Reminder of important clinical lesson

Necrotising granulomatous lymphadenitis

François Alves, Ana Baptista, Helena Brito, Idálio Mendonça

Department of Internal Medicine, Faro's Hospital, Rua leao penedo, Faro, Portugal

Correspondence to François Alves, jeanfrancoisalves@sapo.pt

Summary

Extrapulmonary tuberculosis (EPTB) is defined as *Mycobacterium* TB through Ziehl–Neelsen acid-fast stain and culture in Loewenstein–Jensen in a tissue from a site other than lung parenchyma, in association with clinical or imaging findings compatible with infection locally. The authors report a case of a patient who presented with asthenia, anorexia and weight loss. He complained of fever, chills and night sweats of 1-week duration. The thoracic scan reveals lymph node enlargement in the left axilla and pleural effusion and the histological study revealed a necrotising granulomatous lymphadenitis. It was decided to initiate antituberculous drugs with a good response. EPTB is a difficult diagnostic because lymph nodes contain few tubercle bacilli, leading to a low sensitivity of smear microscopy detection. The introduction of antituberculous agents is the cornerstone of management of such infections and, occasionally, it is the only way to make a diagnosis.

BACKGROUND

A significant number of cases of granulomatous lymphadenitis have an identifiable underlying cause. The differential diagnosis includes malignancy (Hodgkin's lymphoma and non-Hodgkin's lymphoma), infections (tuberculosis (TB), non-tuberculous mycobacteria, cat scratch disease, fungal infection, sarcoidosis and bacterial adenitis) and Kikuchi's disease.¹ The most likely diagnoses will depend upon the clinical setting, especially the age and ethnic background of the patient, immune status, co-existent HIV infection² and the presenting clinical features. Extrapulmonary TB (EPTB) is defined as identification of *Mycobacterium* TB through Ziehl–Neelsen acid-fast stain and culture in Loewenstein–Jensen in a tissue or specimen from a site other than lung parenchyma, in association with clinical and/or imaging findings compatible with infection locally.³ A negative smear for acid-fast bacillus (AFB) or the failure to culture *Mycobacterium* TB should not exclude the diagnosis.⁴

CASE PRESENTATION

We report a case of an 82-year-old Caucasian man, with a medical history of chronic atrial fibrillation and cardiac surgery with placement of mechanical prostheses for severe mitral and aortic valve disease. He had reported asthenia, anorexia and weight loss since 8 months ago and a previous admission in another hospital 3 months before due to a suppurative lesion of the skin on the left wall of the chest (in the suture area). He was discharged from this hospital with the diagnosis of granulomatous disease and medicated with corticosteroids with some improvement. He was admitted in our department with complaints of fever, chills and night sweat of 1-week duration. He did not report cough or haemoptysis. He denied a history of smoking and TB. Physical examination, including neurological examination, did not show significant changes.

INVESTIGATIONS

Laboratory investigations showed anaemia (haemoglobin 9.6 g/dl), C reactive protein 134 mg/l, adenosine deaminase

61.9 UI/l, negative antineutrophil antibodies and antineutrophil cytoplasmic antibodies, negative serology for HIV, coxiella and brucella and blood cultures (including *Mycobacterium* TB) were normal. The chest CT scan reveals lymph node enlargement in the left axilla and pleural effusion. The abdominal CT scan was normal. An excisional node biopsy was performed and histology showed extensive necrosis and epithelioid giant cell granulomas. Ziehl–Neelsen staining and microbiology were negative.

TREATMENT

Given the characteristics of the histology, clinical history and epidemiology (TB is still a prevalent problem in Portugal), it was decided to initiate antituberculous drugs (a 2-month initial phase of isoniazid, rifampicin, pyrazinamide and ethambutol followed by a 7-month continuation phase of isoniazid and rifampicin) with a significant improvement of the symptomatology.

OUTCOME AND FOLLOW-UP

He has been followed up in the outpatient clinic and remains asymptomatic.

DISCUSSION

TB remains a major global public health problem in the world. It is estimated that about one-third of the world's population is infected with *Mycobacterium* TB and nearly nine million people develop disease each year.⁵ Despite improved living standards, the availability of anti-TB medications and the mass BCG vaccination at birth, TB remains an endemic disease in Portugal. The WHO reported that the annual incidence rate of reported TB cases per 100 000 population in our population in 2007 was 30%.

Although TB usually attacks the lungs, resulting in the PTB form, other organs can be affected, leading to EPTB or disseminated TB.⁶ The emergence of extrapulmonary disease as an important form of active TB has been noted in many studies^{6–8} but our understanding of the factors responsible for the occurrence of TB at extrapulmonary sites

is still limited. Some studies have reported that the EPTB is on the rise due to the HIV epidemic.² In fact, in industrialised countries, prior to the HIV epidemic, about 15% of TB cases were declared EPTB.⁹ Since the emergence of HIV, EPTB has been detected more frequently (more than 30%) among HIV-infected individuals in Europe and in the United States.^{10 11} It has been demonstrated that EPTB was also associated with a poor immune status and unfavourable social conditions even in the absence of HIV infection, both in developing and industrialised countries.^{12 13} Another possible cause is the improvement in diagnostic facilities.

Extrapulmonary sites of infection commonly include lymph nodes, pleura and osteoarticular areas, although any organ can be involved with the frequencies of the different clinical sites varying according to country.^{14–16} The most common form of EPTB is tuberculous lymphadenopathy,^{14 15} and its diagnosis remains a challenge, necessitating a high index of suspicion, since granulomatous lymphadenopathy has an extensive differential diagnosis. Several conditions, including atypical mycobacterial infection, fungal infection, sarcoidosis and other inflammatory conditions, can present the same cytology and/or histopathology as tuberculous lymphadenopathy² resulting in a significant delay of the appropriate treatment.

Patients without HIV infection typically present with chronic, non-tender lymphadenopathy.¹⁷ Patients with HIV infection usually present with fever, night sweats and weight loss.¹⁸ The nodes are discrete, firm and non-tender; with time, a firm mass of matted nodes becomes visible.³ Most patients have a positive tuberculin skin test result and a normal result on chest radiography.³

Excisional biopsy of the lymph nodes with histology, AFB stain and mycobacterial culture is the diagnostic procedure of choice.¹⁷ However, owing to the paucibacillary nature of the specimens, a negative smear for AFB, a lack of granulomas on histopathology and failure to culture *Mycobacterium TB* (cultures grow mycobacteria in 39–80% of cases)⁴ do not exclude the diagnosis. Conventional methods and cytological investigations are being used in conjunction with PCR techniques to further help in the detection and characterisation of pathogenic mycobacteria associated with human lymphadenitis.^{4 19} Many reports have demonstrated the value of PCR in the diagnosis of EPTB, including pleural effusion and lymphadenitis.^{4 19–21} Fine-needle aspiration is more reliable in patients with HIV infection because of the higher mycobacterial burden and should be the initial diagnostic procedure in these patients.^{3 17} PCR for *Mycobacterium TB* on the fine-needle aspiration specimen enhances test sensitivity.³ The utility of fine-needle aspiration in patients without HIV infection is highly variable.¹⁷

In general, the same regimens are used to treat PTB and EPTB, and responses to antituberculous therapy are similar in patients with HIV infection and in those without,³ although adverse drug reactions occur more commonly in those with HIV infection. A 6–9 month regimen (2 months of isoniazid, rifampicin, pyrazinamide and ethambutol, followed by 4–7 months of isoniazid and rifampicin) is recommended as initial therapy for all forms of EPTB unless the organisms are known or strongly suspected to be resistant to the first-line drugs.^{3 22} Occasionally, treatment with

steroids may be necessary. Some studies find that adjunctive corticosteroids may be beneficial in patients with tuberculous meningitis, tuberculous pericarditis or miliary TB with refractory hypoxemia.^{23 24}

Our patient had a history of cardiac surgery with placement of mechanical prostheses and a suppurative lesion of the suture area and he improved with corticosteroids, leading to a misdiagnosis of non-infectious disease. When he came to our department, the clinical history and the characteristics of the histology suggested but did not confirm EPTB. PCR or, in the future, the combination of antigens²⁵ could help us to do a more accurate diagnosis of EPTB.

Learning points

- In our case, the introduction of antituberculous agents was the cornerstone of management of this infection.
- They must be introduced as soon as possible and, sometimes, it is the only way to make a diagnosis.

Competing interests None.

Patient consent Obtained.

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