Would you Rather Treat? A Rare Case of Mycobacterium Scrofulaceum.

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WOULD YOU RATHER TREAT? A RARE CASE OF *MYCOBACTERIUM SCROFULACEUM*

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ABSTRACT

Mycobacterium scrofulaceum is a rare cause of non-tuberculous mycobacterial infection in adults, primarily affecting the immunocompromised. Pulmonary involvement has been seen in individuals with pre-existing lung pathology. We report a case of a 63-year-old female who presented with abdominal pain, cough and sputum samples yielding *M. scrofulaceum*, with a normal clinical examination. Initial investigations were unremarkable, prompting abdomen and pelvis computed tomography (CT), revealing minimal pericardial and ascitic fluid. Thoracic CT exhibited calcified tree-in-bud nodules and a trivial left pleural effusion. Given subdued symptoms and limited disease, discerning colonisation versus clinically relevant infection was uncertain. Due to lack of empirical data for guidance, treatment approaches at this juncture remain unclear. The patient was monitored closely for a period of one year with a plan to treat should there be evidence of active disease.

KEYWORDS

Non-tuberculous Mycobacterium, pulmonary Mycobacterium scrofulaceum

LEARNING POINTS

- This case demonstrated an atypical presentation of rare non-tuberculous Mycobacterium.
- Whether the case involves *Mycobacterium scrofulaceum* infection or colonisation needs to be distinguished.
- There is limited utility of clinical diagnostic algorithms for non-tuberculous mycobacteria in *Mycobacterium scrofulaceum*.

INTRODUCTION

Mycobacterium scrofulaceum, a member of the non-tuberculous mycobacteria (NTM) group, got its name from 'scrofula', an infection of cervical lymph. Before the era of antibiotics, in the Middle Ages it was believed that a touch from royalty could heal skin; scrofula was known as 'king's evil'; patients rarely died from it and were unlikely to progress to pulmonary tuberculosis (TB)[1]. Data from the paediatric population may not be readily extrapolated to the adult population as number of reports have not differentiated between NTM organisms, but conflated organisms into an *M. avium*, intracellular, scrofulaceum (MAIS-complex), precluding any species-specific inferences[2]. Studies on NTM cervical lymphadenitis in children indicate that surgical

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excision is the most common and effective treatment, with a high success rate. However, medical treatment and observation are also used, though less frequently. The decision to opt for non-surgical approaches depends on factors such as the severity of the case and the patient's overall condition[3].

CASE DESCRIPTION

A 63-year-old female presented with left upper quadrant abdominal pain and a productive cough for a week, associated with fatigue. The patient denied having any fever, night sweats, and anorexia or weight loss. On clinical examination she was apyrexial, and had a tender left upper quadrant and left inguinal fossa. On auscultation her chest was clear bilaterally and had no added sounds. The rest of her examination was unremarkable. The patient is a well-controlled hypertensive with no history of diabetes, dyslipidaemia or other significant medical conditions; she maintains a healthy and active lifestyle. Her surgical history includes a cholecystectomy and hysterectomy. She has never smoked or consumed alcohol. Originally from Ghana, she has resided in Ireland with her partner for 20 years. She reported no recent travel, sick contacts or exposure to animals, and last visited Ghana several years ago without incident. She has worked as a healthcare assistant for over 15 years.

The patient was initially worked up for diverticular disease. Her C-reactive protein on admission was 68 mg/l, albumin 32 g/l, with normal renal and liver functions. Chest and abdominal X-rays were normal. Computed tomography (CT) abdomen and pelvis with contrast showed no evidence of diverticulosis but small volume of free fluid at the splenic hilum, minimal left pleural effusion with multifocal pleural and parenchymal calcifications in both lung bases. There was also a small volume of pericardial effusion inferiorly, in keeping with polyserositis *(Fig. 1)*. The pleural effusions were minimal, which precluded diagnostic paracentesis *(Fig. 1)*. After the CT scan, three early morning sputum samples were collected, more than 24 hours apart with no growth initially. The patient had an extensive workup including a viral screen, HIV, hepatitis B, hepatitis C, autoimmune screen and syphilis serology, which were all negative. The patient was treated empirically with IV amoxicillin/clavulanic acid. TB sputum cultures were found to be positive after 12, 16 and 37 days. *M. scrofulaceum* resistant to rifampicin was identified. QuantiFERON, blood and urine culture for TB were negative. A CT of the thorax showed calcified tree-in-bud nodularity in both lower lobes and in upper lobes peripherally, and mild bronchial wall thickening *(Fig. 2)*. It was unclear whether the positive sputum cultures were reflective of contamination, colonisation or indolent, slowly progressive infection. However, given the unremarkable imaging and clinical picture there was no clear evidence of active disease, and the clinical judgement was in favour of careful follow-up until the diagnosis was conclusively established or excluded. This would entail radiological surveillance, serum inflammatory markers and multiple sputum sampling for acid-fast bacilli every three months for a year as NTM lung disease is generally associated with slow progression.

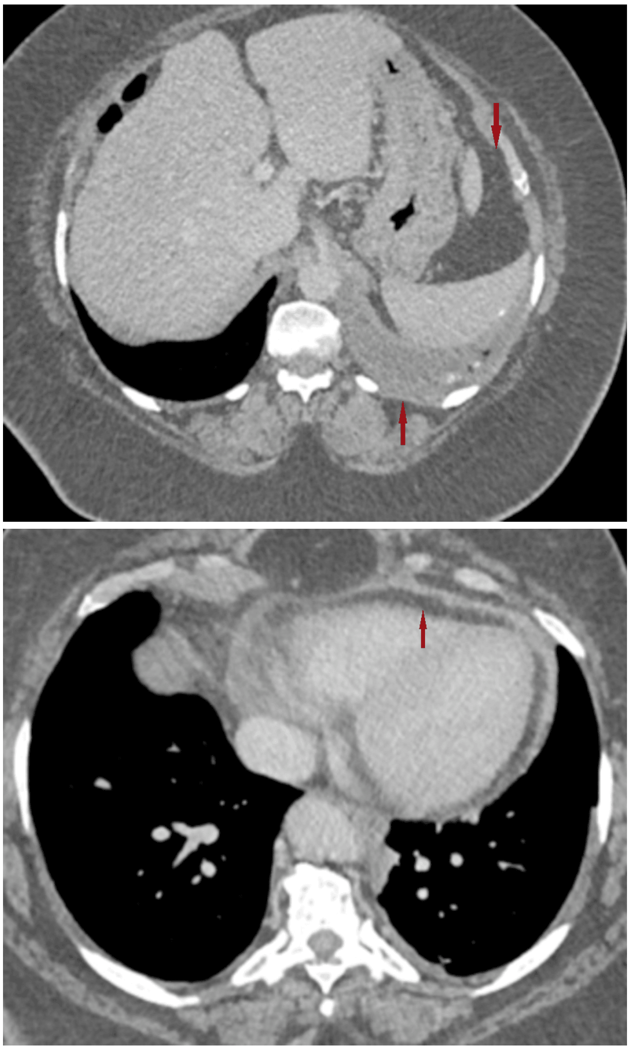

Figure 1. CT of the thorax showing mild pleural effusion, pericardial and ascitic fluid.

Normal levels of inflammatory markers, a clear chest X-ray and subsequent negative sputum samples for acid-fast bacilli follow-up made the diagnosis of active disease less likely. Therefore, it was decided that patient should not be treated due to lack of pulmonary symptoms, non-specific imaging and lack of predisposing lung condition. Subsequent imaging showed complete resolution of pericardial, pleural and ascitic fluid. In light of this, it was decided to discharge the patient from respiratory service.

DISCUSSION

Over 150 NTM species have been identified but *M. scrofulaceum* disease is rarely encountered in adults. A 2019 report from a tertiary medical centre identified only ten patients with *M. scrofulaceum* disease over a 15-year period. A comprehensive NTM collaborative study inclusive of 30 countries from six continents identified that *Mycobacterium avium complex* was consistently identified across these regions. The uniquely high reporting of *M. scrofulaceum* in South Africa was linked with the mining industry[4]. These organisms are ubiquitous and found in house dust,

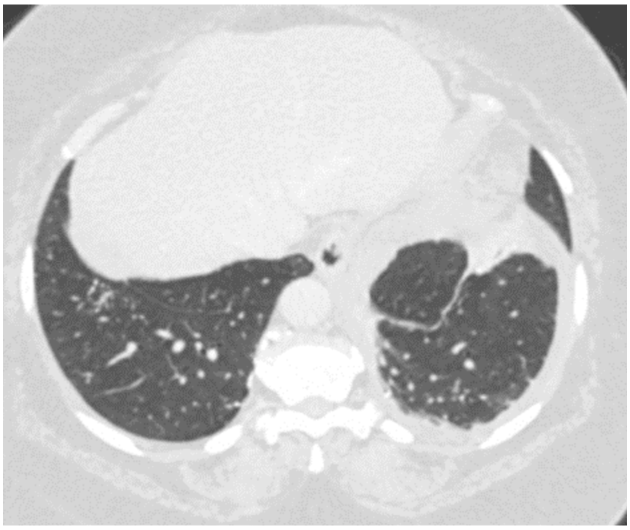

Figure 2. CT of the thorax showing calcified tree-in-bud nodularity in both lower lobes.

soil and water including treated sources of tap water, but have regional variation in distribution[5]. The incidence and prevalence of disease related to NTM is on the rise, and with novel presentations. However, there remains a dearth of empirically derived data to aid diagnosis and treatment protocols.

Pulmonary infections with *M. scrofulaceum* are rare and a characteristic pulmonary lesion is slowly-progressive cavernous pneumonia[6]. The infection is usually symptomatic and present with fever, lymphadenopathy or weight loss. Asymptomatic infections are not common and pose diagnostic and management challenges similar to this case. Those with two or three positive sputum cultures were associated with 90 and 98% development of radiological features of a new cavity or infiltrative lesion respectively. NTM are particularly observed in male patients (likely reflecting lifestyle factors such as smoking and occupational exposures), those with impaired host immune responses, structural lung pathology or older populations[7]. The ATS/IDSA diagnostic criteria are widely used; however, they have not been validated in any (highly susceptible) patient group or specific NTM species including *M. scrofulaceum*[8]. In addition, these criteria define NTM lung disease with no guidance available for extra-pulmonary/disseminated disease.

Polyserositis (PS) is not a well understood entity and is not clearly defined. Nevertheless, it is associated with malignancy, autoimmunity and infectious disease. In a recent systematic review of PS, of the cases with an infectious aetiology, two immunosuppressed patients had *Mycobacterium tuberculosis* disease confirmed on pleural fluid culture and peritoneal biopsy[9].

M. scrofulaceum is listed among NTMs that are generally considered to be contaminants if recovered from a single sample. There is no data to clarify the approach to recovery of *M. scrofulaceum* (or other infrequently encountered species) in more than one sample, given that multiple samples generally optimise the positive predictive value of disease. In addition, expert consensus suggests that samples recovered at bronchoscopy, e.g. bronchial washings, are more sensitive than routine expectorated sputum testing and less likely to be contaminated by tap water. However, invasive sampling is not essential for making the diagnosis. Positive culture results from at least one bronchial washing or lavage; transbronchial or other lung biopsy with mycobacterial histopathologic features (granulomatous inflammation or acid-fast bacteria) and positive culture for NTM or biopsy showing mycobacterial histopathologic features and one or more sputum or bronchial washings that are culture positive for NTM form part of the criteria for NTM lung disease. Colonisation without infection (i.e., tissue invasion) is a contested concept for NTM.

Data from paediatric NTM cervical lymphadenitis provides some evidence as this is the closest disease model to scrofula described in the Middle Ages. Recently, a systematic review and meta-analysis including 1951 children with NTM cervical lymphadenitis showed that 'no intervention' (i.e. no surgical excision or antimycobacterial treatment) was associated with a 70.4% cure rate and prolonged time to resolution. This could explain the non-fatal outcomes observed. *In vivo* and *in vitro* data show that environmental exposure to *Mycobacterium avium/intracellular/scrofulaceum* (MAIS) complex can induce immune responses to tuberculosis that is comparable to that achieved with BCG vaccination[10].

Given this patient's minimal symptoms, resistance to rifampicin, lack of clear evidence of active disease, absence of radiological or symptomatic progression during follow-up, close observation was favoured over immediate treatment. While mycobacterial infections such as *M. tuberculosis* are known causes of polyserositis, its association with NTMs, particularly *M. scrofulaceum*, is unclear.

CONCLUSION

This case highlights the highlights the complexity of managing NTMs, particularly when patients present with either atypical symptoms or are completely asymptomatic. The patient's non-specific symptoms, unremarkable imaging findings and the slow-growing nature of *M. scrofulaceum* presented diagnostic uncertainty between colonisation and infection. Despite multiple positive sputum cultures, the lack of active disease indicators warranted close monitoring rather than immediate treatment. It emphasises the importance of a personalised approach to manage, balancing the risks of treatment against the potential of disease progression. Asymptomatic NTM infections such as in this case require vigilant monitoring to ensure timely intervention if the infection becomes symptomatic, or it begins to spread. Further studies are needed to refine the diagnostic criteria and treatment approaches for rare NTM species, for example *M. scrofulaceum*.

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