CASE REPORT

Miliary tuberculosis in an immunocompetent male with a fatal outcome

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SUMMARY

A man aged 33 years, born in Nepal, but resident in the UK for 7 years presented to the emergency department with a 4-day history of general malaise, fever (temperature 38.6°C) and a non-productive cough. His medical history was unremarkable and no high-risk behaviour was identified. Clinical examination confirmed decreased air entry bilaterally with bibasal crackles. He was tachycardic, with a heart rate of 120 bpm. Further investigation with a 12-lead ECG confirmed supraventricular tachycardia (SVT) which was terminated with vagal manoeuvres. His chest radiograph demonstrated left basal consolidation. His white cell count was $11 \times 10^9/L$ and his C reactive protein was 43.2 mg/L. His blood cultures revealed no growth. He was diagnosed with community-acquired pneumonia and started treatment with amoxicillin and clarithromycin. 3 days post admission, he was intubated for 24 hours in the Department of Intensive Care Medicine. Further episodes of SVT were observed and an ECHO showed a severely dilated and impaired left ventricle. Further chest radiographs illustrated diffuse consolidation with evidence of pulmonary oedema. HIV serology was negative. He developed transaminitis and thrombocytopenia. An ultrasound scan of his liver showed no obvious liver pathology. He remained tachypnoeic and due to worsening pulmonary oedema and extensive consolidation, he was readmitted to the intensive care unit. A CT abdomen with contrast showed an unusual pattern of lymphadenopathy with disproportionately enlarged coeliac axis nodes (5×7×5 cm) and minor para-aortic adenopathy, suspicious for lymphoma. On inserting his central venous catheter in his right internal jugular vein, pus was inadvertently aspirated from his right neck. Acid alcohol fast bacilli (AAFFB) were isolated from the pus and was subsequently identified as *Mycobacterium tuberculosis*. He started treatment with antitubercular medication rifater: a combination of rifampicin 720 mg od, isoniazid 300 mg po od and pyrazinamide 1750 mg. In addition, he received ethambutol 1000 mg po od and pyridoxine 5 mg. He developed worsening metabolic acidosis, pH 7.19, loss of respiratory compensation and pancytopenia. Right heart strain was evident on his Focused Intensive Care Echo. He developed an increased oxygen requirement and respiratory distress on the ventilator. An erect chest radiograph showed bilateral pneumothoraces and bronchopleural fistulae. A chest drain was inserted. Following discussion with the Cardiothoracic Surgeons, pleurodesis was not deemed possible. He developed inotropic-dependent shock with worsening lung compliance. As a result of his deteriorating ventilation, acidosis and hyperkalaemia, he started treatment with continuous veno-venous

haemofiltration. With a diagnosis of miliary tuberculosis and SVT causing cardiogenic pulmonary oedema, this man sadly died with his family at his bedside 10 weeks following initial hospital presentation.

BACKGROUND

Miliary tuberculosis (TB) is a potentially fatal form of TB and results from haematogenous spread of *Mycobacterium tuberculosis* bacilli. Since its first description by John Jacob Manget in 1700, it is estimated that miliary TB accounts for <2% of all cases of TB in immunocompetent individuals and up to 20% of all extrapulmonary TB cases. The clinical presentation of miliary TB is protean and non-specific, thus posing a diagnostic challenge to even the most experienced clinician. Without treatment, miliary TB is uniformly fatal within 12 months. This case report discusses the epidemiology and clinical manifestations of miliary TB, as well as the diagnostic tests, biomarkers and anti-TB drugs. This case report offers an important clinical reminder of maintaining a high index of clinical suspicion and a systematic approach to diagnostic testing to establish an early diagnosis of miliary TB. Furthermore, this case also acts as a timely reminder of the importance of initiating antitubercular therapy in a timely manner as miliary TB is all too frequently diagnosed late, resulting in a fatal outcome, which unfortunately occurred in our case.

CASE PRESENTATION

A man aged 33 years, born in Nepal, but resident in the UK for 7 years, having resided in the USA from 2004 to 2009, presented to the emergency department with a 4-day history of non-productive cough, palpitations and fever, preceded by a sore throat. His medical history was unremarkable and he reported no known drug allergies. He worked as a laboratory technician, was a non-smoker and did not consume alcohol. He denied a history of illicit drug use. His travel history included a 1-month trip to Nepal in 2014 and he denied any exposure to TB. On presentation, his observations were as follows: heart rate 120 bpm, blood pressure 104/65 mm Hg, respiratory rate 16, SpO₂ 94% on air and temperature 38.6°C.

Physical examination revealed no organomegaly, lymphadenopathy or signs of immune-suppression. Respiratory examination confirmed decreased air entry bilaterally and bibasal crackles. A non-productive cough was observed.

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Table 1 Blood results on admission

Hb	134 g/L	Magnesium	0.78 mmol/L
WCC	$11 \times 10^9/L$	Total bilirubin	11 $\mu\text{mol/L}$
Neutrophils	$7.92 \times 10^9/L$	Alkaline phosphatase	142 IU/L
Na	134 mmol/L	ALT	106 IU/L
K	3.5 mmol/L	CRP	43.2 mg/L
Urea	5.8 mmol/L	Platelets	$260 \times 10^9/L$
Creatinine	99 $\mu\text{mol/L}$	eGFR	75 mL/min/L
Adjusted calcium	2.20 mmol/L	TSH	0.85 $\mu\text{U/L}$

INVESTIGATIONS

Haematological investigations confirmed an elevated C reactive protein, with normal renal, liver and thyroid function tests (table 1).

A 12-lead ECG showed supraventricular tachycardia (SVT) with a rate of 120 bpm. The underlying rhythm was sinus, with no evidence of a conduction disorder or ischaemia. His SVT was terminated with vagal manoeuvres. Further investigation with a chest radiograph showed left basal consolidation, with no evidence of an effusion (figure 1). His blood cultures revealed no growth. Further investigation with a venous blood gas confirmed: pH 7.076, bicarbonate 12.8 mmol/L, base excess –13.6 mmol/L and lactate 8.1 mmol/L. His troponin was 35 ng/L.

DIFFERENTIAL DIAGNOSIS

The working diagnosis was of community-acquired pneumonia, CURB-65 score of 2. He started treatment with intravenous amoxicillin (1 g three times daily) and oral clarithromycin (500 mg two times per day). Three days post admission, he deteriorated clinically, with decreased oxygen saturations (SpO_2 80% on air) and pulmonary oedema. A chest radiograph showed extensive ground glass change tending towards consolidation. He started treatment with intravenous piperacillin/tazobactam. His screening swabs on admission isolated methicillin-resistant *Staphylococcus aureus* and he was treated with oral linezolid on microbiology advice.

He remained tachypnoeic and was admitted to the Department of Intensive Care Medicine, requiring intubation and ventilation. He was extubated uneventfully 24 hours later on to nasal high flow oxygen and remained in the intensive care unit (ICU) for 3 days. Further episodes of SVT were noted and corrected with electrolyte replacement. His urine was negative

Figure 1 Chest radiograph. There is left lower zone consolidation, consistent with infection. No pleural effusion.

for *Legionella pneumophila* antigen and Pneumococcal antigen. Influenza A, including H1N1, and influenza B were PCR-negative. A transoesophageal echo showed a globally dilated and severely impaired left ventricle. There was no evidence of infective endocarditis. He was therefore discharged to the coronary care unit for ongoing management of his dilated cardiomyopathy. His HIV serology (1 and 2), hepatitis C and hepatitis B surface antigen screen were negative. A repeat chest radiograph showed hazy, diffuse pulmonary shadowing with the presence of air bronchograms consistent with diffuse consolidation. He developed deranged liver function tests (total bilirubin 29 $\mu\text{mol/L}$, ALP 183 IU/L and ALT 577 IU/L) and his ferritin was >2000 $\mu\text{g/L}$. An ultrasound scan of his abdomen showed no focal hepatic lesions and patency to all hepatic veins. An oedematous thick-walled gallbladder, with no evidence of gallstones or biliary dilation was observed. There was a normal appearance of the spleen and kidneys. He initially improved with diuretic therapy. However, he developed an increased work of breathing and an increased oxygen requirement. His chest radiograph showed worsening pulmonary oedema and extensive consolidation throughout both lung fields, suspicious for acute respiratory distress syndrome (ARDS) (figure 2). He was reviewed by the respiratory physicians and deemed clinically unstable for bronchoscopy. His midstream urine (MSU) cultured *Klebsiella pneumoniae*, sensitive to coamoxiclav. A repeat MSU 3 days later isolated *Enterobacter aerogenes*, sensitive to gentamicin. Immunofluorescence was negative for ANA ELISA and ANCAIF, proteinase 3 0.2 IU and myeloperoxidase 0.3 IU. He developed transaminitis (ALT 705 IU/L) and thrombocytopenia (platelets $67 \times 10^9/L$). Two weeks post admission, a CTPA showed diffuse, widespread consolidation (figure 3). The differential diagnosis included ARDS, pulmonary oedema and atypical infection. Limited images through the upper abdomen demonstrated a fluid attenuation mass-like appearance in the midline measuring 37 mm between stomach and liver anterior to the diaphragmatic crus. The aetiology was unclear.

Consequently, a CT abdomen with contrast was performed (figure 4). An unusual pattern of lymphadenopathy with

Figure 2 Chest radiograph. Extensive bilateral ground-glass change tending towards consolidation particularly on the right, with peripheral sparing, appear similar to the previous study. Appearances most likely due to infection or oedema.

Figure 3 CTPA. No pulmonary emboli identified. There is diffuse bilateral widespread pulmonary ground-glass change becoming more confluent in places, particularly in the upper lobes in keeping with diffuse consolidation. The differential diagnosis included ARDS, pulmonary oedema and atypical infections.

Figure 4 CT abdomen. Extensive low-volume para-aortic lymphadenopathy measuring up to 12 mm short axis. Much larger 5×7×5 cm coeliac axis soft tissue mass noted, which is also presumably lymphadenopathy. The liver, spleen, pancreas, adrenals and kidneys appear unremarkable. No obvious large or small bowel lesion. Unusual pattern of lymphadenopathy with enlarged coeliac axis nodes and minor para-aortic adenopathy suspicious for lymphoma.

disproportionately enlarged coeliac axis nodes (5×7×5 cm) and minor para-aortic adenopathy, measuring up to 12 mm in the short axis was noted. The differential diagnosis included lymphoma and haematology review of his blood film showed anaemia (Hb 90×10^9 g/L, MCV 81.5 fL) and lymphocytopenia (0.58×10^9 /L) which could be explained by chronic infection. He was deemed too unwell for a lymph node biopsy. He developed rigours, hypotension, dyspnoea and was desaturating. Further episodes of SVT were terminated with 12 mg of adenosine.

TREATMENT

He was readmitted to the intensive care unit (ICU) 1 day later and remained an inpatient for 5 days. On inserting his central

venous catheter in his right internal jugular vein, pus was inadvertently aspirated from his right neck, perhaps from a necrotic laterocervical lymph node. In the interim, he was treated empirically with linezolid and piperacillin/tazobactam. His norepinephrine was titrated to maintain a mean arterial pressure >65 mm Hg. Three days later and 2 weeks following this man's admission, TB microscopy of his neck pus revealed numerous acid alcohol fast bacilli (AAFFB). *Mycobacterium tuberculosis* was subsequently isolated, sensitive to rifampicin, ethambutol and isoniazid. Scanty white cell counts were also isolated. *Mycobacterium tuberculosis* PCR also confirmed the diagnosis. He started treatment with antitubercular medication, rifater, a combination of isoniazid 300 mg po od, pyrazinamide 1750 mg and rifampicin 720 mg od.

In addition, he received ethambutol 1000 mg po od and pyridoxine 25 mg. His visual acuity was assessed with the Snellen Chart. His β glucan test was positive, concentration 334 pg/mL.

However, bronchoalveolar lavage did not reveal *Pneumocystis carinii/jiroveci* DNA. No AAFFB were seen on TB microscopy and Cepheid TB PCR was negative. There was no bacterial growth after 24 hours incubation. A repeat β d-glucan 2 weeks later was negative (43 pg/mL). As he required no further ICU support, he was transferred to the respiratory ward for further management. He started treatment with steroids, prednisolone 40 mg once daily due to possible pericardial involvement. He was readmitted to ICU for the third time due to an increased oxygen requirement. He was tachypnoeic and an ABG revealed: pH 7.436, PCO_2 3.25, PO_2 10.30, lactate 0.9, base excess -7.3, HCO_3^- 18.5. Further episodes of SVT were observed (rate 216 bpm) requiring adenosine for termination. On cardiology advice, he started treatment with verapamil 120 mg and bisoprolol 5 mg. His electrolytes were deranged: hyponatraemia (Na 129), hypokalaemia (K 3.3) and low magnesium (Mg 0.6). He was also anaemic; Hb 94, MCV 79.6. A transthoracic ECHO showed a normal-sized left ventricle and wall thickness. His left ventricular systolic function was moderately impaired with an ejection fraction of 42%. Global hypokinesia was evident. His diastolic function appeared mildly impaired. A small pericardial effusion was noted adjacent to his right atrium. He desaturated to 60% on air, with a respiratory rate of 50. He developed worsening metabolic acidosis, pH 7.19, with loss of respiratory compensation and pancytopenia. He required intubation and ventilation.

Right heart strain was evident on his FICE. Owing to persistent hypoxia and tachycardia, a CTPA was performed (figure 5). It showed diffuse ground glass opacification throughout the lungs, increased in size from previous imaging. A necrotic para-tracheal lymph node was slightly larger.

There was no evidence of a pulmonary embolus.

OUTCOME AND FOLLOW-UP

He developed an increased oxygen requirement and respiratory distress on the ventilator. An erect chest radiograph showed bilateral pneumothoraces and bronchopleural fistulae (figure 6). A left Seldinger chest drain and a right surgical chest drain were inserted. A chest radiograph showed a stable left apical pneumothorax. The right pneumothorax appeared resolved.

Continued miliary change and consolidation throughout both lungs was evident. Owing to worsening ventilation, he was discussed with the Cardiothoracic Surgeons. As his lungs were chronically inflamed with TB, it was thought that his lungs may not re-expand. Therefore, pleurodesis was not performed. He started treatment with caspofungin 50 mg intravenous od for possible fungal pneumonia. He developed inotrope-dependent

Figure 5 CTPA. No filling defects are seen in the central and segmental vessels. Diffuse ground-glass opacification throughout the lungs, confluent posteriorly.

Figure 6 Chest radiograph. Bilateral pneumothoraces larger on the left. Background features of miliary TB within the lungs.

shock (0.5 mcg/kg/min) and a worsening lung compliance was noted. He remained on spontaneous ventilation pressure support and this support was increased to try and offset his hypercapnia. He remained feverish with a temperature of 39°C. As a result of his deteriorating ventilation, acidosis and hyperkalaemia, he started treatment with continuous veno-venous haemofiltration (table 2).

With a diagnosis of miliary TB and SVT causing cardiogenic pulmonary oedema, this man sadly died with his family at his bedside 10 weeks following initial hospital presentation.

DISCUSSION

In the year 1700, John Jacob Manget coined the term 'miliary TB' (derived from the Latin word 'miliarius' meaning related to millet seed), to describe the surface of the lung being covered with firm, small white nodules. Mandell, Douglas and Bennett's

Table 2 Blood results

Hb	71 g/L	Magnesium	1.19 mmol/L
WCC	$6.50 \times 10^9/L$	Total bilirubin	11 $\mu\text{mol/L}$
Neutrophils	$4.99 \times 10^9/L$	Alkaline phosphatase	314 IU/L
Na	148 mmol/L	eGFR	31 mL/min/L
K	6.3 mmol/L	Albumin	23 g/L
Urea	15.1 mmol/L	Phosphate	1.30 mmol/L
Creatinine	214 $\mu\text{mol/L}$		
Adjusted calcium	2.03 mmol/L		

textbook 'Principles and Practice of Infectious Diseases' aptly describes the pathogenesis of miliary TB as 'progressive haematogenous dissemination' of *M. tuberculosis* from a pulmonary or extrapulmonary focus and embolisation to the vascular beds of the liver, spleen, bone marrow, lungs and meninges.² The inadequacy of effector T-cell response in suppression of *M. tuberculosis* is thought to be responsible for its development.¹ TB remains one of the most infectious diseases worldwide and is the leading cause of death from an infectious disease. Owing to non-specific clinical symptoms and atypical presentations, the diagnosis of miliary TB poses a formidable challenge to physicians. With the advent of immunosuppressant and biological medications, increasing occurrence of organ transplantation and the global pandemic of HIV, the epidemiology of miliary TB has been altered.³ Historically, before the advent of antitubercular medication, miliary TB was considered a childhood disease, but it is now increasingly recognised in adults. According to the Global Tuberculosis Report 2015, in 2014, there were an estimated 9.6 million new TB cases: 5.4 million among men, 3.2 million among women and 1.0 million among children. There were also 1.5 million TB deaths (1.1 million among HIV-negative people and 0.4 million among HIV-positive people).⁴ In the UK, in 2014, there were 179 case notifications of miliary TB, accounting for 2.8% of all new cases.⁴

The myriad clinical manifestations and atypical radiographic findings perplex even the most experienced clinicians. No single sign or symptom is diagnostic and clinicians should look for a constellation of symptoms such as peripheral lymphadenopathy, hepatosplenomegaly, pleural and pericardial effusions. Morning temperature spikes have a diagnostic significance and are reported to be characteristic, with patients presenting with 'pyrexia of unknown origin' and few systemic clues.³ Several papers have described sweat engraving the patient's silhouette on the bed, closely resembling a body's shadow, otherwise known as the 'damp shadow sign'.⁵

Haemoptysis rarely occurs, but a dry cough, scanty sputum and dyspnoea are observed.

Erythematous macules and papules, otherwise known as TB malaria cutis, offer a valuable clue to the diagnosis. Neurological manifestations, including TB meningitis, have been described in up to 30% of cases. Pott's spine and paraspinal cold abscess formation have been reported. Miliary TB manifesting as Addison's disease has also been described. Choroidal tubercles, located within 2 cm of the optic nerve are pathognomonic. Therefore, ophthalmoscopic examination in all patients with suspected miliary TB is imperative. 'Cryptic forms' of miliary TB, a term coined by Proudfoot, can mimic a metastatic carcinoma.⁶ Acute miliary dissemination may lead to emphysematous changes, thus resulting in a bilateral simultaneous pneumothorax.⁶ There are several reports of miliary TB in

immunocompromised individuals, for example, those with AIDS or those taking immune-suppressant medications, for example, infliximab or antitumour necrosis factor. Individuals with early HIV infection (CD4 count >200 cells/mm³) have a similar clinical presentation to that observed in immunocompetent individuals. However, in advanced disease, macular, pustular or purpuric lesions, indurated ulcerating plaques and subcutaneous abscesses may be evident.

Pulmonary TB complicated by ARDS is often found in the setting of miliary TB. ARDS was first described in 1967 as a life-threatening respiratory condition characterised by hypoxia and stiff lungs. There is increased permeability of pulmonary capillary endothelial cells and alveolar epithelial cells leading to pulmonary oedema, refractory hypoxaemia, multiorgan failure and death. Duration of miliary TB beyond 20 days tends to markedly increase the risk of developing ARDS.⁷ Mohan's paper aptly highlights the difficulties encountered in diagnosing miliary TB as a primary cause of ARDS.⁷ Other reported respiratory complications include pneumomediastinum and acute empyema.⁸ In the acute phase, arterial hypoxaemia due to widening of the alveolar–arterial oxygen gradient and hypercapnia due to tachypnoea are also observed.⁹ Furthermore, cardiovascular manifestations occur in 1–2% of patients with TB and include pericarditis, +/- an effusion, mycotic aneurysm of the aorta, myocarditis, congestive heart failure and infective endocarditis.¹⁰ TB myocarditis may present with rhythm disorders and sudden cardiac death.¹⁰ Miliary TB is also associated with renal failure due to granulomatous destruction of the interstitium and immune complex glomerulonephritis. These rare manifestations may be a component of the multiorgan dysfunction syndrome due to TB or as a manifestation of immune reconstitution inflammatory syndrome.

A number of haematological and biochemical abnormalities are known to occur. Anaemia, caused by chronic infections such as TB, results from the suppression of erythropoiesis by inflammatory mediators. Elevated serum alkaline phosphatase levels and hepatic transaminases indicate diffuse liver involvement. Other laboratory markers such as lymphopenia, thrombocytopenia and hypoalbuminaemia are strongly associated with mortality. Furthermore, hyponatraemia may indicate the presence of TB meningitis and may also be a predictor of mortality.¹¹ Sharma reported a retrospective series of 100 non-HIV adult patients (51 males, 49 females), with a mean age of 35 years, with miliary TB treated in a tertiary care centre.¹¹ Twelve patients died with miliary TB. Other independent predictors of mortality included temperature $>39.3^{\circ}\text{C}$, history of vomiting and the presence of crepitations on auscultation.¹¹ Cognitive, behavioural and an altered mental state have been described in 25% of cases.^{12 13}

Mandell's 'Principles and Practice of Infectious Diseases' aptly describes miliary TB in three groups.² Group 1, acute miliary TB, is associated with a brisk and histologically typical tissue reaction. It presents with non-specific symptoms, including fever, weight loss and headache. Laboratory findings, including a normal white cell count, hyponatraemia and a low haemoglobin, may be noted. A transaminitis and an elevated alkaline phosphatase may be present.² Impairment of pulmonary diffusion capacity can be demonstrated and fulminant miliary TB may be associated with ARDS and disseminated intravascular coagulation. A miliary infiltrate on chest radiograph is the main reason miliary TB is suspected. Group 2, known as cryptic miliary TB, usually describes older patients with miliary TB in whom the diagnosis is obscure due to the clinical picture of fever of unknown origin, a normal chest radiograph and a

negative tuberculin test. Group 3, non-reactive TB, presents with a clinical picture of sepsis and diffuse inconspicuous mottling on chest radiographs.² Gross pathology specimens include soft abscesses involving the liver and spleen.

Miliary TB has clinical, radiological and physiological similarities to other interstitial lung diseases, including a restrictive physiology and impaired gas exchange. The characteristic finding of miliary TB on chest radiography includes tiny (1–2 mm in diameter) 'millet seed' nodular opacities, but this classic miliary pattern may not be evident in up to 50% of chest radiographs of affected individuals, as in our case.^{12 13} At the onset of symptoms, chest radiographs are usually normal, with hyperinflation evident after 14 days. Other associated findings, occurring in $<5\%$ include parenchymal lesions, cavitation, segmental consolidation and thickening of the interlobular septae.¹ The differential diagnosis of a miliary pattern on a chest radiograph also includes histoplasmosis, sarcoidosis, cryptococcus, brucellosis, toxoplasmosis, schistosomiasis, bronchoalveolar cancer and metastatic disease.

Pipavath *et al*¹⁴ have described the high-resolution CT findings, including miliary nodularity, consolidation, ground glass and focal cystic abnormalities. Sharma concluded from his study that CT is superior to chest X-rays in detecting nodular lesions, lymphadenopathy and air trapping in patients with miliary TB.¹⁵ A few months ago, Hunter *et al* described an interstitial pattern with B-lines and comet tail artefacts disseminated throughout multiple lung areas as consistent changes seen in lung ultrasound of 10 patients with miliary TB.^{16 17} Further well-designed studies are required to evaluate its applicability. As well as this, ultrasonography has a role to play in facilitating diagnostic testing, for example, pleural or peritoneal fluid.

Admittedly, histopathological examination of biopsy specimens can provide rapid and sensitive results, but is not without risk in a patient with suspected miliary TB. However, it still remains the gold standard for diagnosis. Three types of media may be used for culture: solid egg-based (Lowenstein Jensen, which takes at least 21 days for a result), solid agar-based and liquid broth. Fibreoptic bronchoscopy in patients with a dry cough, bronchoalveolar lavage, bronchoscopic aspirate, brushings, washings and transbronchial lung biopsy are recommended.¹ With the launch of the GeneXpert MTB/RIF assay, this nucleic amplification has the ability to detect the *M. tuberculosis* complex. It offers the advantage of a rapid diagnosis, within 2 days. Adenosine deaminase is a useful adjunct in the diagnosis. Sputum smear microscopy using the Ziehl-Neelsen staining is useful in detecting AAFB and has a reported sensitivity of 61%. Sputum PCR has a high sensitivity 79%.¹⁸ Among non-invasive methods, enzyme-linked immunospot (ELISPOT) assay has the highest sensitivity (93%) for the detection of *M. tuberculosis* and may be a useful adjunctive test.¹⁹ In addition, a positive tuberculin skin test signifies a possible diagnosis of TB, but a negative test does not exclude it. Strain typing of TB isolates by 24 loci mycobacterial interspersed repetitive unit-variable number tandem repeats is now a routine laboratory tool for TB control, improving the diagnosis of latent and active infection, resulting in enhanced epidemiological investigations.²⁰ The possibility of multidrug-resistant TB should be considered in miliary TB.

Miliary TB is uniformly fatal if untreated within 12 months. Published studies have indicated that the BCG vaccine is effective in reducing the incidence of miliary TB, especially in children.²¹ The National Institute for Health and Clinical Evidence suggest 6 months of treatment (2 months with isoniazid, rifampicin, pyrazinamide and ethambutol or streptomycin, followed

by 4 months of isoniazid and rifampicin).²² Adjunctive corticosteroid treatment may be beneficial in individuals with ARDS, immune complex nephritis and pericardial or pleural effusions. However, further randomised controlled trials are required.

This case report highlights the protean manifestations of miliary TB and aptly describes the diagnostic challenge posed to experienced clinicians. It is imperative to maintain a high index of clinical suspicion and to initiate antitubercular treatment in a timely manner.

Learning points

- Miliary tuberculosis (TB), a term coined by Manget in 1700, is a fatal form of disseminated TB that results from a massive lymphohaematogenous dissemination from a mycobacterium-laden focus and embolisation to the vascular beds of the liver, spleen, bone marrow, lungs and meninges. It accounts for <2% of all cases of TB in immunocompetent individuals and up to 20% of all extrapulmonary TB cases.
- Morning temperature spikes have a diagnostic significance and are reported to be characteristic of miliary TB. Choroidal tubercles, located within 2 cm of the optic nerve, are pathognomonic. A number of haematological and biochemical abnormalities are known to occur, for example, anaemia, lymphopenia, thrombocytopenia, hypoalbuminaemia, hyponatraemia and transaminitis. Atypical presentations, for example, cryptic miliary TB and acute respiratory distress syndrome—often delay the diagnosis.
- Histopathological examination of biopsy specimens remains the gold standard for diagnosis.
- Miliary TB presents differently from typical cavitating pulmonary TB clinically and radiographically. The classic presentation of miliary TB with millet-seed sized infiltrates on chest radiographs may be a late finding and so a high suspicion for miliary TB needs to be entertained with systemic infections of unknown aetiology.
- Antitubercular treatment should be initiated immediately based on a strong clinical suspicion, as mortality is often due to delays in starting treatment.

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