Mycobacterium avium-intracellulare cervical lymphadenitis in siblings: a case report and review

V. L. CUMBERWORTH, B.Sc., F.R.C.S., A. C. ROBINSON, F.R.C.S.

Abstract

We report two cases of cervical mycobacterium avium-intracellulare lymphadenitis in siblings which developed within one month of each other. There was no underlying immunodeficiency but the children lived in close proximity to a pigeon loft.

Key words: *Mycobacterium avium-intracellulare* infection; Lymphadenitis; Sibling relations

Introduction

Lymphadenitis of the anterior cervical or submandibular nodes is the commonest manifestation of atypical mycobacterial infection in children, with *mycobacterium avium-intracellulare* (*MAI*) the commonest organism responsible (Speck and Besunder, 1992).

The mode of transmission of *MAI* infection is uncertain and secondary familial infection, particularly in the absence of immunodeficiency, has been reported only extremely rarely.

Such infections are characteristically resistant to multiple drug regimes and surgical excision of localized lesions is the treatment of choice.

Case reports

Case 1

A two-and-a-half-year-old girl presented with a one-month history of a 5 × 5 cm right-sided submandibular swelling. The initial pain and erythema had resolved with oral antibiotics and her history was otherwise unremarkable. Aspiration yielded 7 mls of green pus, examination of which was unhelpful. Her full blood count was normal.

After a negative preliminary panendoscopy, incision and drainage was performed which yielded caseous, necrotic material. Histological examination showed necrotising granulomatous inflammation with epithelioid histiocytes and giant cells. Ziehl-Neelsen staining demonstrated acid-fast bacilli and a diagnosis of mycobacterial cervical lymphadenitis was made and initial treatment commenced with isoniazid and rifampicin.

However, after Reference Laboratory confirmation, the diagnosis of *MAI* was established with multiple drug resistance. After persistence of the cervical swelling with recollection of the abscess, medical therapy was discontinued and the necrotic swelling excised. Her post-operative course was uneventful and one year later she remains well.

Case 2

Her three-and-a-half-year-old brother had developed a 2 × 2 cm right-sided jugulodigastric swelling one month before his sister. He had a year-long history of monthly recurrent tonsillitis and four weeks later underwent adenotonsillectomy, panendo-

scopy and fine needle aspiration of his neck swelling. Cytological examination was negative and histology of the tonsillar and adenoid tissue normal. His ESR was marginally raised at 14 mm/hr and full blood count was normal.

Three months later the right anterior cervical triangle swelling had increased in size to 3 × 2 cm and one month after the definitive surgical treatment for his sister (detailed above) his cervical swelling was explored. A multi-lobulated mass adherent to the common carotid artery and internal jugular vein, and with central caseation, was removed. Histological examination showed necrotising, granulomatous inflammation, consistent with mycobacterial infection. Subsequent microbiological investigation confirmed *MAI* cervical lymphadenitis. Like his sister, his post-operative recovery was uncomplicated and he remains well 11 months later.

The only factor of possible relevance elicited by detailed history taking was that a few months prior to development of the cervical lymphadenitis the family had moved to a house next-door-but-one to a pigeon loft.

Discussion

In the early 1950s non-tuberculous mycobacteria were increasingly recognized as important human pathogens after culture rather than smearing for acid-fast bacilli became routine and the prevalence of tuberculosis had rapidly declined (Wolinsky, 1979). Mycobacteriae of complex avium-intracellulare (*MAI*) are the most important agents of non-tuberculous mycobacteriosis throughout the world, with the two species being grouped together due to the difficulty in differentiating them except by seroagglutination, thin-layer chromatography, enzyme-linked immunosorbent assay (ELISA) and DNA probes. *MAI* strains are particularly associated with pulmonary disease, childhood lymphadenitis and disseminated infections in patients with AIDS (Wolinsky, 1992).

MAI occur in soil (where they can maintain viability for four years), water and dust but are common in animals, particularly birds, poultry and small wild animals (Christie, 1987).

From a series of 330 pulmonary cases of atypical mycobacteriosis, Corpe (1964) found no secondary cases in spouses or the same family, highlighting the difference in epidemiology from mycobacterioum tuberculosis infection.

Circumstantial evidence suggests that cervical lymph nodes become infected with myobacteria by a pathway originating in the mouth or oropharynx, with infection acquired from natural sources in the environment (Wolinsky, 1979).

The only proven examples of direct animal to man transfer of atypical mycobacteriosis concerns *M. marinum* acquired from fish handling; there is no evidence for direct person to person transmission, even when sputum is heavily laden with organisms (Christie, 1987; Citron and Girling, 1987). Secondary cases in families have been reported extremely rarely and may represent either person to person transmission or acquisition of infection from a common source in the environment (Wolinsky, 1979). Uchiyama *et al.* (1981) described fatal disseminated MAI infection in two siblings, although extensive immunologic evaluation in one revealed a monocyte killing defect. Chakraborty *et al.* (1981) found a significant predominance of the haplotype A2-B12 from that expected from a series of 41 consecutive cases of *M. intracellulare* and suggested that there may be a possible predisposing genetic factor in this disease.

From a nine year review Wickman (1986) found that lymphadenitis was the commonest non-tuberculous mycobacterial infection of children, with *MAI* responsible in 30 of 33 cases, although none of the children were BCG vaccinated. Indeed Katila *et al.* (1987) postulated that neonatal BCG vaccination may protect children against non-tuberculous mycobacterial infection, particularly under the age of four.

From a review of 118 children with culture-positive mycobacterial lymphadenitis under the age of seven, Pang (1992) found MAI in 74 per cent, *M. scrofulaceum* in 20 per cent and *M. tuberculosis* in 4 per cent in contrast to adults where the respective frequencies were 2 per cent, 4 per cent and 89 per cent. *M. tuberculosis* predominates as the cause of mycobacterial cervical adenitis in adults (Lai *et al.*, 1984).

The differential diagnosis of non-tuberculous mycobacterial lymphadenitis (NTML) includes tuberculosis, sarcoidosis, pyogenic infection, cat scratch disease, infectious mononucleosis and malignancy (Citron and Girling, 1987).

Diagnosis may be difficult since *MAI* has fastidious growth requirements and in 30 per cent of cases the organisms may fail to grow (Sigalet *et al.*, 1992), furthermore the histology on biopsy is generally considered indistinguishable from that of tuberculosis (Citron and Girling, 1987). However, the presence of 'atypical histological features' such as a poorly defined, nonspecific, sarcoid-like or irregular granulomatous response or a lack of caseation tend towards NTML in children. Specific DNA probes have been developed for MAI which can identify only two organisms, although data on identification of different pathogenic mycobacteria from paraffin embedded specimens has yet to be reported (Pinder and Colville, 1993).

From a review of 19 children with NTML White *et al.* (1986) found a mean age at diagnosis of just over five years, with most having no systemic upset and lymphadenopathy for a mean duration of six weeks, principally in the cervical nodes. Chest X-rays were clear, standard tuberculin testing negative in two-thirds of the cases tested and anti-tuberculous drugs ineffective due to high resistance with total excision the treatment of choice.

Sigalet *et al.* (1992) reported similar findings from a review of 53 cases; incision and drainage or anti-tuberculous medication was unsuccessful in all 12 cases so managed whereas primary excision succeeded in 33 of 37 cases. Sixteen cases required secondary surgical excision and all were successful.

MAI are the most resistant of the non-tuberculous mycobacteria to chemotherapy, although strains may vary in susceptibility (Christie, 1987). Combinations of four to six drugs have been used for disseminated *MAI* typically associated with immunodeficiency or immunosuppression (Speck and Besunder, 1992).

Disseminated *MAI* has occurred with increasing frequency in AIDS and has been present in up to 50 per cent of such patients undergoing autopsy in some American cities; even with intensive combination drug therapy case fatality is very high in disseminated *MAI* infection (Wolinsky, 1992).

Cervical lymphadenitis in young children is more commonly of atypical mycobacterial rather than tuberculous origin, with *MAI* the most frequent pathogen. Due to the lack of evidence for direct person to person transmission and immense rarity of secondary cases in families, the occurrence of similar *MAI* infection in siblings within one month is of particular interest. The role of the nearby pigeon loft remains uncertain.

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Address for correspondence:
Mr V. L. Cumberworth,
14 Grafton Road,
Harrow,
Middlesex
HA1 4QT.