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Primary multi-drug resistant tuberculosis presented as lymphadenitis in a patient without HIV infection

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ABSTRACT: ***Primary multi-drug resistant tuberculosis presented as lymphadenitis in a patient without HIV infection. S.M. Mirsaeidi, P. Tabarsi, M.O. Edrissian, M. Amiri, P. Farnia, S.D. Mansouri, M.R. Masjedi, A.A. Velayati.***

Primary multi-drug resistant extrapulmonary tuberculosis is an uncommon form of the disease, but it seems that by increasing the number drug resistant tuberculosis around the world, the number of cases of primary multi-drug resistant tuberculosis with extrapulmonary presentation also is going to rise. In this report, we describe a 19-year old, HIV negative man with primary multi-drug resistant TB lymphadenitis, presented with cervical lymphadenopathy and sinus discharge at the site of involved lymph nodes. The Acid Fast Bacilli (AFB) smear of sputum was negative but the AFB smear of discharged fluid as well as the excisional biopsy of the lymph nodes confirmed the *M. tuberculosis* infection. The patient underwent the treatment with a combination of isoniazide, clofazimine, pyrazinamide, ofloxacin and amikacin with promising results. By increasing the number of drug resistant tuberculosis patients around the world, appropriate diagnosis and treatment of different presentations of the disease need a special attention.
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Keywords: HIV Antibodies, Iran, Lymphadenitis, Tuberculosis, Multidrug-Resistant.

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Introduction

Tuberculosis (TB) is an infectious disease with various clinical presentations. Due to the fact that the proportion of TB cases caused by drug-resistant strains has increased around the world in recent years, appropriate diagnosis and management of these patients is vital in controlling the disease.

Among the immunocompetent primary multi-drug resistant TB patients, extra pulmonary presentation of TB is not very common and experience in the management of drug resistant extrapulmonary TB is limited [1, 2]. In this report, we presented a HIV-seronegative primary multi-drug resistant TB patient with lymphadenitis presentation.

Case presentation

A 19 year old Afghan man presented to the outpatient clinic of Tuberculosis in Dr. Massih Daneshvari Hospital with a lump in the right submandibular region, mild anorexia and weight loss. The mass appeared on his neck 2 years ago with a progressive trend. The patient was admitted to the TB ward of the hospital for further evaluation. He had not received any specific management for his problem up to the time of admission. He had a positive history of non-specific fever and chills but he did not mention any history of dyspnea, chest pains, coughs, sputum production and night sweating. He is a non-smoker and the past medical history for any specific disease was negative. He did not mention the history of any close contact with a recognized TB patient. He immigrated to Iran 4 years ago and he was working as a construction worker.

In the physical examination, a movable prominent palpable mass with 2x3 cm diameters was observed in left submandibular region along with three less prominent lymph nodes in left anterior lymphatic chain of the neck. No palpable nodes were found in axilla or supraclavicular areas. The physical examination of other organs was normal. Hematological and biochemical parameters were normal and a Tuberculin skin test (with PPD) for *Mycobacterium tuberculosis* showed a 14 millimeter induration. Microscopical examination of sputum smear was negative for *Mycobacterium tuberculosis* bacilli. An Anti-HIV antibody (ELISA) test was negative. Immunoglublin measures, Nitroblue tetrazolium test and adenosine deaminase test were normal. The flow cytometery result was normal except for a slight decrease in CD3/CD4 percent (table 1). The patient also underwent the

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

	Result		Result
Hematological variables:		***Immunologic variables & other TB-related laboratory tests***	
Red cell count (per mm^3)	4,350,000	Immunoglobulin G (SRID) (mg/dl)	1,700
Hematocrit (%)	35.5	Immunoglobulin A (SRID) (mg/dl)	250
Hemoglobin (g/dl)	11.7	Immunoglobulin M (SRID) (mg/dl)	150
Mean corpuscular volume (μm^3)	81.6	Immunoglobulin G (ELISA) (mg/dl)	106
White-cell count (per mm^3)	6,900	T helper lymphocytes	
Differential count (%)		(CD3/CD4) (%) (Normal range: 28.5-60.5)	24
Neutrophils	72	Anti-HIV antibody (ELISA)	Negative
Lymphocytes	24	Tuberculin skin Test	14mm
Monocytes	1	AFB smear of sputum (repeated 4 times)	Negative
Eosinophils	3	AFB smear of lymph node tissue	Positive
Platelet count (per mm^3)	349,000	AFB smear of discharged fluid from Lymphadenitis	Positive
Prothrombin time (sec) (activity 100%)	13	Mycobacterial culture and DST	
Erythrocyte sedimentation rate (mm/hour)	32	*M.tuberculosis* (confirmed by PCR)	resistant to H+R+S+E
		Nitroblue tetrazolium test (%)	100
Blood Chemical Variables:		Adenosine deaminase test (negative if <45 U/l)	42
Fasting blood sugar (mg/dl)	108		
Urea (mg/dl)	28		
Creatinine (mg/dl)	0.7		
Sodium (mEq/dl)	139	***Urine analysis:***	
Potassium (mEq/dl)	4.2	Sugar	Negative
Aspartate aminotransferase (IU/l)	25	White blood cell	1-2
Alanine aminotransferase(IU/l)	17	Red blood cell	0-1
Alkaline phosphatase (IU/l)	270	Hemoglobin	Negative
Billirubin Total (mg/dl)	0.4	Urine culture	Negative

excisional biopsy of the mass in his neck which the result of pathological examination showed chronic necrotizing granulomatosis inflammation consistent with TB. The Acid Fast Bacilli smear of the specimen was positive for *Mycobacterium tuberculosis*. The specimen was also sent for mycobacterial and mycological culture and antibiogram. Mycology culture of the specimen was negative. The results of the laboratory tests are summarised in table 1. The chest X-ray was normal (fig. 1), but the computed tomography of chest with intravenous contrast showed calcified hilar and subcarinal nodes and a small pleural tag in posterior segment of right upper lobe (fig. 2). Computed tomography of neck revealed numerous peripherally enhancing lymph nodes (fig. 3). By diagnosing the TB infection in the patient, the standardised treatment regimen [3] commenced for the patient (patient's weight was 50 kg) as follows: isoniazid 250

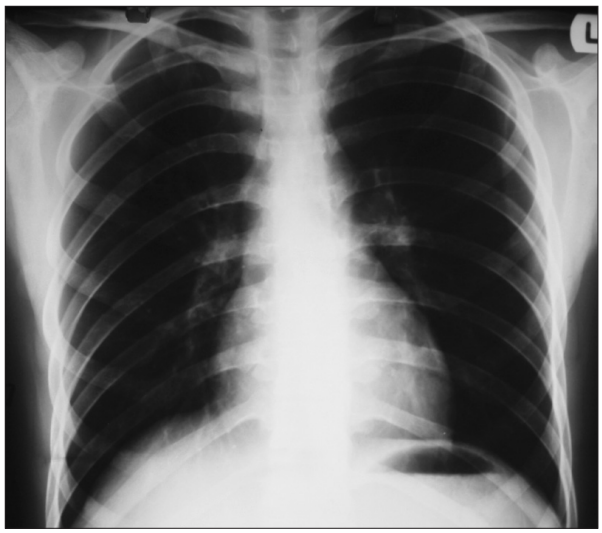

Fig. 1. - The chest X-ray was normal.

mg daily, rifampicin 600 mg daily, pyrazinamide 1250 mg daily and etambutol 1000 mg daily.

Two months after beginning the treatment, not only was no improvement observed in the patient's condition, but also several lymphadonpathies had appeared in the posterior and anterior lymphatic chains in the patient's neck with fistulisation in both sides and thick purulent discharge (fig. 4). The AFB smear of discharged fluid and polymerase chain reaction of the specimen confirmed the infection by *Mycobacterium tuberculosis* bacilli. At the time, the results of culture in Löwenstein–Jensen (LJ) medium and anti-TB drug susceptibility testing (DST) performed by proportion method showed a multi-drug resistance *M. Tuberculosis* which was resistant to isoniazid (H), rifampicin (R) streptomycin (S), and ethambutol (E). Repeating the culture and DST confirmed the previous results, later. The patient was re-interviewed by different interviewers and no history of previous anti-TB therapy was taken. At this time, repeating the physical examination revealed developing of a 1x1 cm lymphadenopathy in the left retroauricular region as well as a 1x1 cm right auxiliary lymph node and 1x1 cm right inguinal lymph node. The treatment strategy was changed by diagnosing tuberculosis with primary drug resistance and the following regimen considered for the patient: isoniazide 500 mg daily, pyrazinamide 1500 mg daily, ofloxacin 600 mg daily, amikacin 500 mg daily and clofazimine 200 mg daily.

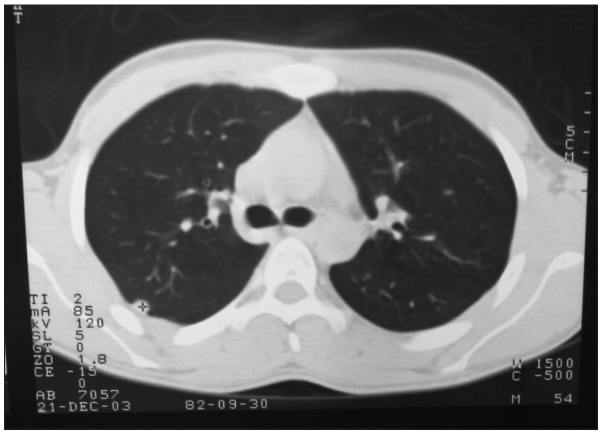

Fig. 2. - Computed tomography of chest with intravenous contrast. It shawed a small pleural tag, in posterior segment of right upper lobe.

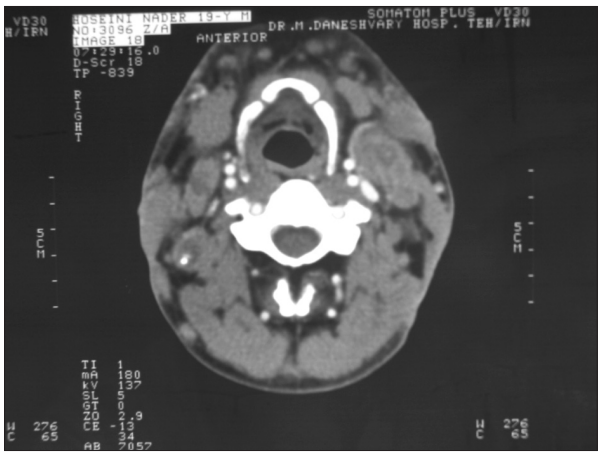

Fig. 3. - Computed tomography of neck; revealed numerous pripherally enhancing lymphnodes.

Two weeks after beginning the new treatment, lymphadenitis and fistula discharge subsided obviously (fig. 4) and a month after the treatment, the result of the smear of discharged fluid changed to negative. We plan to continue the treatment for at least 18 months with precise monitoring and follow up.

Discussion

Drug resistant TB has become a major public health problem since early 1990's globally [4, 5]. The prevalence of new cases of multidrug resistant TB in Iran was estimated 5.0 percent; however this prevalence is 48.2 percent among previously treated cases [6]. Drug-resistant TB was significantly higher ($p < 0.05$) in the foreign-born TB patients than in indigenous patients in Iran [7]. Cervical lymphadenitis is a common extrapulmonary manifestation of TB; nevertheless, it seems that the primary multidrug resistant extrapulmonary TB is an uncom-

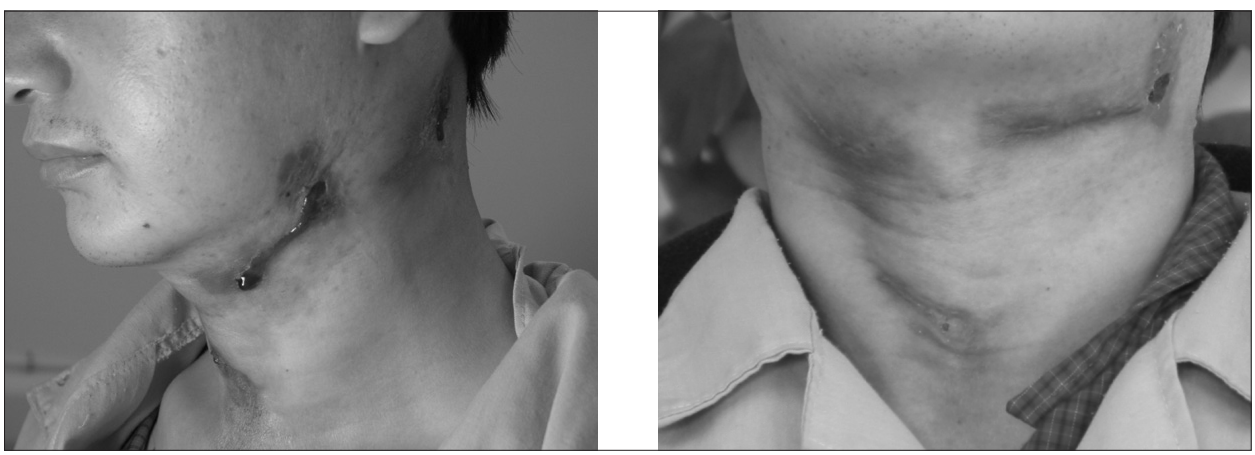

Fig. 4. - Before and after treatment photos of the patient neck.

mon form of the disease [1]. The reported patient is the first immunocompetent patient with primary multi-drug resistant TB in the National Research Institute of Tuberculosis and Lung Disease that is the main referral center for TB in Iran and else where (as our knowledge). The case does not report any previous exposure to TB. In lymphadenitis TB, less than 20% of patients have a history of previous exposure to TB patients [8]. The chest-X-ray in this patient was normal and the primary site of TB was found in his lungs by performing computer tomography scan. This is not a surprising finding because only in 24-46% of patients with TB lymphadenitis, radiographic abnormalities consistent with TB can be observed [9, 10].

While the treatment response in cases with multi-drug resistance had a significantly higher failure rate than those who were susceptible [2, 11], we have had a desirable response to treatment with isoniazide, clofazimine, pyrazinamide, ofloxacin and amikacin in our case with the changing of the discharged fluid smear to negative, significant subsiding the lymphadenitis and general well being. Nevertheless, this may be due to the lack of serious involvement of vital organs like the lung in the patient.

By increasing the number of the drug resistant TB cases around the world, facing the various manifestation of this type of the disease, including the primary multi-drug resistant TB with extrapulmonary presentation is expected to be higher than before [1], which brings more emphasis on rapid and unambiguous diagnosis and suitable management of the disease as a consequence.

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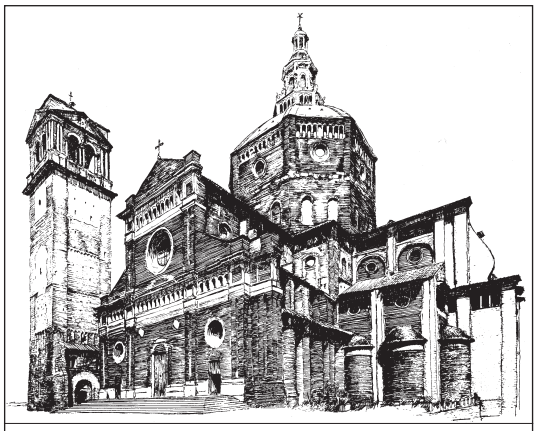

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