CASE REPORT

An unusual presentation of miliary tuberculosis

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SUMMARY

A young Bangladeshi woman presented to the emergency department with vaginal discharge on a history of fevers and rigours. Although initially treated for pelvic inflammatory disease, the patient rapidly developed respiratory failure with acute respiratory distress syndrome. An axillary biopsy and a high-resolution CT of the chest confirmed miliary tuberculosis (TB). She was initiated on anti-TB medication and made a rapid recovery.

BACKGROUND

This case highlights the many different ways tuberculosis (TB) may present and that, in an at-risk population, it should remain at the top of your differentials.

CASE PRESENTATION

A 25-year-old Bangladeshi woman presented to the emergency department following a 6-week history of fevers and rigours. She had also noticed multiple pustules over her abdomen and vulva that had developed in the preceding 3 days with offensive vaginal discharge and dysuria. In addition, she presented with a dry cough.

Her medical history included three previous surgical terminations of pregnancies in Bangladesh.

She had one previous sexual partner, her husband, from whom she was separated. She denied any sexual activity or foreign travel in the previous 2 years and had moved to the UK in 2010. She was normally fit and active, did not smoke, did not drink and was working as a carer.

On initial assessment she was febrile at 40.2°C, tachycardic and mildly tachypnoeic, oxygen saturation at room air was 97%. Besides a solitary abdominal pustule and several vaginal pustules with associated discharge, examination was otherwise unremarkable. Of note, she had no peripheral lymphadenopathy and her chest was clear on auscultation.

DIFFERENTIAL DIAGNOSIS

- ▶ Pelvic inflammatory disease (PID)
- ▶ Herpes simplex
- ▶ *Mycobacterium tuberculosis*

TREATMENT

The patient was initially treated for PID with intravenous ceftriaxone and acyclovir with additional oral doxycycline while her TB investigations were pending. Despite treatment, the patient's symptoms progressed and subsequently developed oral ulcerations and tender cervical lymphadenopathy.

FiO2	0.6
pH	7.42
pCO2	5.00
pO2	8.69
HCO3	24.2
BE	0.5

Figure 1 Arterial blood gas; significant hypoxia with poor alveolar-arterial gradient.

She remained febrile and tachycardic, becoming more tachypnoeic and hypoxic (figure 1). A repeat chest X-ray (CXR) showed marked deterioration from admission CXR (figures 2 and 3). A CT pulmonary angiogram was performed to rule out pulmonary emboli. This demonstrated ground glass shadowing and small pleural effusions bilaterally (figure 4) consistent with acute respiratory distress syndrome. Owing to severe hypoxaemia, the patient was transferred to the high-dependency unit for additional respiratory support.

Peripheral blood and sputum cultures were negative thus far. Viral serology and sexually transmitted infection screens were negative and the decision was taken to start anti-TB treatment. She was started on rifampicin, isoniazide, ethambutol and pyrazinamide with additional steroid cover. A radiologically guided axillary lymph node biopsy was performed and confirmed the presence of acid-fast bacilli (AFB). A high-resolution CT chest was taken which demonstrated miliary TB (figure 5) and axillary lymphadenopathy (figure 6). In order to exclude spread to the central nervous system (CNS), a lumbar puncture (LP) and MRI of the head were performed, both of which were normal. A comprehensive list of microbiology specimens is included in figure 7.

Figure 2 Admission chest X-ray.

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Figure 3 Chest X-ray (day 2 of admission): bilateral pleural effusions with probable bibasal consolidation.

OUTCOME AND FOLLOW-UP

Following initiation of anti-TB medications the patient improved dramatically. She remained afebrile, her tachycardia and tachypnoea settled and her hypoxia resolved. She was stepped down to a level 1 bed, where she completed her recovery. She was counselled on the risks and side effects of her anti-TB medications and appropriate investigations, including visual acuity and colour vision testing, were carried out prior to discharge.

DISCUSSION

The diagnosis of miliary TB can be fraught with difficulties. The insidious course that the infection takes, the non-specific symptoms it may present with and the delays in obtaining a microbiological or histological diagnosis all contribute to the delay to diagnosis and consequent high morbidity and mortality.¹

Our patient had the constitutional symptoms associated with TB and was from a country with high TB prevalence. However, her symptoms were predominantly gynaecological and, although TB had been considered as part of the differential diagnosis initially, due to her relative lack of respiratory symptoms and chest radiograph findings, alternative diagnoses were considered more likely. The aetiology of the vesicles remains unclear although given the underlying diagnosis of TB, they may represent

Figure 5 High-resolution CT of the chest; multiple nodules in keeping with miliary tuberculosis.

papulonecrotic tuberculids. These remain a distinct entity from cutaneous tuberculosis infection; instead they represent a hypersensitivity reaction to mycobacterial antigens. Although lesions typically fail to culture or stain for mycobacteria species, in half the cases PCR for mycobacterial DNA will be positive and therefore worthwhile investigating.

The key point in this case was to revisit the initial differential diagnosis when the patient failed to improve with conventional treatment. As her symptoms developed further, investigations were arranged and some repeated (figure 3). A common theme in the literature is that a high index of clinical suspicion is needed to correctly diagnose TB and it is far more reliant on clinical acumen than investigations.²

Specific to this case is the rapid respiratory decompensation from fulminant miliary TB. During the course of several days the patient became acutely hypoxic and developed pronounced bilateral consolidation and ground glass shadowing in keeping with an ARDS presentation.

TB is an uncommon but treatable cause of ARDS. Historically it has been estimated that some 1–2% of cases of ARDS were associated with miliary TB.³ The majority of cases described in the literature are anecdotal case reports. A recent retrospective case series identified 85 patients with miliary TB who subsequently developed ARDS.⁴ This case series demonstrated that mortality from miliary TB and ARDS is high (47%) and the main barriers to survival were delay in diagnosis and initiation of treatment. The series also found that patients who were

Figure 4 CT pulmonary angiography ground glass shadowing and bibasal pleural effusions.

Figure 6 High-resolution CT of the chest; significant axillary lymphadenopathy (see arrow).

Blood MCS (x5)	Coag negative S.Aureus (insignificant)
Urine MCS (x 3)	No growth
Pleural fluid	MCS: No growth
	AFB Smear: Negative
	Cytology: Blood + Mononuclear cells
	LDH: 984
	Protein: 20
Cerebrospinal fluid	MCS: No growth
	AFB Smear: Negative
	Cell count: WBC <1, RBC 810
	Cytology: Blood, Scanty lymphoid cells
	Glucose: 3.9
Lymph Node	Protein: 690
	AFB: Smear positive, fully sensitive
	FNA: Acellular

Figure 7 Microbiology specimens; lymph node biopsy was able to confirm *Mycobacterium tuberculosis*.

mechanically ventilated soon after diagnosis fared better and a number of independent predictors for development of ARDS in miliary TB were identified: diabetes mellitus, alanine transaminase, aspartate transaminase, D-dimer, haemoglobin and albumin. Further case reports have also demonstrated pregnancy and length of illness (>1 month) to be independent predictors for developing ARDS.^{5 6}

The diagnosis in this case was initially a clinical one and treatment was started when the clinical suspicion of TB was high. Although culture positivity may take weeks, smear for AFB can be performed rapidly and biopsies showing caseating granuloma also help to signpost the diagnosis. Sources for tissue diagnosis in miliary TB can be difficult to find and, again, clinical examination and imaging should be used to guide this. All specimens should be sent for histopathology and cytology as well as mycobacterial smear and culture. In this instance, a bronchoalveolar lavage (BAL) was not performed but had the diagnosis not been reached with the lymph node biopsy it would have been the next investigation of choice with the diagnostic yield reported to be around 46.8%.⁷ In this age of increasing drug resistance, specimens for culture and sensitivity are crucial but can be sought simultaneously to starting treatment.

Miliary TB is a life-threatening condition that left untreated is often fatal, usually within a year.⁸ Most leading bodies including the WHO and the National Institute for Health and Care Excellence (NICE) advocate 6 months of treatment with prolonged courses in the case of bone, joint or CNS involvement.^{9 10} There is no clear evidence to show the benefit of corticosteroids in the management of miliary TB alone. However, in the presence of hypoadrenalism there is an absolute indication for the use of corticosteroids. There is evidence of benefit in CNS involvement, pericardial or pleural effusions, endobronchial TB, IRIS, ARDS, immune complex nephritis or histiocytic phagocytosis syndrome but further work is needed in this field.⁸

In conclusion, a prompt diagnosis and early intervention is key to survival in cases of ARDS and miliary TB. Given the

barriers for prompt microbiological or histological diagnoses, much emphasis is placed on clinical judgement and this case highlights how important it is to revisit diagnoses and repeat investigations according to the patient's clinical course.

Learning points

- ▶ Diagnosis of tuberculosis (TB) can be difficult, particularly in miliary TB.
- ▶ Acute respiratory distress syndrome can be an uncommon but serious feature of tuberculosis.
- ▶ If there is a high index of clinical suspicion of TB, treatment should be started promptly in conjunction with attempts to seek microbiological confirmation of the diagnosis.
- ▶ Microbiological confirmation can be exceedingly difficult and it is through a combination of smear, culture, PCR and histopathology from multiple sites that a diagnosis may finally be reached.

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REFERENCES

- Sharma SK, Mohan A, Sharma A, *et al.* Miliary tuberculosis: new insights into an old disease. *Lancet Infect Dis* 2005;5:415–30. <http://www.ncbi.nlm.nih.gov/pubmed/15978528> [cited 19 June 2013].
- Poyrazoglu OK, Timurkan M, Yalniz M, *et al.* Clinical review of 23 patients with tuberculous peritonitis: presenting features and diagnosis. *J Dig Dis* 2008;9:170–4. <http://www.ncbi.nlm.nih.gov/pubmed/18956596> [cited 24 July 2013].
- Dyer RA, Chappell WA, Potgieter PD. Adult respiratory distress syndrome associated with miliary tuberculosis. *Crit Care Med* 1985;13:12–15. <http://www.ncbi.nlm.nih.gov/pubmed/3965242> [cited 24 July 2013].
- Deng W, Yu M, Ma H, *et al.* Predictors and outcome of patients with acute respiratory distress syndrome caused by miliary tuberculosis: a retrospective study in Chongqing, China. *BMC Infect Dis* 2012;12:121. <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3407496&tool=pmcentrez&rendertype=abstract> [cited 24 July 2013].
- Sharma SK, Mohan A, Banga A, *et al.* Predictors of development and outcome in patients with acute respiratory distress syndrome due to tuberculosis. *Int J Tuberc Lung Dis* 2006;10:429–35. <http://www.ncbi.nlm.nih.gov/pubmed/16602408> [cited 24 July 2013].
- Isobe Z, Suga T, Hamaguchi S, *et al.* [A case of miliary tuberculosis showing acute respiratory failure during pregnancy]. *Nihon Kokyuki Gakkai Zasshi* 2007;45:874–8. <http://www.ncbi.nlm.nih.gov/pubmed/18051791> [cited 24 Jul 2013].
- Ray S, Talukdar A, Kundu S, *et al.* Diagnosis and management of miliary tuberculosis: current state and future perspectives. *Ther Clin Risk Manag* 2013;9:9–26.
- Sharma SK, Mohan A, eds Disseminated and miliary tuberculosis. In: *Tuberculosis*. 2nd edn., New Delhi: Jaypee Brothers Medical Publishers, 2009:493–518.
- World Health Organisation. *Treatment of tuberculosis: guidelines for national programmes*. 3rd edn. 2003.
- National Institute for Health and Clinical Excellence. *Tuberculosis: Clinical diagnosis and management of tuberculosis and measures for its prevention and control*. 2006.

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