Unusual association of diseases/symptoms

Mycobacterium malmoense: dissemination causes a popliteal aneurysm in a 74-year-old manAndrew Stewart Brereton,¹ Hassan El Teraifi²¹Medical Assessment Unit, Eastbourne DGH, Eastbourne, UK;²Histopathology Department, Eastbourne DGH, Eastbourne, UK**Correspondence to** Dr Andrew Stewart Brereton, andy_koala@hotmail.com**Summary**

Mycobacterium malmoense is recognised as an environmental pathogen predominantly affecting populations in Northern Europe. In immunocompetent individuals, isolated pulmonary disease remains the commonest presentation. The authors report a rare case describing a mycotic popliteal aneurysm caused by *M malmoense* in a 74-year-old man from Hastings, UK with co-existing pulmonary *M malmoense* disease. Primary pulmonary disease was confirmed by a combination of history, examination and positive radiological and microbiological findings. Tissue analysis of the aneurysm wall during popliteal aneurysm repair confirmed the presence of disseminated *M malmoense*. Histological analysis of the aneurysm wall showed non-caseating granulomata. The patient completed a 2 year course of rifampicin, ethambutol and clarithromycin which eradicated the organism from his sputum. Further progress has been complicated by the development of an aspergilloma at the site of his eradicated pulmonary *M malmoense* disease and the need for angioplasty to his bypass grafts 1 year postsurgery.

BACKGROUND

The patient presenting with unilateral calf swelling is a common presentation to the emergency department or medical assessment unit. In this particular patient there was a unifying theme that linked his acute presentation with his chronic pulmonary disease. It is important to reflect on complex cases encountered during 'on take' periods to improve knowledge and ultimately develop as a clinician. I feel that this rare case of a mycotic popliteal aneurysm caused by disseminated *Mycobacterium malmoense* in an adult should be shared with the wider medical audience as there have been no previous cases such as this published in any previous worldwide literature.

Infection with non-tuberculous mycobacteria (NTM) is often reported as a rather benign process. I wanted this case report to highlight that delaying treatment of pulmonary disease can lead to disseminated disease and subsequent harm to the patient.

CASE PRESENTATION/INVESTIGATIONS/TREATMENT

A 74-year-old retired lorry driver presented to the respiratory outpatient clinic in January 2009 with a 4 month history of worsening dyspnoea associated with a 'slimy cough.' There had been no preceding history of haemoptysis, fevers, night sweats or weight loss or history of tuberculosis. The patient had lived on a farm as a child and occasionally drunk unpasteurised milk. He had a medical history of chronic obstructive pulmonary disease (COPD) which was managed with a single agent – tiotropium 18 mcg (1 puff) once daily and he continued to smoke cigarettes with a 40 year pack history.

Clinical examination at this time had been unremarkable but a chest x-ray (CXR) had revealed the presence of right upper lobe infiltrates (figure 1). Three separate expectorated sputum samples had each tested positive for acid fast bacilli (AFB) during the period from January to

March 2009. Subsequent culture isolation and speciation had confirmed the AFB to be *M malmoense*. Before commencing drug therapy for primary pulmonary *M malmoense* infection he had presented to the emergency department, in May 2009, with a gradual onset of right calf and ankle oedema.

Figure 1 Posteroanterior chest radiograph showing infiltrates in the right upper lobe.

Figure 2 Doppler ultrasound showing the right popliteal aneurysm measuring 23 mm at its widest point – labelled 'A'.

A Doppler ultrasound of his right leg revealed the presence of a 2.7 cm popliteal artery aneurysm causing adjacent popliteal vein compression (figure 2).

There was no history of diabetes, hypercholesterolaemia, hypertension or a family history of aneurysms.

On examination the patient appeared well, was slim and afebrile. His pulse was 84 bpm and his blood pressure was 110/70. Heart sounds were normal. Respiratory examination revealed the occasional scattered wheeze, RR 22 and saturations of 96% on air. Abdominal examination was unremarkable with no evidence of aortic or iliac aneurysms. There were prominent femoral pulses bilaterally. He had a palpable popliteal aneurysm in the right popliteal fossa with a swollen right leg from beneath the knee with mild erythema at the ankle. Right dorsalis pedis was easily palpable with a biphasic signal and there was an impalpable right posterior tibial artery. Left leg examination was unremarkable revealing normal pulses throughout.

There was no clinical evidence of any skin, ophthalmic, cardiac or renal manifestations of endocarditis or disseminated mycotic disease.

Bloods results confirmed a normal full blood count, renal and liver function. His lymphocyte count was 1.7. Bone profile revealed an albumin 25, C reactive protein 26 and an erythrocyte sedimentation rate of 30.

CT angiography confirmed a leaky popliteal aneurysm with oedema of the surrounding tissues.

He subsequently underwent an exploration of his right popliteal fossa with bypass of the leaking popliteal aneurysm using reversed a contralateral long saphenous vein graft. Microbiological analysis of tissue taken from around the popliteal aneurysm confirmed the presence of *Stenotrophomonas maltophilia*, mixed anaerobes and AFB.

Culture isolation and speciation further classified the AFBs as *M. malmesense*.

Microscopic examination of the popliteal aneurysm showed ulceration of the lining surface of the popliteal artery. There were multiple non-caseating granulomata within the wall of the blood vessel as shown in (figure 3). These granulomata were made out of histiocytes with elongated nuclei with sparse mixed chronic inflammatory cells in the background. Special stains such as Ziehl-Neelsen for acid fast bacilli were negative but microbiology culture confirmed the presence of *M. malmesense*.

OUTCOME AND FOLLOW-UP

Following a normal initial assessment by a Consultant Ophthalmologist, the patient was commenced on rifampicin, ethambutol according to British Thoracic Society (BTS) Guidelines and clarithromycin based on advice from the department of microbiology who confirmed the isolated *M. malmesense* to be sensitive to this drug. This gentleman had no side effects of the treatment with regular full blood counts/liver function tests remaining within normal ranges for his entire 2 year treatment course. One year after the popliteal aneurysm repair the patient began to complain of claudication in the right lower leg on exertion. He subsequently required angioplasty of the superficial femoral artery (SFA) and the SFA vein graft anastomosis. He has had no further vascular problems since this procedure.

The patient completed 2 years of anti-NTM drug regime without re-isolation of *M. malmesense* in his sputum. He had three monthly CXR with respiratory outpatient review and had made good progress until May 2011 when he had fatigue and the production of blood streaked sputum.

Figure 3 Histology shows a close up view of a granuloma at the wall of the aneurysm made out of elongated histiocytes forming a rounded shaped granuloma with no caseation in its centre. Magnification X200 H&E stain.

Unfortunately his most recent CXR, and subsequent CT chest identified a new cavitating lesion in his right upper lobe suggestive of an aspergilloma. His sputum has remained negative for all Mycobacteria and fungal species but his blood tests were strongly positive (>200 mgA/l) for *Aspergillus* IgG antibodies (normal range <40). He has now been commenced on itraconazole for presumed aspergilloma and is progressing well.

DISCUSSION

The gram positive, acid-fast *M malmoense* is a member of a large family known as NTM.

Most documented cases of opportunistic *M malmoense* infection are in children causing cervical lymphadenitis or in adults presenting with isolated pulmonary disease.

Opportunistic NTM disease is most often associated with underlying comorbidities such as COPD, bronchiectasis, cystic fibrosis and chest wall disorders, oesophageal motility disorders and immuno-compromised states such as HIV infection.¹⁻³

In immuno-competent individuals, extra pulmonary disease is rare. Previous case reports have highlighted extrapulmonary manifestations such as synovitis and limited skin disease.^{4 5} There have been no previous documented cases of mycotic aneurysms secondary to disseminated pulmonary *M malmoense*. The patient has not provided any history of recurrent illnesses or risk factors that are classical for exposure to HIV and subsequent infection. On presentation, he had a normal full blood count and was not lymphopaenic. He has not been screened for autoantibodies, immunoglobulin deficiency or had a HIV test. We believe that this patient is immuno-competent but accept that only by completing these investigations could we conclude this beyond all reasonable doubt.

The diagnostic criteria for NTM pulmonary disease (American Thoracic Society/British Thoracic Society guidelines ATS/BTS) is a three pronged approach. This involves combining a compelling history and clinical assessment with positive CXR or HRCT findings consistent with NTM disease. Furthermore, within 1 year, bacteriology should confirm disease (two or more positive culture results from separate expectorated samples) or one or more positive cultures from either bronchial alveolar lavage/wash or a transbronchial biopsy.^{3 6}

ATS/BTS guidelines specify a maximum timeframe of 1 year to complete confirmation of NTM disease with positive microbiology results.^{3 6}

For the diligent physician who is keen to adhere to current guidelines and maintain best medical practice a prolonged period of clinical, radiological and microbiological investigation is required before NTM infection can be accurately diagnosed. In this patient it took 4 months to conclusively diagnose him with a pulmonary opportunistic *M malmoense* infection, 2 months later he presented with disseminated disease.

Current ATS/BTS guidelines for the treatment of disseminated *M malmoense* stipulate a minimum 18 month treatment regime of rifampicin, ethambutol +/- macrolide such as azithromycin or clarithromycin with frequent repeat sputum samples to confirm eradication of AFB.^{3 6-10}

Antituberculous medication are well reported for their infamous side effects and the difficulty that patients may find maintaining compliance with such a prolonged treatment plan makes the decision to treat, a decision not entered into lightly by either the clinician or the patient. In this case the mycotic aneurysm developed 6 months after he first presented to the respiratory outpatient clinic. It is unclear why the organism had such a vascular affinity

given the absence of classical risk factors for developing an aneurysm in this gentleman. The pleasing eradication of *M malmoeense* from his sputum after 2 years of treatment has been offset by the unfortunate development of an aspergilloma at the site of his previous opportunistic *M malmoeense* infection. This latest development poses a treatment conundrum. The patient was not a candidate for surgical removal leaving long-term antifungal medical therapy as the next best step. Evidence supporting one antifungal class over another for the treatment of an aspergilloma is currently weak and thus the choice of which agent is used is influenced by previous clinical experience. In this case, the patient was commenced on itraconazole and is currently progressing well although a clinical, biochemical or radiological response to this drug is not always guaranteed.¹¹

Learning points

- ▶ Although rare, disseminated *M malmoeense* does occur in adults and can cause the development of a mycotic aneurysm.
- ▶ Delaying treatment of pulmonary disease caused by NTM can lead to disseminated disease and subsequent harm to the patient.
- ▶ Further guidance from BTS/ATS is required on the appropriate treatment regime for disseminated *M malmoeense* as its current treatment is based on the drug regime for disseminated *Mycobacterium avium* complex.
- ▶ Complex cases such as this are best managed with multi-disciplinary team input from beginning to end.

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