A paediatric case of non-tuberculous mycobacterial infection in the neck

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Abstract

We discuss a case of rapid onset neck swelling in a paediatric patient with an underlying *Mycobacterium avium* infection. Surgical excision of the tissue revealed epithelioid granulomata with central caseating necrosis, background chronic inflammation and scanty acid-fast bacilli. Diagnosis of non-tuberculous mycobacterial infection can be reached using histological features, cultures and molecular techniques. Granulomatous inflammation has a range of infective and non-infective causes to consider when determining a diagnosis.

Keywords caseous necrosis; granuloma; infectious pathology; mycobacteria; paediatric pathology

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Case report

A previously well 2-year old white male presented with a rapid onset, painless left neck swelling. An initial ultrasound scan suggested the swelling was due to a reactive lymph node. No improvement was seen over the course of several weeks and after treatment with oral antibiotics. Clinical examination demonstrated two painless masses in the left submandibular region with no overlying cellulitis. Further ultrasound scans revealed an organized abscess. The patient was otherwise asymptomatic, afebrile and had no history of immunocompromise.

The patient was treated with incision and drainage of the neck abscess tissue and further oral antibiotics. Multiple fragments of pale, yellow tissue were seen macroscopically. On microscopy, sections showed inflammatory tissue with epithelioid granulomata, focally coalescing around central areas of caseous type necrosis (Figure 1). Multinucleated giant cells were present and the surrounding tissue showed a prominent infiltrate of chronic inflammatory cells, composed mainly of plasma cells (Figure 2). Ziehl-Neelsen and Wade-Fite special stains were negative for acid-fast bacilli.

Initial tissue and pus microbiology cultures were negative. Tissue sent for molecular testing for mycobacteria revealed the presence of *Mycobacterium avium* on whole genome sequencing.

Five months after the initial surgery, symptoms recurred and the patient proceeded to a left lower parotidectomy with removal of a facial node, overlying skin and level 2 nodes. On microscopy, only the facial node and overlying skin demonstrated inflammatory changes. The skin showed granulomatous inflammation, extending through the entire thickness of the dermis. Epithelioid granulomata with coalescing central areas of caseous type necrosis were again identified (Figures 3 and 4). There was marked chronic inflammation with many multinucleate giant cells in the background. Ziehl-Neelsen and Wade-Fite special stains showed scanty acid-fast bacilli (Figure 5) and likely acid-fast material within histiocytes (Figure 6). The features were consistent with the earlier diagnostic features of infection with *Mycobacterium avium*.

After further surgical excision, the patient recovered fully and had no disease recurrence.

Discussion

Mycobacterium avium is a subtype of *Mycobacterium avium complex (MAC)* species and one of a large group of non-tuberculous mycobacteria, responsible for causing infections (pulmonary disease, lymphadenitis and disseminated disease) in humans.[1] The term "non-tuberculous mycobacteria" encompasses all Mycobacterial species, with the exception of *Mycobacterium tuberculosis* and *Mycobacterium leprae*.[2]

MAC species are widely present in the environment and infections may be contracted through inhalation, ingestion or skin contact, usually from environmental exposures (such as soil or contaminated water) or medical devices.[1,2] Other common pathogenic non-tuberculous mycobacterial (NTM) species include *Myocobacterium abscessus complex* and *Mycobacterium kansasii*.[1] These pathogens cause disease in both immunocompromised and healthy patients, and symptoms may be non-specific, resulting in delayed presentation and diagnosis.[2]

Granulomatous inflammation is a form of chronic inflammation, composed of activated macrophages with associated T lymphocytes.[3] Examples of common aetiologies of granulomatous inflammation to be considered in a differential diagnosis are

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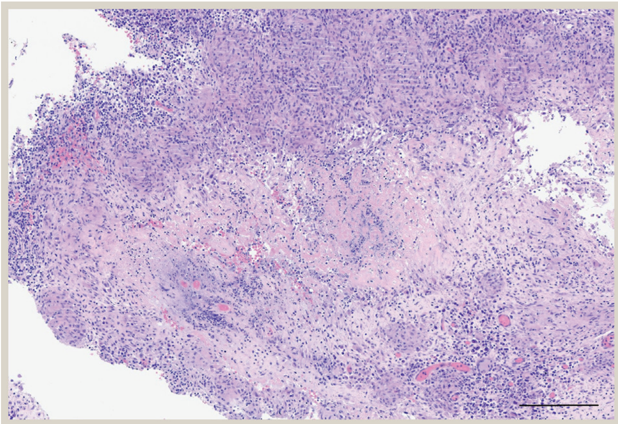

Figure 1 Epithelioid granulomata with central caseous necrosis (200 µm scale).

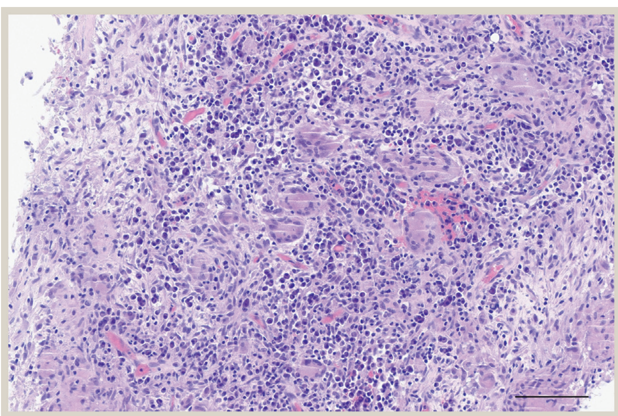

Figure 2 Multinucleated giant cells and prominent chronic inflammation (100 µm scale).

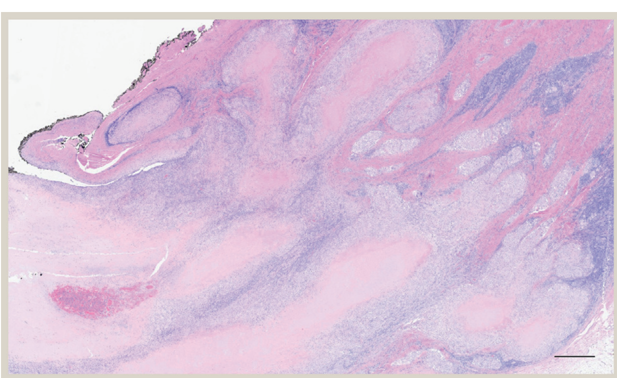

Figure 3 Epithelioid granulomata with central caseous necrosis (500 µm scale).

shown in Table 1. Granulomas develop to contain material that is difficult to break down or eradicate.[3,4] These can be grouped into two histological patterns:

- Foreign body granulomas – result from groups of macrophages encompassing material (such as talc, suture, starch, food material and hyaluronic acid) that is too large to be broken down by phagocytosis and that does not provoke a specific immune response.[3–5]
- Immune granulomas – may be caused by a range of infective and non-infective agents that are difficult to eradicate and induce a granuloma producing T cell-mediated immune response.[3,4]

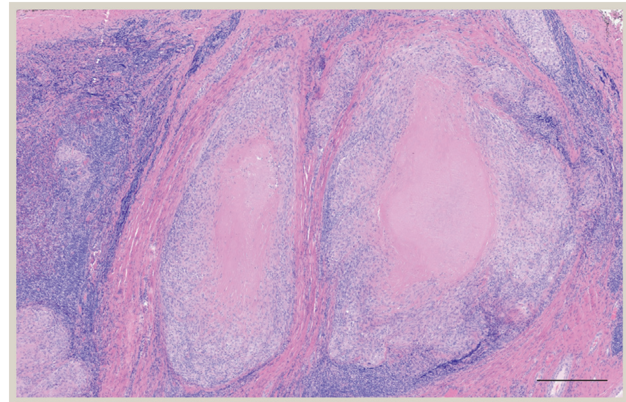

Figure 4 Epithelioid granulomata with central caseous necrosis and background chronic inflammation (400 µm scale).

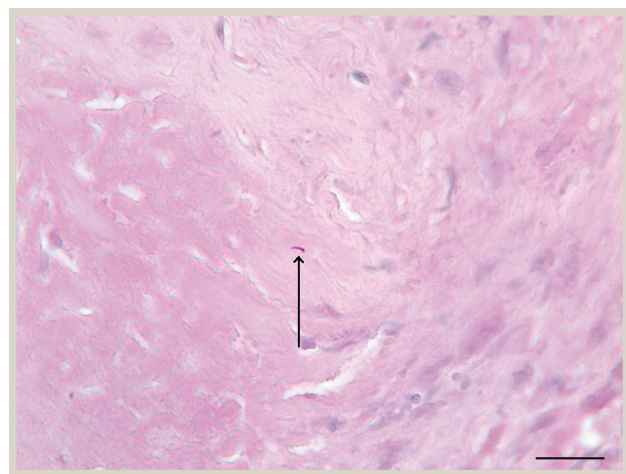

Figure 5 Acid fast bacillus (arrow) in necrotic debris on Wade Fite staining (20 µm scale).

Central necrosis forms within some granulomas and creates an ideal environment for growth and dissemination of infective

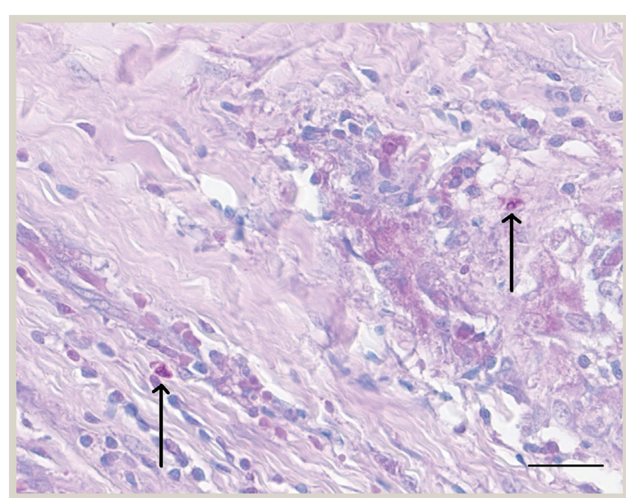

Figure 6 Likely acid fast material (arrows) within histiocytes on Wade Fite staining (30 µm scale).

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Examples of aetiologies of granulomatous inflammation[3–5]

Infection
- Bacterial: *Mycobacterium tuberculosis*, *Mycobacterium avium*, *Treponema pallidum*, Nocardia, *Francisella tularensis*.
- Fungal: Aspergillus spp., *Histoplasma capsulatum*, Cryptococcus spp.
- Viral: cytomegalovirus, Epstein-Barr virus
- Parasitic: Toxoplasma gondii, Leishmania spp.

Malignancy e.g. haematological malignancies, sarcomas, disseminated metastases.
Autoimmune/immunological e.g. Churg Strauss, Crohn's disease, primary biliary cholangitis, sarcoidosis. systemic lupus erythematosus
Drugs: antibiotics, methotrexate, non-steroidal anti-inflammatory drugs
Foreign body/occupational diseases e.g. pneumoconioses, berylliosis

Table 1

pathogens, including *M. tuberculosis,* non-tuberculous mycobacteria and fungal species such as *Coccidiodes immitis and Coccidiodes posadasii*.[4]

In addition to examination of the histological pattern of disease, other tests can assist with determining an underlying diagnosis. Special stains such as Ziehl-Neelsen, Grocott methenamine silver and a modified acid-fast stain (Wade-Fite) can be useful in detecting mycobacterial species.[4] Correlation with clinical and any radiological findings is required and sampling for cultures is essential where there is suspicion of an infective cause.[4,6] Both fresh and formalin-fixed, paraffin-embedded tissues can be sent for PCR and sequencing for bacteria and fungi, although in formalin fixed, paraffin embedded material the sensitivity is reduced and a negative result in such material may not exclude infection.[4]

Conclusion

This case demonstrates an infective cause of granulomatous inflammation due to a non-tuberculous mycobacteria infection. There can be a range of underlying causes of granulomatous inflammation and there may be varied histological appearances. Diagnosis may require consideration of clinical history, radiological features, histological and special stain appearances, culture results and molecular findings. ◆

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Practice points

- Consider a range of infective and non-infective causes when encountering granulomatous inflammation
- Non-tuberculous mycobacteria may be an underlying cause necrotizing granulomas
- Perform ancillary testing (acid-fast bacilli stains (Ziehl Nielsen, Wade-Fite stains etc.)) and even if negative, refer for microbiology testing
- There are two key patterns of granuloma formation (foreign body granulomas and immune granulomas)
- Diagnosis of underlying aetiology of granulomatous inflammation may require consideration of clinical history, radiological features, histological and special stain appearances, culture results and molecular findings.

Self-assessment questions

1. Which of these best summarises the description "non-tuberculous mycobacteria"?

a. All mycobacterial species, excluding *Mycobacterium tuberculosis*
b. All mycobacterial species
c. All mycobacterial species excluding *Mycobacterium tuberculosis, Mycobacterium leprae* and *Mycobacterium kansasii*
d. All mycobacterial species excluding *Mycobacterium tuberculosis* and *Mycobacterium leprae*

2. Which of these is LEAST likely to cause foreign body granuloma formation?

a. Sutures
b. Hyaluronic acid
c. Melanin
d. Starch

3. Which of these stains would be LEAST useful in a case of granulomatous inflammation due to an underlying infection?

a. Periodic acid-Schiff
b. Congo red
c. Wade-Fite
d. Grocott methenamine silver

Answers
1 – d
2 – c
3 – b

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