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Pulmonary Mycobacterium Simiae infection and HTLV1 infection: an incidental co-infection or a predisposing factor?

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ABSTRACT: ***Pulmonary Mycobacterium Simiae infection and HTLV1 infection: an incidental co-infection or a predisposing factor? S.M. Mirsaeidi, P. Tabarsi, A. Mardanloo, G. Ebrahimi, M. Amiri, P. Farnia, M. Sheikhleslami, V. Bakayev, F. Mohammadi, S.D. Mansouri, M.R. Masjedi, A.A. Velayati.***

There is little information on atypical mycobacterium and human T lymphothropic virus Type I (HTLV-I) co-infection. We present the first case of pulmonary *M. simiae* infection in co-infection with HTLV-1, confirmed by ELISA antibody test and Western Blot. We discuss the clinical characteristics and laboratory tests of the patient and presumptive immunological relation. We propose that in patients with the HTLV infection and pulmonary symptoms and signs compatible with tuberculosis, evaluation for atypical mycobacteriosis may be recommendable.
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Keywords: Mycobacterium simiae, Pulmonary infection, human T lymphothropic virus Type I.

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There are few reports of infection due to *Mycobacterium simiae*, particularly in non-Human Immudeficiency virus (HIV) patients. *Mycobacterium simiae*, an atypical mycobacterium, is recognised as an infection-causing agent in immunocompromised patients. We report a case of pulmonary infection due to M.simiae, associated with human T lymphothropic virus Type I (HTLV1) seropositivity, which to our knowledge, is the first case of *Mycobacterium simiae* and HTLV1 co-infection.

Case presentation

A 51 year old married woman was referred to our hospital as a multi drug resistant case from Tabriz TB centre in the north western province of Iran (Eastern Azerbaijan). The disease had presented with cough and productive sputum since one year before admission. After 3 months, the patient, being diagnosed as a case of smear positive pulmonary tuberculosis, had received a 6 month anti tuberculosis regimen including first line drugs (Isoniazid, Rifampin, Ethambutol, and Pyrazinamid) according to standard World Health Organization (WHO) recommendations.

The sputum culture was positive in the end of 5th month of treatment, and antibiogram showed resistance to all first line anti tuberculosis drugs. The patient was referred to our hospital for further investigation and subsequent treatment.

At the time of admission, she presented with mild cough and dispnea, chest pain, fever, night sweat and mild anorexia. She was a passive smoker without any history of TB or any other lung diseases. No tuberculosis history was found in patient's family.

Upon physical examination, she was neither ill nor cachectic.Vital signs were within normal range. In lung, fine disseminated, early inspiratory crackles were present in both fields. No organomegaly or lymphadenopathy was present.

The chest radiography and spiral thorax Computed Tomography scan are shown in figures 1 and 2.

Sputum culture in Lowenstein-Johnson medium revealed slowly growing photochromotogen, colonies. The organism was niacin positive, whereas it failed to reduce nitrate, and was also negative in Tween hydrolysis. Polymerase chain reaction and restriction fragment length polymorphism using primers (439-bp segment of gene encoding the 65-kDa heat shock protein) was performed in two separately cultured colonies mediums [1]. The mycobacterium was identified as *Mycobacterium simiae* by RFLP (figure 3).

We found more than 6 positive cultures in one year and repeated sputum smear positive in joint to new clinical and radiological characters of mycobacterial infection without the presence of *M.tu-*

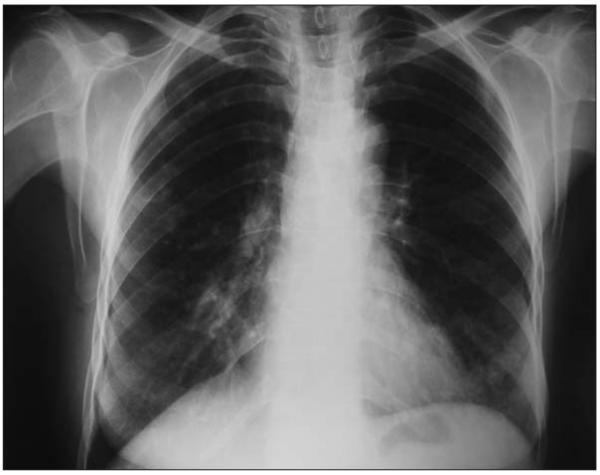

Fig. 1. - Chest X- ray revealed middle lobe infiltration and right lower lobe honey-comb.

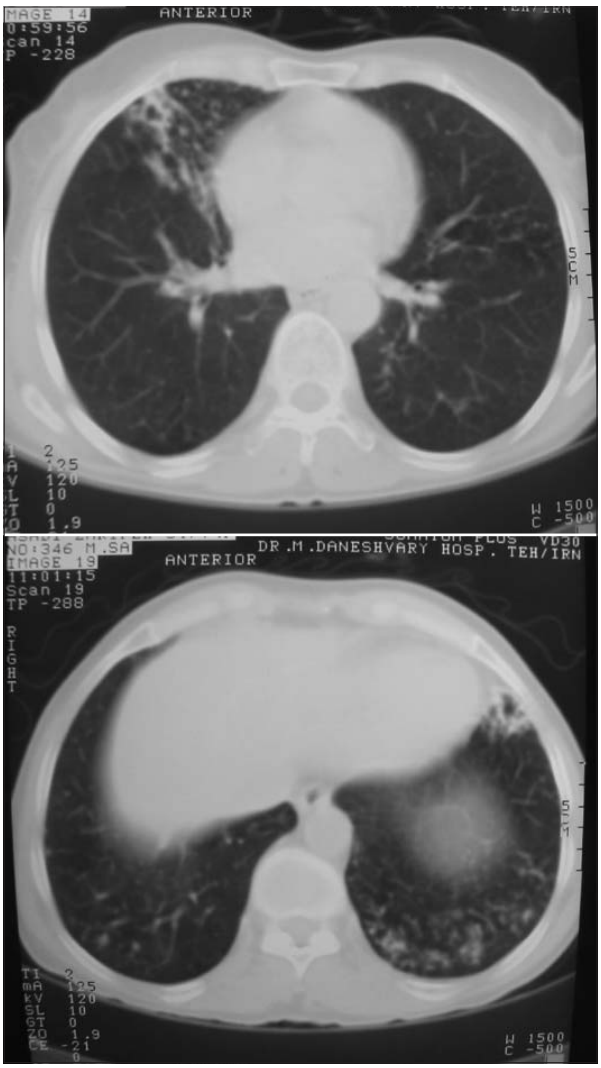

Fig. 2. - Spiral computed tomography of thorax (axial without contrast). Three in bud pattern of infiltration is seen in right upper lobe, right middle lobe, lingula and left lower lobe, with bronchiectasis and partial loss of volume in right middle lobe.

berculosis. In this case, for confirmation of absence *M.tuberculosis*, we also used molecular study.

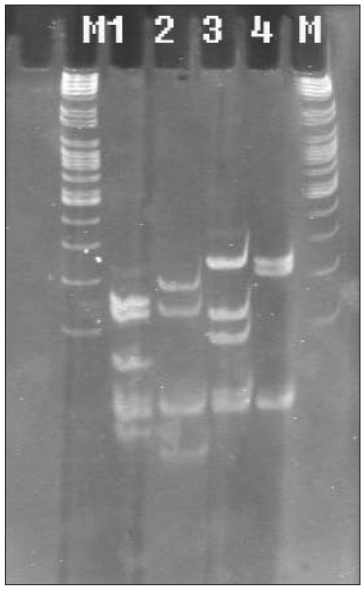

Fig. 3. - Result of PCR. Test procedure: PCR-RFLP (companion with genetic pattern of standard strains from Pasture institute in Paris).
Result: *Mycobacterium Simiae*.
Two different samples:
Negative for *Mycobacterium Tuberculosis.*
Positive for *Mycobacterium Simiae.*
M: Marker, lane 1,2: Digesting with Hae 3 endonuclcease, Lane 3,4: Digesting with BSTE 2 endonuclease
Lane 1: H37RV, Lane 2: Patient Sample, Line 3: H37RV, Lane 4: Patient Sample

The patient was referred to bronchoscopy, bronchoalveolar lavage and transbronchial lung biopsy when she was hospitalised. The pathology results revealed granulomoatous reaction that was compatible with mycobacterial infections.

The immunological variables were detected by the means of serology tests, flow cytometry and detecting antibodies of HIV and HTLV1.

The results of the laboratory tests of patient, including hematological, biochemical, immunological and Mycobacteriological tests are shown in table 1.

The patient went under multidrug-resistant regimen therapy with daily Ofloxacin (600 mg), Amikacin (500 mg), Cycloserine (500 mg), and Pyrazinamid (1500 mg).

With regard to the American Thoracic Society (ATS) criteria [2], the diagnosis of non-tuberculous mycobacteria had been fulfilled and the therapeutic regimen was changed to Clarithomycin 500 mg BID, Ciprofloxacin 500 mg BID and Amikacin 500 mg daily.

The patient had negative smears and her clinical symptoms and signs were alleviated after three months.

Check-ups after six months of the treatment initiation, the patient's smears and cultures were repeatedly without any clinical complaint.

Discussion

There are reports of *Mycobacterium simiae* isolation from clinical specimens and different body sites, including the lungs as the most frequent site blood and bone marrow, skin, urine,lymphnode,brain, umbilical cord [3-9]. Yet, clinical disease reports are rare.

Mycobacterium simiae, originally isolated from monkeys in 1965, has been recovered from environmental origins such as soil samples, tap water, water supply and dental unit waterlines in different parts of world such as Israel, Gaza, central Africa, Europe, USA, Cuba and Australia as well [7, 9-11].

Table 1 - The results of the laboratory tests of the patient

Results		Results	
Immunological variables		**Hematological variables**	
Immunoglobulin G (SRID)	1480	Red cell count (per mm^3)	4830000
Immunoglobulin A (SRID)	175	Hematocrit (%)	38.4
Immunoglobulin M (SRID)	48	Hemoglobin (g/d)	3.3
Immunoglobulin E (ELISA)	42	Mean corpuscular volume (μm^3)	79.5
Anti-HTLV (1&2)	positive	Mean corpuscular Hematocrit	27.5
Anti HTLV (western blot)	positive	RDW	13.7
Anti-HIV	negative	White cell count (per mm^3)	5400000
HBS AG (ELISA)	negative	Differential count (%)	
Anti-HBS (ELISA)	negative	Neutrophils	58
Anti-HCV (ELISA)	negative	Lymphocytes	36
Anti-HIV (ELISA)	negative	Monocytes	2
Anti-HBC (ELISA)	negative	Eosinophils	4
C3 (SRID)	71	Platelet count (per mm^3)	199000
C4 (SRID)	34	Pro thrombin time (sec) (activity 100%)	13
CH50 (u/ml)	110	Partial thromboplastine time	39
Flowcytometry		Erythrocytesedimentation rate (mm/hour)	16
CD4	36	**Blood chemical variables**	
CD8	24	Fasting blood glucose (mg/dl)	90
CD4/CD8	1.5	Urea (mg/dl)	49
CD16	5	Creatinin (mg/dl)	0.8
CD19	13	Uric acid (mg/dl)	3.8
CD56	1.5	Cholesterol (mg/dl)	208
Absolute count CD4	653/µl	Triglyceride (mg/dl)	137
CD2	73.4	Aspartae amino transferase (IU/l)	44
CD3	69	Alanin amino transferase (IU/l)	39
CD14	15.2	Alkaline phosphatase (IU/l)	352
CD16 (FC Gamma Receptor III)	9.7	Bilirubin Total (mg/dl)	1
CD19 (PAN B cell)	21.8	Calcium (mEq/dl)	10
CD56 (NK cell, T cell subset)	12.3	Sodium (mEq/dl)	142
Mycobacteriological tests		Posphorous (mEq/dl)	4.1
Tuberculin skin test	27 mm	Potassium (mEq/dl)	4.1
AFB smear of sputum (repeated 3 times)	positive	Albumin (mg/dl)	4.5
Mycobacterial culture and DST		Rheumatoid factor (RF)	negative
M. Simiae (confirmed by PCR)…		C reactive protein (CRP)	negative
Resistant to I+R+S+E+P (repeated 2 times), mycobacterium photochromogen, slow growing		**Cerebrospinal fluid analysis (CSF)**	
Nirtroblue tetrazolium test (%)	100	Examination of one smear revealing no cellular elements:	acelular specimen
Adenosine deaminase test (negative if <45)	57	Appearance	turbid
		Red blood cell	44000*
		Glucose	49
		Protein	40
		Lactate dehydrogenase (LDH)	11
		Urine analysis	
		Glucose	negative
		Protein	1+*
		Microscopic:	
		WBC	2-3
		RBC	35-40*
		Epithelial cells	3-4
		Urine bacteria	negative

Although in some cases it may be attributed to the contamination or colonisation of *Mycobacterium simiae*, there is evidence, albeit rare, of active disease due to *Mycobacterium simiae* [3-6, 8, 12].

The infection reported in both immunocompetent [5, 6, 8] and immunocompromised patients [2, 3, 8, 11] is thought to occur in immunocompromised patients including patients suffering from AIDS [3, 9] or other causes of immunocompromised states including corticosteroid therapy and solid organ tumour [4].

To our knowledge, this is the first case of infection with *Mycobacterium simiae* together with HTLV1 seropositivity. Furthermore; this is the first case of *Mycobacterium simiae* pulmonary infection, reported from Iran.

However, there has been a recent report of pulmonary mycobacterium avium complex (M.A.C)

infection in HTLV1 carriers, showing that pulmonary MAC infection causes more diffused and widespread lesions in HTLV1 carriers than in non-carriers [13], suggesting the strong inhibition of lymphocyte activation in HTLV1 carriers which may account for the severity of pulmonary M.A.C. infection in HTLV1 carriers [14].

Considering afore mentioned reports, Immunologic status seems to be a main determinant of disease development. With regard to the recent findings about altered immunologic status in HTLV1 carries [15-17], HTLV1 carrier state might be considered to be a predisposing factor for the infection with *Mycobacterium simiae* in this case.

North eastern parts of Iran have been recognised as endemic regions of HTLV1 carrier state [18], but there has been no report of any seropositivity or infection due to HTLV1 in other parts of Iran, such as the eastern Azerbaijan province, located in the north west of Iran, where the patient is from. It seems that in world regions such as Iran, where an endemicity of HTLV1 is documented, there must be a high index of suspicious to infection with atypical mycobacterium, especially *Mycobacterium simiae* in patients presenting with signs and symptoms of mycobacterium tuberculosis infection. Therefore, appropriate diagnostic tests and evaluation procedures should be considered.

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