Reminder of important clinical lesson

Extra-pulmonary primary multidrug-resistant tubercular lymphadenitis in an HIV negative patient

Surya Kant, S Saheer, Ghulam Hassan, Jabeed Parengal

Department of Pulmonary Medicine, CSMMU, Lucknow, India

Correspondence to Professor Surya Kant, dr.kantskt@rediffmail.com

Summary

A 28-year-old woman without any history of prior antituberculosis treatment presented with cervical lymphadenopathy and a cold abscess near medial end of clavicle of 5 months duration. Pus culture and sensitivity revealed *Mycobacterium tuberculosis* resistant to rifampicin and isoniazid. Thus she was diagnosed as a case of primary multidrug-resistant tuberculosis and treated with second line drugs according to culture susceptibility pattern. On completion of therapy, patient showed good clinical response. This case highlights the observation that even extra-pulmonary primary multidrug-resistant tuberculosis can be successfully treated with currently available second line drugs.

BACKGROUND

Tuberculosis (TB) is an infectious disease with varied clinical presentations, extra-pulmonary forms being more common in HIV patients.¹ Tubercular lymphadenitis involving cervical region is the most common form. The diagnosis is very difficult requiring high index of suspicion. Definitive diagnosis is made by demonstration of *Mycobacterium tuberculosis* in tissues or fluids. There is scanty information regarding extra-pulmonary primary drug resistant TB in the literature.² Here we report such a case of bilateral cervical adenopathy with a cold abscess, wherein the patient showed favourable clinical recovery with second line regimen.

CASE PRESENTATION

A 28-year-old non-smoker woman with no prior history of antiTB treatment or contact with a case of TB, presented to our department with bilateral cervical adenopathy, more on right side with multiple discharging sinuses and cold abscess in lower part of neck anterior to medial end of clavicle of 5 months duration (figure 1). Rest of the general physical examination was normal. Chest examination showed no clinical abnormality, and again the examination of cardiovascular, abdominal and neurological systems was unremarkable. There was no clinical evidence of any immunosuppression.

INVESTIGATIONS

Blood investigations revealed haemoglobin of 14.5 g/dl, total leucocyte count 6400/μl with differential counts (neutrophil 66%, lymphocyte 33% and eosinophils 1%) and platelets of 3 24 000/μl. She had normal liver and renal function tests. Chest radiograph did not reveal any abnormality. Tuberculin testing showed induration of 18 mm. Sputum smears for acid fast bacilli were negative. Serological evidence for HIV infection was negative. Histopathological examination of cervical lymph node revealed multiple granulomas with caseating necrosis suggestive of TB. Pus was aspirated from the cold abscess

which showed acid fast bacilli and the material was sent for culture and drug susceptibility testing for *M tuberculosis* using MGIT 960.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for cervical lymphadenopathy is given in table 1.^{3 4}

TREATMENT

She was initially treated with conventional daily regimen of antiTB drugs including rifampicin, isoniazid, ethambutol and pyrazinamide according to body weight awaiting drug susceptibility results. Subsequently on account of resistance to primary drugs, she was treated with second line

Figure 1 Initial photograph showing multiple sinuses (black arrows) and cold abscess at medial aspect of clavicle (white arrow).

Table 1 Differential diagnosis for cervical lymphadenopathy

Diseases	Clinical features	Investigatory findings
Infectious mononucleosis	Fatigue, malaise, fever, atypical lymphocytosis	Monospot, IgM early antibody or viral capsid antigen
Toxoplasmosis	80% to 90% of patients are asymptomatic	IgM toxoplasma antibody
Cytomegalovirus	Often mild symptoms; patients may have hepatitis	IgM CMV antibody, viral culture of urine or blood
Initial stages of HIV infection	'Flu-like' illness, rash	HIV antibody
Cat-scratch disease	Fever in one third of patients; cervical or axillary nodes	Usually clinical criteria; biopsy if necessary
Pharyngitis due to group A streptococcus, gonococcus	Fever, pharyngeal exudates, cervical nodes	Throat culture on appropriate medium
Tuberculosis lymphadenitis	Painless, matted cervical nodes and scrofula (chain of cervical lymphadenopathy)	Purified protein derivative, biopsy
Lymphoma	Fever, night sweats, weight loss in 20% to 30% of patients	Biopsy
Leukaemia	Blood dyscrasias, bruising	Blood smear, bone marrow
Serum sickness	Fever, malaise, arthralgia, urticaria; exposure to antisera or medications	Clinical criteria, complement assays
Sarcoidosis	Hilar nodes, skin lesions, dyspnoea	Biopsy
Kawasaki disease	Fever, conjunctivitis, rash, mucous membrane lesions	Clinical criteria
Measles	Fever, conjunctivitis, rash, cough	Clinical criteria, serology
Rubella	Rash	Clinical criteria, serology
Tularemia	Fever, ulcer at inoculation site	Blood culture, serology
Secondary syphilis	Rash	Rapid plasma reagin
Hepatitis B	Fever, nausea, vomiting, icterus	Liver function tests, HBsAg
Lymphogranuloma venereum	Tender, matted inguinal nodes	Serology

CMV, cytomegalovirus; HBsAg, hepatitis B surface antigen.

drugs based on susceptibility pattern and hospital treatment protocol with the regimen consisting of kanamycin (0.75 g every day), clofazimine (100 mg twice daily), clarithromycin (500 mg twice daily), cycloserine (750 mg every day), ethionamide (750 mg every day) and levofloxacin (750 mg every day). After 6 months of treatment kanamycin was stopped and rest of the drugs were continued for eighteen months.

OUTCOME AND FOLLOW-UP

Following completion of the therapy for the multidrug-resistant isolates, patient showed good clinical response (figure 2), without any relapse. She is regularly following us for the last 1 year.

DISCUSSION

Globally drug resistant TB has become a major health problem since early 1990 and for failure of anti-TB treatment, drug resistance must be considered.⁵ The four different categories of drug resistant TB are mono-resistance, poly-resistance, multidrug-resistance TB (MDR-TB) and extensive drug-resistance TB (XDR-TB). MDR-TB is defined as resistance to at least rifampicin and isoniazid and XDR-TB is defined as MDR-TB plus resistance to any fluoroquinolone, and at least one of three injectable second-line drugs (capreomycin, kanamycin and amikacin). Extra-pulmonary TB among the immunocompetent individuals constitutes about 15% to 20% of all cases of TB,⁶ and, in HIV patients it accounts for more than 50%.⁷ In majority of the patients it occurs as a result of lymphohematogenous dissemination during primary infection.⁸ To our best of knowledge there is no literature available on the prevalence of extra-pulmonary drug resistant TB, and only few reports are found.⁹ Like pulmonary, extra-pulmonary TB should also be confirmed microbiologically and if resistance is suspected, it should be studied for culture and susceptibility. High failure rates

Figure 2 Corresponding photograph showing healing of the sinuses (black arrows) and cold abscess (white arrow), on completion of therapy.

are usually seen in the treatment of drug resistant TB compared with drug susceptible ones.^{2 10} In our case with extra-pulmonary disease there was favourable outcome because of adequate treatment and adherence to the prescribed regimen. As there is an increase in the number of pulmonary MDR-TB cases throughout the world, it is predicted that extra-pulmonary presentation would be higher than before.^{1 11} As, drug resistance is a man made problem, its emergence and spread can be prevented by prompt diagnosis and effective treatment of all drug susceptible and resistant cases.¹²

Learning points

- After any failure of initial antiTB treatment drug resistance must be considered.
- Extra-pulmonary TB should preferably be confirmed microbiologically.
- MDR-TB can be adequately treated with proper regimen and adequate adherence.

Competing interests None.

Patient consent Obtained.

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