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Non-tuberculous mycobacterial infections presenting as salivary gland masses in children: investigation and conservative management

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Abstract

Non-tuberculous mycobacterial (NTM) infections in children commonly present as cervicofacial masses. The importance of early diagnosis is in the exclusion of infection requiring treatment, particularly tuberculosis and the rare case of malignancy. Five children with NTM presenting with salivary gland masses illustrate the value of skin testing with new tuberculins and the place of fine-needle aspiration cytology in the investigation of these infections.

Four children who were skin tested reacted specifically to one of the new tuberculins, two indicating infection with *Mycobacterium malmoense*, confirmed by culture, the others responding to tuberculins from *M. scrofulaceum* and *M. avium-intracellulare*, neither having a positive culture. The one case not skin tested produced *M. avium-intracellulare* on culture.

All five patients were managed conservatively. The place for conservative management when the facial nerve is at risk and extensive skin excision is indicated are discussed.

Key words: Mycobacterium, atypical; Salivary gland; Biopsy, needle; Skin tests; Child

Introduction

Non-tuberculous mycobacteria (NTM) are increasing in importance with the decline in the incidence of tuberculous (TB) infections. The most common presentation of NTM in children is a cervicofacial mass (Del Becarro *et al.*, 1989). This typically has the characteristics of a 'cold abscess'. Although acute bacterial or viral infections are usually distinguishable, the features are not diagnostic. The importance of rapid confirmation of NTM is in the exclusion of TB and rare malignancy, both of which require prompt treatment.

The availability of new tuberculins from NTM for skin testing and increasing experience with fine-needle aspiration (FNA) cytology has improved diagnostic ability. The place of these investigations in five children presenting with masses in the region of the major salivary glands is evaluated and the indications for conservative management are discussed.

Patients and methods

Five children presenting to the ENT Department with masses in the region of the parotid or submandibular gland over an 18-month period between 1991 and 1993 were studied. All the children were examined, their history included any contacts with tuberculosis, and initial investigation undertaken included full blood count and chest X-ray

All five patients then underwent examination under general anaesthesia. FNA cytology was undertaken unless incipient or actual skin breakdown was observed when an incisional technique was used. The material obtained was examined histologically as well as microbiologically, for fungi and mycobacteria.

The advantage of the anaesthetic was taken, in four of these children, to undertake skin testing using both tuberculin in 1 in 10 000 and new tuberculins from *Mycobacterium avium*, *M. avium-intracellulare* (*MAI*), *M. malmoense* (*M.mal.*) and *M. scrofulaceum* (*M. scrof.*). These latter four preparations were obtained from Dr Stanford at the University College of London Medical School.

The procedure followed was to inject 0.1 ml of each solution into the volar aspect of either forearm ensuring a distance of at least 10 cm between each site which was marked and labelled (Figure 1). Reading the response took place after 72 hours. Two diameters of the resultant induration were measured; a positive response being taken as 2 mm or greater.

Following confirmation of an NTM infection all these patients were managed conservatively. Reg-

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FIG. 1
Forearm skin testing sites.

ular observation of the mass was maintained and assessment of the overlying skin changes included a photographic record (Figures 2-5).

Case reports

One male and four female children aged between three and six years old presenting with masses in the region of the parotid or the submandibular gland were studied.

Case 1

A three-year-old presented with three masses of 1 to 2 cm diameter in the left pre-auricular and submandibular areas. Cytological examination of FNA material revealed no specific features but acid-fast bacilli (AFB) were seen and culture identified *M. avium-intracellulare* as the organism. The masses continued to progress over three months but wound breakdown did not occur. After 18 months the masses had resolved leaving raised irregular scarring in the pre-auricular and submandibular regions.

Case 2

A three-year-old female presented with a 2 cm mass in the left parotid region. Ultrasound demonstrated the mass to be part cystic and present within the substance of the salivary gland. FNA produced 3 ml of pus, microscopical examination of which demonstrated cells compatible with the presence of necrotizing granulomata in a lymph node. Skin testing was attempted without general anaesthesia but equivocal results were obtained probably due to a failure to inject the full 0.1 ml intradermally. A subsequent repeat biopsy through an area of skin breakdown produced necrotic cells only. Microbiological examination failed to demonstrate AFB. Repeat skin testing on the second occasion produced a positive result for *M. scrofulaceum*. After 27 months she had a small hypopigmented patch overlying the area of skin involvement.

Case 3

A four-year-old female presented with a right submandibular mass progressing over two months to 2 cm diameter despite one course of broad spectrum antibiotics. Ultrasound confirmed the mass to be within the substance of the submandibular gland. FNA for cytology and culture were not diagnostic. One month later a biopsy obtained from a skin dehiscence revealed chronic inflammatory cells but no organisms were identified. Skin testing at this stage produced a positive result for *M. avium-intracellulare*. A short flat nonlinear scar remained after 21 months follow-up.

Case 4

A three-year-old female presented with a three-week history of a right submandibular mass associated with overlying erythema. FNA was undertaken through an area of incipient skin dehiscence. Skin testing at this time produced a positive response to *M. malmoense*. Subsequent culture results supported the result with isolation of *M. malmoense*. After 14 months the residual scar remained erythematous and raised.

Case 5

A six-year-old male presented with a two-week history of a 4 cm left submandibular mass. FNA revealed acute inflammatory cells only. Skin testing gave a positive result for *M. malmoense* with an equivocal response to *M. scrofulaceum*. *M. malmoense* was subsequently isolated. After eight months his scar remained erythematous and raised though dry.

All of these children came from a rural area, none had a history of known contact with tuberculosis. No responses to TB tuberculin were obtained.

Discussion

The tubercle bacillus was first identified by Koch (1882) but it was not until the 1950s that reports of human disease due to NTM appeared. Now they are recognized as a significant cause of pulmonary and

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FIG. 2
Case 1 showing parotid and submandibular infection.

nonpulmonary disease and are increasing in importance particularly in the immunocompromised.

In adults pulmonary disease predominates. The most common NTM infection in children is head and neck lymphadenitis, NTM being implicated in 18–34 per cent of cervical node biopsies (Del Beccaro *et al.*, 1989). With the decline in the incidence of TB cervical lymphadenitis, NTM has become increasingly important, now being the most common cause of paediatric mycobacterial neck masses. In the USA only 10 per cent of culture-positive mycobacterial neck masses were due to TB in children as compared with 90 per cent of adults (American Thoracic Society, 1990). There are no published data including both tuberculous and NTM lymphadenitis in children in the UK. However in the North West Region between 1982 and 1987, 14 culture-positive cases of NTM lymphadenitis were collected from children under 15 years of age with no cases of tuberculous lymphadenitis in Caucasian children. The increase in NTM infections has been postulated as being associated with the loss of cross-immunity previously conferred by the BCG vaccination (Hallberg *et al.*, 1980), although not applicable in Britain where pre-school vaccination has never been routinely practised.

NTM are widespread in the environment having been isolated from soil, water and house dust in addition to animals and birds. In occasional patients the portal of entry is apparent including puncture wounds of the skin. In the majority however the exact portal of entry is not defined, the mouth, throat, gingiva, lips and the tonsils having been implicated (Wolinsky, 1979; Wickham, 1986). In salivary gland infection the possibility of retrograde passage of the mycobacteria along the duct exists, thumb sucking being a possible risk factor in children. Two of the children in this series were habitual thumb suckers.

The most common presentation is of a rapidly progressive mass in the one to five years age group, some studies indicating a female preponderance (Del Becarro *et al.*, 1989). The mass is normally unilateral and solitary but may represent matted

FIG. 3
Case 1 after 17 months.

nodes and occurs typically in the upper cervical or pre-auricular region. The skin becomes adherent to the underlying tissues surrounding the mass, increasing in vascularity, but despite this erythema the skin temperature is not raised. These characteristic skin changes, easily recognized when previously seen (Figure 2), may not be present. The infection may progress to fluctuation, thinning of the skin with eventual dehiscence and development of a chronic sinus. The course of the disease is to spontaneous healing with calcification (Saitz, 1981). Progression to systemic dissemination is rare in the nonimmunocompromised but death has been reported (Margileth *et al.*, 1984).

The differential diagnosis is from acute bacterial or viral infection, actinomycosis, tuberculosis and neoplasia as well as specific salivary gland pathology. There may be clinical characteristics which point to a particular pathology; systemic disturbance is rare in NTM infection, tuberculous masses characteristically occur in the supraclavicular or posterior triangle and may have positive chest X-ray findings but none of these clinical findings are specific.

When the mass occurs in the region of the major salivary glands the diagnosis becomes more difficult (O'Connell *et al.*, 1993). Presentation of a child with a salivary mass rapidly increasing in size without the typical appearance of inflammation raises the possibility of malignancy, granulomatous diseases including NTM and TB, as well as the other well

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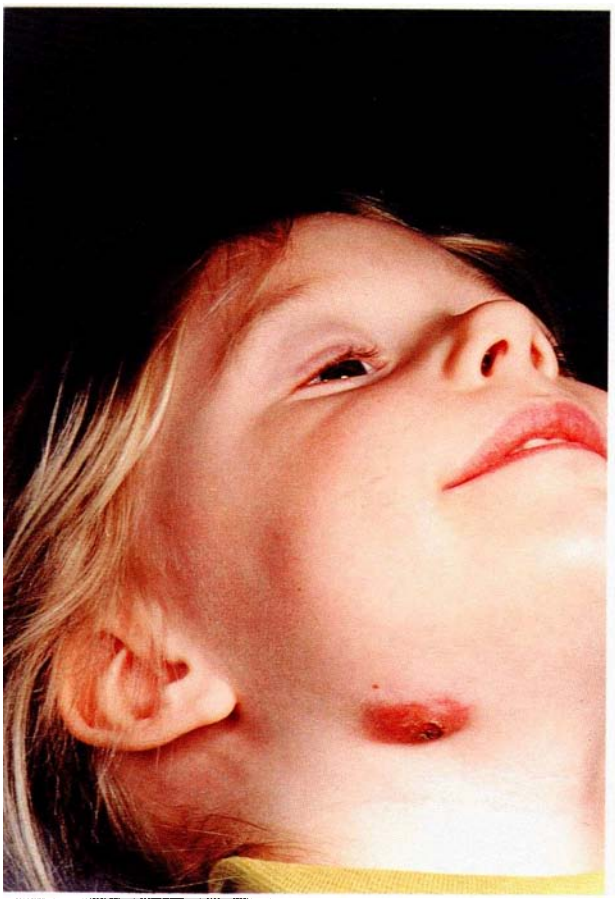

FIG. 4
Case 3 showing submandibular infection.

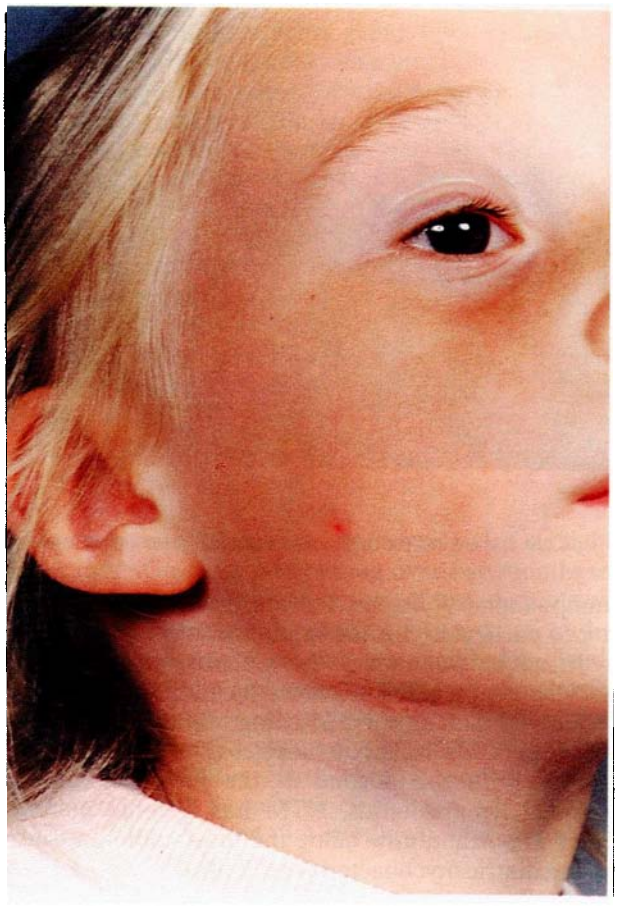

FIG. 5
Case 3 after 21 months.

recognized causes of cervical lymphadenopathy. The clinical features and general investigations including blood count, ESR and chest X-ray are not sufficiently specific to distinguish between neoplasm and chronic infection. They were normal in all these patients.

The use of FNA is a reliable, accurate, inexpensive, rapid means of obtaining a diagnosis (Derias *et al.*, 1992). A specificity of between 95 and 100 per cent, and a sensitivity of between 91 and 95 per cent have been described for neoplasia (Frable and Frable, 1982; Wakely *et al.*, 1988; Cohen *et al.*, 1989; Silverman *et al.*, 1991), and for TB a specificity of 93 per cent and a sensitivity of 77 per cent (Lau *et al.*, 1990). Material can also be obtained for microbiological investigation (Davis *et al.*, 1993).

TABLE I
INVESTIGATION RESULTS

Case no.	1	2	3	4	5
Site	Parotid + submandibular	Parotid	Submandibular	Submandibular	Submandibular
FNA biopsy	FNA	FNA-biopsy	FNA-biopsy	FNA	FNA
Histology	Debris	Granuloma + caseation	Langerhans giant cell	Chronic inflammation	Acute inflammation
AFB micro	Negative	Negative	Negative	Positive	Negative
AFB culture	Positive *MAI*	Negative –	Negative –	Positive *M. mal.*	Positive *M. mal.*
Skin test Response Type	Not done	7 mm *M. scrof.*	10 mm *MAI*	5 mm *M. mal.*	7 mm *M. mal.*
Skin breakdown	No	Yes	Yes	Yes	No
Review (months)	17	27	21	14	8
Scar	Extensive	Minimal	Minimal	Early	Early

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Although FNA and open biopsy have been implicated in skin breakdown and subsequent chronic sinus formation, the former has provided valuable clinical information where there is doubt, particularly with respect to malignancy. In this series open biopsy was only used where skin breakdown had already occurred or was incipient.

Histology for NTM infections is not specific, showing varying stages of granuloma including caseation (Schuit and Powell, 1978; Aleva *et al.*, 1988). This may suggest mycobacterial infection, as in *Case 2*, but is not specific. AFB may be seen on microscopy (49 per cent of the culture negative group) but false positives have been described with organisms other than mycobacteria (Huebner *et al.*, 1992) and there was no differentiation from TB. In only one of our cases were AFB seen in the aspirate. Culture is the most reliable investigation but positive results of less than 50 to 85 per cent for excised nodes are reported, when a diagnosis of NTM was expected (White *et al.*, 1986; Huebner *et al.*, 1992). Even then the result may take weeks or months. Positive cultures were obtained in three out of five of our patients.

The availability of the new tuberculins in addition to tuberculin from TB, has greatly improved diagnostic ability. In this series all of those tested had positive reactions to the specific new tuberculin. Of these, half were negative on culture and only one had AFB detected by microscopical examination. In *Case 2* a repeat skin test was required due to inaccurate intradermal administration of the initial test, although it is recognized that repeat testing may prove necessary (American Thoracic Society, 1990). The accurate intradermal administration of five injections in young children is difficult without general anaesthesia.

Therapy is aimed at preventing prolonged recovery which may include skin dehiscence and sinus formation. NTM particularly those implanted in lymphadenitis, *M. avium-intracellulare* and *M. scrofulaceum*, are relatively resistant to antituberculous therapy. Additionally any *in vitro* drug activity is not realized clinically. In view of the spontaneous recovery and drug resistance of NTM, chemotherapy with its adverse effects is not indicated, in contrast to TB. There is no evidence of person to person transmission obviating the need for contact tracing.

The recommended treatment is for total excision of the diseased tissue including involved skin (American Thoracic Society, 1990). When this includes a salivary gland, as in this series, there is a risk to the facial nerve, particularly when the parotid is involved and total parotidectomy is indicated (Rieu *et al.*, 1990). In all these cases it was considered that the nerve was significantly at risk and that, with the amount of skin involved requiring removal, an at least equally good cosmetic result could be obtained by conservative management with regular review and scar revision after healing if required.

Case 1 has scarring which may require revision but the area requiring excision would have been very extensive, involving the parotid and submandibular glands and overlying skin (Figures 2 and 3). *Cases 2* and *3*, after more than 18 months follow-up have healed with a good cosmetic result (Figure 5). *Cases 4* and *5* , have residual erythematous scars which are still improving. All the wounds are dry.

The absence of any risk of transmission of infection to family and close contacts is fully explained. The presence of a discharging sinus has then been well accepted by parents and GPs when the spontaneous recovery expected in this condition and alternative surgical management are discussed.

Conclusions

A child presenting with a cervicofacial mass having the features of a 'cold abscess' should be considered for early skin testing with the new tuberculins in addition to tuberculin from TB. The clinical findings may suggest NTM as opposed to TB infection but none are specific. Skin test confirmation of an NTM infection excludes both the need for biopsy and antituberculous or other drug therapy in the nonimmunocompromised patient.

When the possibility of malignancy is considered, FNA will provide a rapid, reliable result although the risk of precipitating skin dehiscence must be considered, with the possibility of a chronic sinus (which may occur spontaneously). Additionally FNA provides material for microbiological examination and culture. Incisional biopsy should be avoided with intact skin.

Total excision of the mass has been the recommended treatment but in the presence of extensive skin involvement and risk to the facial nerve conservative management should be considered for the optimal cosmetic result.

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