techniques for identification of emerging NTM strains become more advanced [6]. The newly discovered NTM, *M. riyadhense*, is potentially pathogenic to humans, a claim supported by its close relation to *Mycobacterium szulgai*, *Mycobacterium kansasii* and *Mycobacterium malmonese*, the most pathogenic NTM species [5,7].

Most of the reported cases in literature (including our patients) were isolated from Saudi Arabia [2–4,8–10], few cases from France, Bahrain [11], Korea [12] have been documented. The majority of cases were in adults aged 18–54 years, only one case was seen in a child [10]. Although *M. riyadhense* has been reported to cause infection mostly in immunocompetent patients, few cases recently have documented the isolation of this infection from HIV patients [3,4]. This is however the second report in which HIV patients unusually manifest their disease with this rare infection. While pulmonary involvement is by far the most frequent manifestation, occurring in 5 of 9 cases reported, extra-pulmonary infections have been encountered as well [2,8–10].

Establishing diagnosis of *M. riyadhense* is challenging since it is not only indistinguishable from TB [11], but from other NTM as well. In both of our patients, the organism was initially misidentified, respectively, as *M. terrae* complex and *M. smegmatis*, mandating a high index of suspicion for potential misidentification.

Because of the limited number of cases reported in literature, no specific agent is approved to treat *M. riyadhense* infections. Although resistance to isoniazid was common [12], several cases reported that nearly all patients have been cured with Rifampicin, ethambutol, pyrazinamide (first line treatment of –TB) [2–4,8–12]. Surprisingly, in one case [11], the patient had a relapse after being

Table 1
clinical characteristics of all *Mycobacterium riyadhense* cases reported in the literature.

Case no	Author	Country	Age, gender	Clinical manifestation	Initial regimen	Modified regimen	Outcome	HIV status
1	van Ingen et al. [2]	KSA	19, M	Extrapulmonary (bone, maxillary sinus)	INH,RIF,EMB	INH,RIF	Cured	Not reported
2	Gordreuil et al. [11]	France	39, F	Pulmonary	INH,RIF,EMB	INH, RIF	Cured	Not reported
3	Gordreuil et al. [11]	Bahrain	43, F	Pulmonary	CLR,CIP	INH,RIF,PZA,EMB,CLR,CIP	Relpsed then Cured	Not reported
4	Choi et al. [12]	Korea	38,F	Pulmonary	INH,RIF,EMB,PZA	RIF, EMB,PZA	Cured	Not reported
5	Garbati and Hakawi [4]	KSA	54, M	Pulmonary	INH,RIF,EMB, PZA, CLR	EMB,RIF,CLR	Cured	Positive
6	Saad et al. [8]	KSA	18, F	Extrapulmonary (bone and skull frontal lobe)	INH,RIF,EMBPZA,MOX	RIF,EMB	Cured	Not reported
7	Saad et al. [8]	KSA	24, F	Extrapulmonary (spine)	INH,RIF,EMB,PZA	RIF,EMB	Cured	Not reported
8	AlAmmari et al. [3]	KSA	30, M	Pulmonary	INH,RIF,EMB,PZA	INH,MOX, EMB,PZA	Cured	Positive
9	Al-Dossary et al. [10]	KSA	7, M	Extrapulmonary (lymph node)	CIP,CLR,RIF, EMB	CIP,CLR	Cured	Not reported
10	Varghese et al. [9]	KSA	25, M	Pulmonary	CLR/INH/RIF	N/A	Cured	Not reported
11	Varghese et al. [9]	KSA	55, M	Pulmonary	INH/RIF/EMB/PZA	N/A	Cured	Not reported
12	Varghese et al. [9]	KSA	39, F	Pulmonary	INH/RIF/EMB/PZA	N/A	Cured	Not reported
13	Varghese et al. [9]	KSA	77, M	Pulmonary	INH/RIF	N/A	Cured	Not reported
14	Varghese et al. [9]	KSA	37, M	Extrapulmonary (lymph node)	INH/RIF/CLR	N/A	Cured	Not reported
15	Varghese et al. [9]	KSA	82,M	Pulmonary	CLR/INH/RIF	N/A	Cured	Not reported
16	Varghese et al. [9]	KSA	18, M	Pulmonary	INH/RIF/EMB/PZA	N/A	Cured	Not reported
17	Varghese et al. [9]	KSA	32, M	Pulmonary	CLR/INH/RIF	N/A	Cured	Not reported
18	Varghese et al. [9]	KSA	61,M	Pulmonary	INH/RIF	N/A	N/A	Not reported
19	Varghese et al. [9]	KSA	8, M	Extrapulmonary (lymph node)	CLR/INH/RIF	N/A	Cured	Not reported
20	Varghese et al. [9]	KSA	82, M	Pulmonary	INH/RIF	N/A	Died	Not reported
22	Varghese et al. [9]	KSA	28, M	Extrapulmonary (lymph node)	INH/RIF	N/A	Cured	Not reported
23	Current	KSA	44, F	Pulmonary	EMB,PZA,MOX,CLR	MOX,EMB, AZT	Cured	Positive
24	Current	KSA	51, M	Pulmonary	MOX,CLR,EMB	MOX,CLR	Cured	Positive

Abbreviations: M: male; F: female; INH: isoniazid; RIF: rifampicin; EMB: ethambutol; PZA: pyrazinamide; CLR: clarithromycin; CIP: ciprofloxacin; MOX: moxifloxacin; AZT: Azithromycin; N/A: not applicable.

started on a combination of clarithromycin and ciprofloxacin (first line treatment of anti-NTM) despite the demonstration of in-vitro drug susceptibility to this combination and patient only improved after adding anti tuberculous therapy to his failing regimen. Different regimens of anti TB have been used as shown in Table 1. Duration of treatment varied mainly according to the site of infection. The median duration of treatment was 13.5 months. In the first patient, we tried a regimen that included azithromycin, ethambutol and moxifloxacin and continued for 12 months. In the second case, the patient was on clarithromycin and moxifloxacin for 10 months. Our patients showed significant response within 2 months from starting the treatment and remained negative at 8 months' follow-up with a significant clinical and radiological improvement.

Conclusion

M. riyadhense infections are extremely rare, and only limited knowledge of this infection in HIV patients is available. Diagnosis often poses a challenge to physicians as it is difficult to distinguish from TB clinically and radiologically. It responds well to anti-tuberculosis therapy. This report serves to remind clinicians with the possibility of HIV infection to present initially with this infection in spite of its rare occurrence, and further enriching the existing limited knowledge of such unusual pathogen in HIV patients.

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Competing interests

None declared.

Ethical approval

Not required.

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