Non-tuberculous mycobacterial lymphadenopathy

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Abstract

The surgical and antimicrobial treatment of non-tuberculous mycobacterial lymphadenopathy in 17 children was reviewed. Node excision was curative, but most nodes were still incised leaving discharging lesions. Standard antituberculous treatment was unhelpful, but a new macrolide/quinolone combination appeared to be effective in three cases.

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Non-tuberculous mycobacteria, usually harmless commensals, occasionally produce disease or latent infection in children, most commonly cervical lymphadenopathy. The differential diagnosis includes bacterial abscess, tuberculosis, and malignancy. The dilemma for clinicians is to distinguish tuberculous from non-tuberculous mycobacterial infection, as treatment differs.

Patients and methods

Seventeen children with non-tuberculous mycobacterial lymphadenopathy seen in the Newcastle area between 1989 and 1993, were reviewed. Fifteen were identified from culture reports from the Regional Tuberculosis Laboratory, two from the presence of acid fast bacilli on histology together with differential skin testing.

Results

There were 12 girls and five boys, aged 6 months to 8·5 years (mean 3·2 years); all were white. Fifteen had no systemic upset and two experienced lethargy and anorexia. Submandibular nodes were involved in 13, cervical in two, and preauricular in two. *Mycobacterium avium-intracellulare* was cultured from 13, *M malmoense* from one, and *M chelonei* from one.

A chest radiograph was normal in the 15 who had radiography performed. Fourteen were tuberculin tested, of whom none had received a previous BCG vaccination. In only seven receiving a Mantoux test (10 U tuberculin) was the area of induration documented. Two gave a response greater than 5×5 mm, considered positive. These two were among five tested against a panel of atypical mycobacterial skin test reagents (research reagents from Dr J Stanford, University College London, positive where induration greater than 2 mm) as well as Mantoux tests. Four of these five children had *M avium-intracellulare* lymphadenopathy (table 1).

Eleven nodes were incised and drained, five were excised, and one spontaneously discharged. The incised and excised groups were not significantly different with respect to age, sex, disease duration, size or inflammation of node, site, or organism.

There was complete healing within 1–3 months in all five cases where the nodes were totally excised (irrespective of drug treatment), but in only one of the 11 incised. The remaining non-excised nodes became indolent, taking between five and 18 months to heal.

No drug treatment was started until after either histology or culture result had been received. Ten were given antimicrobial agents; seven antituberculous chemotherapy, and three azithromycin and ciprofloxacin, with or without septrin. The antituberculous regimens varied (table 2).

All 15 isolates were resistant to rifampicin, isoniazid, ethambutol, pyrazinamide, and streptomycin. Of two tested against clarithromycin one was sensitive, and one borderline sensitive, and both were resistant to ciprofloxacin. One tested against azithromycin had borderline sensitivity. Five children were continued on antituberculous drugs even after sensitivity testing showed resistance to all the drugs being given.

Twelve nodes were not excised and four of these children received no drugs: one healed well, one slowly, and two required further excision. Five received standard antituberculous treatment and three a macrolide, ciprofloxacin combination. No side effects were noted from any drugs. Although those receiving macrolide treatment started with large indurated discharging scars, these healed slowly, but satisfactorily, while the two with similar lesions treated with standard antituber-

Table 1 Skin tests

	Positive	*Negative*	*Total*
Mantoux test	2	5	7
M avium	5	0	5
M intracellulare	5	0	5
M malmoense	4	1	5
M scrofulaceum	2	2	4
M vaccae	1	0	1

Table 2 Drug regimens used (duration (months) in parentheses)

	No of children
Rifampicin, isoniazid (4)	1
Rifampicin, isoniazid (9), pyrazinamide (3)	3
Rifampicin, isoniazid, pyrazinamide (9)	1
Rifampicin, isoniazid, pyridoxine (6), pyrazinamide (5)	1
Rifampicin, isoniazid (12), pyrazinamide (3), ethambutol (9)	1
Azithromycin 10 mg/kg, ciprofloxacin 15 mg/kg (5) (clarithromycin 10 mg/kg refused by patient)	1
Azithromycin 10 mg/kg, ciprofloxacin 12·5 mg/kg, co-trimoxazole 48 mg/kg (6)	1
Azithromycin 10 mg/kg, ciprofloxacin 12·5 mg/kg (5)	1

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culous chemotherapy both required further surgical excision. The remaining three receiving antituberculous treatment had less severe induration initially and had healed satisfactorily by one year.

Discussion

Our series reaffirms the excellent outcome when the node is excised.[1 2] Unfortunately incision and drainage remains the most common surgical intervention; this increases the risk of sinus formation and discharge, producing scarring and a poor cosmetic outcome.

Early diagnosis from recognition of the clinical features with or without differential skin testing might ensure node excision. Culture of fine needle aspirates is of little help as later excision may be made more difficult. Differential skin testing with atypical mycobacteria purified protein derivative has been investigated[3]; we suggest this is useful, although there can be cross reactivity between mycobacteria, sensitivity and specificity are not defined, and the reagents are not commercially available at the moment. All those tested in this study had positive results, although two also gave positive Mantoux responses. Further work is needed to see if they are indeed useful in diagnosis.

Treatment remains a problem for nodes which are difficult to excise; standard antituberculous drugs have little effect on non-tuberculous mycobacteria, which are usually highly resistant, and so should no longer be prescribed.[1 2]

Studies on bacteraemia caused by non-tuberculous mycobacteria in patients with AIDS[4] and in vitro studies suggest azithromycin and clarithromycin may be beneficial.[5] Although not licensed for this indication in children, the safety profiles and side effects of the new macrolides and quinolones make them acceptable for use in non-tuberculous mycobacterial lymphadenopathy, and individual clinicians are using them.[6] In our small series we gained an impression that they enhanced resolution and healing.

A larger, multicentre study, is needed to see whether these new regimens are truly effective both as a rescue treatment postoperatively and in treating disease not amenable to surgery. Until all non-tuberculous mycobacterial nodes are excised the search for effective drug treatment continues.

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