

Multidrug resistant tuberculosis with multiple organ involvement

Aylin BABALIK, Haluk Celalettin ÇALIŞIR

SB Süreyyapaşa Göğüs Hastalıkları ve Göğüs Cerrahisi Eğitim ve Araştırma Hastanesi, Göğüs Hastalıkları Kliniği, İstanbul.

ÖZET

Çoklu organ tutulumu ile seyreden çok ilaca dirençli tüberküloz

Çok ilaca dirençli tüberküloz durumu, klinikte tedavisi ve yönetimi oldukça güç tablolar oluşturmaktadır. Bakteri popülasyonunun az olduğu lezyonlarda direnç gelişme olasılığı düşüktür. Bu olgu skrotal kitle ile başvuran hastalarda infertiliteye sebep olabilen genital tüberkülozun akılda tutulması gerektiğini vurgulamak ve nadir görülen bir ekstrapulmoner tutulumlu bir pulmoner çok ilaca dirençli tüberküloz olgusu olduğu için sunulmuştur.

Anahtar Kelimeler: Çok ilaca dirençli tüberküloz, ekstrapulmoner tutulum, genital tüberküloz.

SUMMARY

Multidrug resistant tuberculosis with multiple organ involvement

Aylin BABALIK, Haluk Celalettin ÇALIŞIR

Clinic of Chest Diseases, Sureyyapaşa Chest Diseases and Chest Surgery Training and Research Hospital, İstanbul, Turkey.

Multidrug resistant tuberculosis has been a challenging situation in the clinical practice with respect to appropriate clinical treatment and management of the disease. The likelihood of resistance development is known to be lower in lesions with lesser percentages of the bacterial population. The present paper was designed to present a rare case of pulmonary multidrug resistant tuberculosis with extrapulmonary involvement to emphasize the consideration of genital tuberculosis with possible infertility in patients admitting with a scrotal mass.

Key Words: Multidrug resistant tuberculosis, extrapulmonary involvement, genital tuberculosis.

Yazışma Adresi (Address for Correspondence):

Dr. Haluk Celalettin ÇALIŞIR, SB Süreyyapaşa Göğüs Hastalıkları ve Göğüs Cerrahisi Eğitim ve Araştırma Hastanesi, Göğüs Hastalıkları Kliniği, İSTANBUL - TÜRKİYE

e-mail: aylinbabalik@gmail.com

INTRODUCTION

Tuberculosis remains to be an important healthcare issue both worldwide and in our country. Multidrug resistant tuberculosis defined as *Mycobacterium tuberculosis* that is resistant to the two most effective anti-tuberculous agents, i.e. isoniazid and rifampicin, leads to quite difficult cases to treat and manage. Multidrug resistant tuberculosis often arises from either history of irregular use of medications or contamination from a patient with resistant tuberculosis. The risk of development of resistance is reduced in lesions with low bacterial count. Bacterial count is very low in granulomas compared to cavities, therefore development of resistance is lower in granulomas (1-3).

According to the data from the Ministry of Health, 18.452 cases have been diagnosed with tuberculosis in Turkey in 2008 and 90.8% (16.760 patients) are newly diagnosed cases. The rate of patients with previous history of tuberculosis treatment was 9.2% (1692 patients). A total of 263 (5.3%) patients were multidrug resistant tuberculosis constituting a rate of 5.1% among all patients, 3% among newly diagnosed patients, and 18.6% among previously treated patients (4). WHO and International Union Against Tuberculosis and Lung Diseases (IUATLD) have performed a drug resistance study in 114 countries between the years 2002 and 2007 and reported the prevalence of multidrug resistance tuberculosis as 0% to 22.3% among newly diagnosed cases and 0% to 85.9% among previously treated cases (5).

Extra-pulmonary form of tuberculosis constitutes 10-20% of all cases of tuberculosis among immunocompetent cases and 60% in HIV infected patients (6). Genital tuberculosis might develop following contamination of *M. tuberculosis* via blood or urinary system. The most common form of genital tuberculosis is epididymal involvement. About 80% of the cases present with concomitant renal involvement (7).

In this paper, we present a case who initially presented with scrotal mass to demonstrate a rare clinical picture of pulmonary multidrug resistant tuberculosis with extrapulmonary involvement and to stress the importance of genital tuberculosis as a cause of infertility.

CASE REPORT

A 64-year-old male patient was referred to our clinic with treatment resistant testis tuberculosis and complained of secretion from the left testis. Medical history revealed that patient had complaints of fever, sweating and swelling in the right side of the neck in April 2001 and had been diagnosed with tuberculous lymphadeni-

tis following histopathological examination of excisional biopsy specimen of cervical lymph node. Treatment with isoniazid (H) 300 mg, rifampicin (R) 600 mg, morfazinamide (M) 1500 mg, and ethambutol (E) 1500 mg had been initiated. The treatment regimen had been arranged as HRME for the first two months and HR for the following 10 months with addition of ciprofloxacin and clarithromycin at month six. Patient had received clarithromycin for two months and ciprofloxacin for six months. At the end of the treatment period no tuberculosis bacilli were determined in the direct microscopic examination of secretion from cervical lymphadenopathy, however the microorganism was reproduced in culture and resistance against HRS was reported in susceptibility testing. The patient had been diagnosed with orchitis in September 2004 when he had complaints of mild sensitivity and increase in volume in right testis, frequent urination and mass lesion in right scrotum in physical examination. Non-specific antibiotic therapy had been initiated and administered for 20 days. Scrotal ultrasonography had been performed upon persistence of swelling and an extra-testicular mass of 35 mm x 4 mm x 22 mm size was observed in the inferior of right testis with 50% cystic-necrotic ingredient. The lesion had been interpreted as tuberculous epididymitis since no vascularity was determined inside the mass and the lesion was not painful, and right radical inguinal orchiectomy and partial scrotal excision was performed for the purposes of diagnosis and treatment. Histopathological examination had revealed several granulomas with multiple caseification necrosis, multinuclear giant cells and histiocytes in testicular tissue and dermis. No acid-resistant bacilli (ARB) were determined in the three direct microscopic examinations of sputum or urine samples. Additionally, ARB were not determined in the direct microscopic examination of scrotal secretion and fasting gastric fluid. Urogenital system had been evaluated as normal in intravenous pyelography, and HRZE (isoniazid, rifampicin, pyrazinamide, ethambutol) antituberculous therapy had been initiated due to histopathological findings. ARB had been reproduced in BACTEC cultures of samples of testicular tissue, scrotal secretion, sputum and fasting gastric fluid in the following period. Sensitivity testing had revealed tuberculosis bacilli resistant to HRES in scrotal secretion, HRE in tissue, to HRS in sputum and HRES in gastric fluid. Family history revealed that the patient's father and two uncles had received treatment for tuberculosis between the years 1980-1983. Resistance patterns of the relatives were not known. Patient presented to our clinic with complaints of swelling in left testis, wound with secretion and pain. Complete blood count and biochemical signs we-

re normal. Sedimentation was 55. Left paracardiac and left perihilar infiltrations had been observed in the X-rays obtained in 2005. Complete blood count and routine biochemistry proved normal. No ARB were determined in the direct microscopic examination and culture of sputum. Similarly, no tuberculosis bacilli were determined in smear and culture of the secretion from left testis. According to the anamnesis, previous laboratory findings, treatment history and clinical picture the patient was evaluated as a case of multiple drug resistant tuberculosis with pulmonary as well as epididymal and testicular involvement, despite no bacilli were determined in the bacteriological examinations performed at our hospital. Treatment with amikacin 750 mg/day, PAS 12 mg/day, cycloserine 750 mg/day, prothionamide 800 mg/day, moxifloxacin 400 mg/day were initiated on May, 2005. Significant improvement was determined in left scrotal swelling following the start of treatment. Parenteral amikacin therapy was stopped at month six. Cycloserine therapy was stopped and antipsychotic therapy was added at month 13 upon the emergence of psychological complaints. This complaint was observed to improve in time. Drug regimen was continued with the remaining medications and completed at month 20. Periodical bacteriological controls revealed no reproduction and clean direct microscopic examination. Treatment was discontinued at 20 months and the patient was improved clinically.

DISCUSSION

In this case presentation, we presented a case diagnosed with and treated for multidrug resistant tuberculosis who had a 20 years old history of tuberculosis in family members, history of tuberculous lymphadenitis in 2001, and pulmonary tuberculosis with genital involvement in 2004.

Distribution of genitourinary system tuberculosis among all cases of tuberculosis differs by the epidemiology of each country. According to the 2005 data of Turkish Ministry of Health published in 2007, 273 (1.4%) cases of genitourinary tuberculosis were encountered among 18.753 cases of tuberculosis (4), whereas this rate was 5.2% in United States of America according to the 2005 data (8). Genitourinary system tuberculosis often emerges in the kidneys secondary to hematogenous distribution of primary pulmonary infection. Disease might emerge immediate in some patients or years after the primary infection in others (9). Studies have defined a latent period as long as 15-22 years. Therefore; this clinical picture might be encountered at advanced ages. Tuberculosis of the genitourinary system often accompanies pulmonary involve-

ment, however isolated genital involvement might also be encountered in some patients. Previous history of pulmonary tuberculosis had been determined in 25.8% of 31 cases with genitourinary tuberculosis in Taiwan, 23.3% of 81 cases in Spain (10,11). Christensen has reported concomitant pulmonary involvement in 38% of 102 cases of genitourinary tuberculosis reported from USA (12). Forty cases of isolated tuberculous epididymitis have been reported in the literature research performed by Viswaroop et al., in 2005 (13). Tuberculous epididymitis results from hematogenous dissemination and most commonly occurs caudally due to high vascularity of this area. Testicular tuberculosis is often secondary to epididymal infection. Isolated tuberculous orchitis without epididymal involvement is quite rare (9,13).

Multidrug resistant tuberculosis is a healthcare issue of increasing importance, and infection with multiple drug resistant bacilli is quite rare in extrapulmonary organ involvement. Pulmonary involvement with tuberculosis and its resistant forms have become a healthcare issue due to high infectivity and great bacterial population. Extrapulmonary forms of tuberculosis are often not contagious, therefore this manifestation should be deemed as a result of a healthcare issue rather than the cause of a healthcare issue. Extrapulmonary involvement gains importance particularly in HIV infected patients in direct proportion with the severity of immunosuppression. Determination of multidrug resistant tuberculosis in an extapulmonary involvement in the absence of HIV infection is an important finding.

Right inguinal orchiectomy plus partial scrotal excision were performed in our patient for diagnostic and treatment purposes. Fine needle aspiration and open biopsy has been compared in a literature study performed on 40 patients with chronic epididymal lesions, and tuberculous epididymitis has been determined as the most common cause of chronic epididymal lesions. Sensitivity and specificity of fine needle aspiration biopsy in diagnosing tuberculous epididymitis has been determined as 87% and 93%, respectively; therefore authors have stressed the importance of fine needle aspiration biopsy as the primary examination in patients with epididymal lesions (14). In our case, ultrasonography findings were compatible with tuberculous epididymitis and pathology specimens of testicular tissue revealed several granulomas with caseification necrosis containing multinuclear giant cells compatible with tuberculosis. Genital involvement was deemed as epididymo-orchitis. Our patient was considered as a case of pulmonary plus genital tuberculosis with no renal involvement since no acid-resistant bacilli were demonstrated

in the direct smear examination and *M. tuberculosis* could not be reproduced in the culture of urine specimen, and IVP proved normal. The diagnosis of pulmonary tuberculosis was supported with the positive culture results of fasting gastric fluid and sputum cultures.

Patient had 20-year-old family history of tuberculosis in three relatives. Results of resistance testing of cervical lymphadenopathy secretion obtained in 2001, scrotal secretion and resected tissue sample were identical and HR resistance was the least common. Patient had been treated with the primary medications adequately and regularly in 2001 and relapse had been observed three years later. Results of resistance testing of right scrotal secretion and resected tissue sample obtained in 2004 were the same as those of fasting gastric fluid and sputum sample and HR resistance was the least common. Previous history of HR resistance, relapse despite regular use of medications, re-determination of HR resistance, failure to control the infection with recurrence in left testis despite right orchiectomy and regular use of medications, and resistance results with H and R resistances being the least common were compatible with the clinical history and picture.

It has been noted that the patient benefited from the initial standard treatment. Short-termed improvement despite multidrug resistant tuberculosis was associated with the low bacilli count in extra-pulmonary lesions and use of pyrazinamide and ethambutol in addition to H and R in the treatment. Next, swelling was observed in the opposite testis with no acid-resistant bacilli in the sputum examination; whereas bacilli were determined in gastric fluid examination and rapid response was obtained to treatment against multidrug resistant tuberculosis.

We presented this significant and alerting case of pulmonary tuberculosis with genitourinary involvement with multidrug resistant tuberculosis bacilli to demonstrate the extent of public healthcare issue of multidrug resistant tuberculosis.

CONFLICT of INTEREST

None declared.

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