Non-tuberculous mycobacterial lymphadenitis

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SUMMARY   Most cases of mycobacterial lymphadenitis in children are caused by non-tuberculous mycobacteria, previously called the atypical mycobacteria. It is important to differentiate non-tuberculous mycobacterial lymphadenitis from tuberculous lymphadenitis as the treatment is different.

We reviewed 19 children (12 girls and seven boys) with non-tuberculous mycobacterial lymphadenitis to define likely presenting features, helpful diagnostic measurements, and optimum management. Mean age at diagnosis was 5·2 years. Most had no systemic upset and clear chest x ray films. Cervical nodes were the commonest affected, and enlargement was usually unilateral. Mean duration of swelling was 6·6 weeks, and 63% of the nodes had an appearance suggestive of cold abscess.

Routine haematology was unhelpful, and standard tuberculin testing performed in 47% yielded negative results in two thirds. Differential Mantoux testing with human purified protein derivative and an avium-intracellular antigen may be more useful. Antituberculous drugs were ineffective. The organism was usually highly resistant. Total excision is the treatment of choice. Antituberculous drugs are unnecessary.

In developed countries most cases of mycobacterial lymphadenitis are caused by non-tuberculous mycobacteria.[1] Several series have been reported.[2–12] It is important to differentiate non-tuberculous mycobacterial lymphadenitis from tuberculous lymphadenitis as the treatment is different. Antituberculous drugs are ineffective in non-tuberculous mycobacterial lymphadenitis, and the treatment of choice is total excision.[4 6–8 10 12]

We have reviewed the management of 19 children with non-tuberculous mycobacterial lymphadenitis. We have sought to define the likely presenting features of these infections and helpful diagnostic measurements.

Patients and methods

Nineteen cases of non-tuberculous mycobacterial lymphadenitis occurring between February 1982 and May 1984 were reviewed. Two cases were seen in Glasgow and the remainder in other British centres. The cases from outside Glasgow were known to the Mycobacterium Reference Unit in Cardiff, and with their help the consultant concerned with the case was contacted and the records obtained.

There were 12 girls and seven boys. All were white, with a mean age of 5·2 years (range 1·8–9·7 years).

Results (Tables 1 and 2)

Cervical nodes were the commonest affected (47%) followed by submandibular (31·5%) and preauricular (21%). In 16 (84%) of the children the lymphadenopathy was unilateral. Mean duration of swelling was 6·6 weeks (range 2 weeks–4 months). Appearance of the nodes varied but in 12 (63%) was suggestive of cold abscess with absent or minimal tenderness and fluctuation. Of the other seven, five (26%) had an appearance suggestive of bacterial abscess, one was cystic, and the other was a non-tender, mobile swelling. Glands varied from 1·5–7 cm in length. Two were described as a large mass, and three were fixed to underlying tissues. In one (case 16) infection developed after trauma to the area. Only two children had systemic upset. This was an intermittent fever and mild cough (case 1) and persistent cough (case 8).

Routine haematology was unremarkable. One case had a raised white cell count (15 000×10⁹/l

Table 1 *Tuberculin tests used, mycobacteria cultured, and drugs used for treatment in 19 cases with non-tuberculous mycobacterial lymphadenitis*

Case No	Tuberculin tests	Mycobacterium cultured	Antituberculous drugs used	
1	Tuberculin PPD 1/10 000, 10 mm AV-INT antigen 1/10 000, 15 mm	—	Rifampicin Isoniazid	} 6 months
2	Tuberculin PPD 1/10 000 negative AV-INT antigen 1/10 000, 15 mm	*M. avium-intracellulare* —	Rifampicin Isoniazid	} 3 months
3	Tuberculin PPD 1/10 000 negative	*M. avium-intracellulare*	Rifampicin Isoniazid	} 7 months
4	Tine test negative	*M. avium-intracellulare*	Rifampicin Isoniazid	} 6 weeks
5	—	*M. avium-intracellulare*	Rifampicin Isoniazid Pyrazinamide one dose	} 4 months
6	Tuberculin PPD 1/1000 negative	*M. avium-intracellulare*	Rifampicin Isoniazid Ethambutol	} 1 week
7	Tine test negative	*M. avium-intracellulare*	Rifampicin Isoniazid	} 3 months
8	—	*M. malmoense*	Rifampicin Isoniazid	} 6 months
9	—	*M. avium-intracellulare*	—	
10	— —	*M. avium-intracellulare*	Ethambutol Isoniazid Streptomycin Ethionamide	} 5 months } 3 months
11	Tuberculin PPD ? dilution—negative —	*M. malmoense*	Isoniazid Rifampicin Ethionamide	} 9 months 8 months
12	Tuberculin PPD ? dilution—negative —	*M. avium-intracellulare*	Isoniazid Rifampicin Ethambutol Erythromycin	12 months } 15 months 4 months
13	—	*M. malmoense*	Rifampicin Isoniazid	} 6 months
14	—	*M. avium-intracellulare*	Rifampicin Isoniazid Ethambutol	6 months 18 months 15 months
15	—	*M. malmoense*	—	
16	—	*M. malmoense*	Ethambutol Rifampicin Isoniazid	1 month } 6 months
17	—	*M. avium-intracellulare*	—	
18	Tine test positive	*M. avium-intracellulare*	Rifampicin Ethambutol	} 8 months
19	—	*M. avium-intracellulare*	—	

PPD=purified protein derivative; AV-INT antigen=an avium-intracellulare composite antigen.

with 60% neutrophils) and two an appreciable rise in the erythrocyte sedimentation rate. Chest x rays performed in 17 cases were clear in 15 (88%). One had minor inflammatory changes in the right upper lobe (case 6) and another a prominent right hilum (case 8).

No child had received prior BCG vaccination. Only nine (47%) had a standard Mantoux or tine test performed, and this yielded positive results in only three. Differential Mantoux test with human purified protein derivative and an avium-intracellular composite antigen (obtained from the Mycobacterium Reference Unit in Cardiff) were performed in two cases and indicated non-tuberculous mycobacterial infection in both. This was taken as sole proof of non-tuberculous mycobacterial infection in case 1 while the remaining cases had bacteriological proof, most of the isolates being mycobacteria of the avium-intracellulare complex. Mean time in obtaining culture results was 7·9 weeks (range 3–16 weeks) and sensitivity results was 11·5 weeks (range 5–16 weeks). Histology was obtained in 13 cases (68%), and acid fast bacilli were seen in the specimen in eight (61%) of these. The histology was variable and described as caseating granulomas (cases 2, 10, 11, 16, and 17), giant cell granulomas (case 13), chronic granulomas (cases 3, 6, and 18), non-caseating granulomas (case 8), and

Table 2   *Surgical procedures performed in 19 cases with lymphadenitis, the outcomes, and subsequent surgery*

Case No	Initial surgery	Outcome	Repeat surgery
1	—	Prominent scar	—
2	Needle aspiration	Sinus 5 months	Total excision at 5 months
3	Incision + biopsy	Sinus 2 months Prominent scar	Incision + drainage at 2 months
4	Incision + biopsy	Sinus 4 months Prominent scar	—
5	Incision + biopsy	Sinus 3 months Indurated wound	—
6	Total excision	Uncomplicated	
7	Incision + drainage	Sinus 2 months Scab over wound 6 months	
8	Partial excision	Uncomplicated	
9	Incision + drainage	Slow resolution No sinus	—
10	Incision + biopsy	Sinus 6 months	Total excision at 6 months
11	Needle aspiration	Sinus 7 months Indurated wound	Needle aspiration 1 month Partial excision 3 months
12	Needle aspiration	Sinus 5 months Prominent scar	—
13	Partial excision	Slightly indurated wound	—
14	Incision + drainage	Sinus 6 weeks Discoloured scar	—
15	Incision + drainage	Uncomplicated	
16	Incision + biopsy	Sinus 4 months Indurated scar	—
17	Total excision	Uncomplicated	
18	Incision + biopsy	Sinus 2 months Discoloured scar	Incision + biopsy 1 month
19	Incision + drainage	Uncomplicated	

chronic inflammation with or without giant cells (cases 4 and 5). Histology in case 14 was said to have confirmed the diagnosis, but details were not available. Pus sent for examination for acid fast bacilli in 14 cases was positive in six (43%) and grew non-tuberculous mycobacteria on culture in 12 (85%).

Ten cases (53%) had family screening for mycobacterial disease, and all yielded negative results. Prior antibiotic treatment was received in 14 cases (74%) with no improvement.

Incision and drainage was the commonest surgical procedure (61%) but, together with needle aspiration, led to a high incidence of sinus formation and scarring. After surgery 11 cases (61%) had a draining sinus for a mean of 15·0 weeks (range 6 weeks–7 months), and this only occurred after incision and drainage (eight out of 11 cases) and needle aspiration (three out of three cases). Five of these patients required further surgery, and five are left with a prominent scar. In one (case 16) sinus formation preceded surgery. In contrast, the four children who underwent total or partial excision as a primary procedure had an uncomplicated course that in two (cases 6 and 17) could not be attributed to antituberculous drugs.

Antituberculous drugs given to 15 (79%) for a mean of seven months (range 1 week–18 months) seemed to be ineffective even in the three cases (10, 11, and 13) where the organism was sensitive (rifampicin and streptomycin). In most the organism was highly resistant to all the usual first line antituberculous drugs. Prominent scarring occurred in the one child (case 1) treated by antituberculous drugs alone, whereas three of the four children treated with surgery alone (cases 15, 17, and 19) had an uncomplicated course. Drug side effects were uncommon. Case 5 developed generalised erythema after one dose of pyrazinamide. In case 10 anorexia, weight loss, and peripheral eosinophilia developed after three months of treatment with streptomycin and ethionamide and resolved on their withdrawal.

The mean duration of follow up was 10·5 months (range 3–18 months).

Discussion

We have reviewed 19 cases of non-tuberculous mycobacterial lymphadenitis in children. Presenting features are similar to other reported series.[3–5] [7] [8] [10–12] Young children are affected, and there is usually no systemic upset or evidence of haematogenous spread. In contrast to tuberculosis, unilateral node enlargement is common and occurs particularly in cervical, submandibular, and preauricular areas. The node may look like a cold abscess, but this is not invariable. It might resemble a cyst or typical bacterial abscess. It is tempting to

perform needle aspiration or incision and drainage, but these procedures increase the risk of sinus formation[2] [4] [9] [10] and also in our series scarring. Diagnosis before surgical intervention is therefore important. A chronic, unilaterally enlarged node in a typical area in a young, otherwise well child should suggest non-tuberculous mycobacterial disease, particularly if there is no response to antibiotics, no family history of tuberculosis, and a clear chest x ray film. Routine haematology is usually normal and does not help in making the diagnosis.

Can tuberculin tests help? Cross reactivity with tuberculin purified protein derivative occurs, and tuberculin tests may yield positive[9] or negative results.[7] In our series most yielded negative results, but only 47% had tuberculin testing. Differential testing with tuberculin purified protein derivative and purified protein derivatives obtained from non-tuberculous mycobacteria is more helpful but not always conclusive and may need to be repeated.[3] [4] [9] [12]

In non-tuberculous mycobacterial infections the response to tuberculin diminishes in time, thereby improving the diagnostic ability of dual skin tests if repeated weeks or months later.[9] There are other problems. Non-tuberculous mycobacterial antigens for skin testing are specific for the organism or complex from which they are derived. Thus the avium-intracellular composite antigen will not detect *Mycobacterium malmoense* infection (for which the appropriate skin testing antigen is not yet available). Perhaps some of these difficulties will be overcome when the highly specific 'new tuberculins'[13] are commercially available.

Non-tuberculous mycobacteria are usually highly resistant to antituberculous drugs.[1] [14] Despite this they continue to be prescribed (79% in this series) and continued even when the sensitivity is known. Mandell suggested a useful role for rifampicin in non-tuberculous mycobacterial infection.[15] This has not been borne out in our series where only two isolates (both *M. malmoense*) were rifampicin sensitive, and despite treatment one required further surgery for a draining sinus. The other's uncomplicated course could equally be attributable to initial surgery (partial excision). All 11 (61%) who developed a draining sinus had been treated with antituberculous drugs, which included rifampicin in 10. Sinus formation was common after incision and drainage, as in previous studies.[2] [4] [9] [10]

Several series have recommended total excision of the node as the only treatment necessary,[4] [6-8] [10] [12] and we would agree. This confirms the diagnosis and carries less risk of sinus formation and scarring.

Antituberculous drugs are ineffective and carry the risk of side effects.

Do we need to treat non-tuberculous mycobacterial lymphadenitis at all? The natural history of these infections is still unclear.[14] In most cases they are benign, and subclinical infections (based on skin testing) probably occur.[14] Pulmonary and disseminated non-tuberculous mycobacterial disease is rare in children, but fatalities have been reported even in the absence of an immune deficiency.[5] Treatment therefore should be optimal and not carry the risk of side effects. As person to person transmission has never been proved[1] [14] contact tracing is unnecessary and children need not be kept from school.

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