Cervical mycobacterial infection

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THE pattern of mycobacterial infection has changed in recent years, the incidence of the pulmonary form having decreased, whilst the extra-pulmonary has not shown a similar tendency (Llewelyn and Dorman, 1971; Newcombe, 1971; Hooper, 1972). Whilst laryngeal (Maran and Stewart, 1971) and aural (Palva *et al.*, 1973) tuberculosis are by no means rarities, the most common form of mycobacterial infection encountered in otolaryngological practice presents as a cervical adenitis (Toremalm and Wihl, 1968). Recent publications have indicated that the incidence of the latter may be increasing (Newcombe, 1971; Ord and Matz, 1974; Wong and Jafek, 1974).

Kent (1967) regarded tuberculous cervical lymphadenitis as a local manifestation of a systemic infection, but a striking feature of many reports in the literature is the infrequent occurrence of systemic, and especially pulmonary, involvement (Wilmot *et al.*, 1957; Black and Chapman, 1964; Newcombe, 1971; Ord and Matz, 1974; Wong and Jafek, 1974). It has been recognized for centuries that tuberculous cervical lymphadenitis, or scrofula, had often a benign course, and spontaneous resolution may have accounted for the apparent efficacy of the king's touch. A possible explanation is that at least some of the cases of scrofula may have been due to an unrecognized infection with atypical mycobacteria.

Human tuberculosis is due to infection either with Mycobacterium tuberculosis or M. bovis. It has been known since the turn of the century that other forms of mycobacteria are to be found widely distributed in nature, but these were for a long time regarded as non-pathogenic for humans. Following the introduction of effective anti-tuberculous chemotherapy, it became apparent that forms of mycobacteria other than M. tuberculosis and M. bovis were occasionally recoverable from patients with diseases similar to tuberculosis. These organisms have been termed atypical, or anonymous, mycobacteria, and have been classified according to their bacteriological growth characteristics into the following four groups: group I, photochromogens; group II, scotochromogens; group III, non-photochromogens, and group IV, rapid growers (Runyon, 1959).

The first descriptions of cervical lymphadenitis due to atypical mycobacterial infection appeared in 1956 (Prissick and Masson, 1956; Weed

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et al., 1956). Since then there have been many reports, especially in the paediatric literature (Chapman and Guy, 1959; Davis and Comstock, 1961; Hsu, 1962; Mackellar *et al.*, 1967). A review of the otolaryngological literature has surprisingly produced only one publication on atypical mycobacteria (Olson, 1967).

As the clinical features, management and prognosis of tuberculous and atypical mycobacterial infections of the neck differ in several respects, it is important that also otolaryngologists be aware of this possible differential diagnosis.

Material

In the three-year period 1971 to 1973 we have seen seven patients with cervical mycobacterial infections. The relevant clinical features of these cases are summarized in Table I. It will be seen that only case 7 had positive chest X-rays. This patient was also febrile, the E.S.R. was 101, and she had pronounced constitutional symptoms. All other patients presented with cervical lymphadenopathy as the sole complaint. Both case 6 and case 7 had a previous history of tuberculosis, cervical lymphadenopathy in the former, and renal tuberculosis in the latter.

All patients were admitted to hospital with the diagnosis of a lump in the neck, and were subjected to a routine battery of investigations. Prior to our becoming aware of the existence of atypical mycobacteria, incision of the neck abscesses was performed in order to obtain material for bacteriological examination. Routine aerobic and anaerobic culture studies were, however, negative. Histological examination of biopsy material revealed chronic granulation tissue with giant cells and central necrosis.

Cutaneous testing with tuberculin was performed routinely, whereas testing with atypical mycobacterial antigens was performed retrospectively in most cases. Skin testing with antigens representative of the four groups of atypical mycobacteria were performed, the antigens being supplied by the Norwegian Veterinary Institute. A summary of the investigations, treatment and clinical course is shown in Table II.

Mycobacterium tuberculosis was successfully cultured from cases 6 and 7, which is conclusive evidence for a tuberculous aetiology. Bacteriological investigations were negative for cases 1 to 5, although acid-fast bacilli were noted on direct microscopic examination of infected tissue from one of these patients (case 3). Skin testing in cases 3, 4 and 5 produced larger reactions to the atypical than to the tuberculous antigen. In case 1, the skin reactions to tuberculin and group III antigen were similar, but the patient had recently received BCG vaccination, and this could account for the response to tuberculin. In case 2, the response to group III antigen was slightly less than to tuberculin, but a period of two years had elapsed between the time of infection and the date for cutaneous testing.

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TABLE I.

RELEVANT CLINICAL FEATURES OF THE SEVEN PATIENTS WITH CERVICAL MYCOBACTERIAL INFECTION

Case	Sex	Age in years	Duration in weeks symptoms	Constitutional	Chest X-ray	Lymphadenopathy
1	Female	12	16	0	Negative	Mandibular
2	Female	1½	2	0	Negative	Mandibular and submandibular
3	Female	6	3	0	Negative	Submandibular
4	Female	3½	3	0	Negative	Submandibular
5	Female	63	3	0	Negative	Submandibular
6	Female	45	16	0	Negative	Submental
7	Female	73	6	+	Positive	Supraclavicular

TABLE II.

RESULTS OF INVESTIGATION AND TREATMENT OF THE SEVEN PATIENTS WITH CERVICAL MYCOBACTERIAL INFECTION

Case	Direct microscopy acid-fast bacilli	Culture	Skin tests erythema/induration in mm.		Treatment		Course
			Tuberculin	Atypical antigen	Chemotherapy	Surgical	
1	0	0	6/4	6/4 Group III	0	Incision	Prolonged drainage
2	0	0	5/2	3/2 Group III	+	Incision	Prolonged drainage
3	+	0	4/0	7/4 Group III	+	Incision	Prolonged drainage
4	0	0	3/0	6/4 Group III	0	Extirpation	Rapid healing
5	0	0	14/10	18/12 Group I	+	Extirpation	Rapid healing
6	0	M. tuberc.	8/7	6/5 Group I	+	Extirpation	Slow healing
7	+	M. tuberc.	5/4	0	+	0	Slow healing

Extirpation of the diseased nodes was performed in cases 4 and 5 and resulted in rapid healing, whereas the three earliest cases were incised and had prolonged suppuration and drainage. Both of the patients with M. tuberculosis infection (cases 6 and 7) had a protracted clinical course.

Discussion

All cases of cervical lymphadenitis due to atypical mycobacterial infection had unilateral involvement of the submandibular or lower facial areas. This has previously been reported as the characteristic localization and presentation of this form of the disease (Jones and Campbell, 1962; Black and Chapman, 1964; Mackellar *et al.*, 1967). In a review of 63 cases of cervical mycobacterial infection, Wong and Jafek (1974) noted that the incidence of concomitant pulmonary involvement was higher in patients with supraclavicular than in those with submandibular lymphadenopathy. It may be noted that cutaneous testing for atypical mycobacteria was not performed in the latter study. All of our cases with atypical mycobacterial infection had negative chest X-rays, the previous medical history was non-contributory, and there was no history of contact with known cases of tuberculosis. On the other hand, the sole case of supraclavicular lymphadenopathy had previously been treated for a renal tuberculosis, and the chest film revealed evidence of prior pulmonary involvement.

The age of the patient is also an important diagnostic feature. All authors agree that atypical mycobacterial cervical adenitis is predominantly a disease of childhood, although there is some dissent as to the precise age group affected (Hsu, 1962; Kendig, 1967; Chapman, 1967). On the basis of a series of thirty cases, Black and Chapman (1964) concluded that atypical mycobacterial infection was not seen under 1 year of age, and that 60 per cent of cases occurred between 20 and 24 months. However, Jones and Campbell (1962) noted that anonymous mycobacterial infection tended to occur in slightly older children, the 7 to 13-year age group, whilst tuberculosis predominantly affected younger children.

In the present series, cases 1 to 4 cover the characteristic age group for atypical mycobacterial infection, i.e. 1 to 12 years. Our case No. 5, aged 63 years, is not representative in this respect, although the results of cutaneous testing are suggestive of infection with group I bacteria. This would appear to be the fourth case of cervical infection due to atypical mycobacteria in an adult (Wade *et al.*, 1969; Hooper, 1972).

The almost exclusive occurrence of this disease in young children, and the preferential localization high in the neck, have been adduced as evidence for incriminating the tonsils as the portal of infection (Prissick and Masson, 1956; Jones and Campbell, 1962; Kendig, 1967). Infection

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has also been causally connected with eruption of the deciduous molars (Chapman and Guy, 1959).

In a retrospective study of eleven patients with 'tuberculous' cervical adenitis, Girard (1972) found that three of four children had positive cutaneous tests for atypical mycobacteria, whilst the fourth was considered suggestive of an atypical infection. Culture was negative in all four children, but produced growth of M. tuberculosis in the majority of the seven adults. A similar trend was reported by Mackellar *et al.* (1967), who found positive cutaneous tests for atypical mycobacteria in twenty-eight of thirty children previously diagnosed as having tuberculous lymphadenitis. Exposure to atypical mycobacteria is probably common. Kendig (1967) reported that only 2·7 per cent of children in the age group 4 to 16 years reacted to tuberculin, whilst 10 per cent had positive skin tests to the atypical mycobacteria. Hsu (1962) has also reported that positive cutaneous responses to group III atypical mycobacteria were five times more common than to ordinary tuberculin. It is, therefore, not improbable that many cases of atypical mycobacterial infection have gone unrecognized, and been labelled as tuberculous lymphadenitis in the past. This applies especially to series which have contained large numbers of children, where culture of infected tissue has been negative, and the clinical course suspiciously benign.

Diagnosis is more a problem of awareness of the condition. Unilateral, upper cervical lymphadenitis in a child, without constitutional disturbances (Wolinsky, 1963), which, however, proceeds rapidly to formation of abscess or sinus (Salyer *et al.*, 1968), is characteristic of the disease. The lymphadenitis of M. tuberculosis infection is generally bilateral and more slowly progressive, with abscess formation occurring at a later stage (Chapman and Guy, 1959; Jones and Campbell, 1962; Kendig, 1967; Mackellar *et al.*, 1967). However, Black and Chapman (1964) were of the opinion that the clinical course and features did not permit differentiation between tuberculous and atypical mycobacterial lymphadenitis. Biopsy is not reliable in differential diagnosis, since Reid and Wolinsky (1969) have shown that the histological features of atypical mycobacterial infection are not sufficiently characteristic to allow differentiation from other conditions which may produce caseous necrosis of lymph nodes. Included in the list of possible differential diagnoses, in addition to tuberculosis, are tularemia, mycoses, lymphogranuloma venereum, brucellosis and cat-scratch disease (Hooper, 1972).

Diagnosis is finally established by cutaneous testing and bacteriological studies. Testing with tuberculin may give a negative or weakly positive reaction (Chapman and Guy, 1959; Davis and Comstock, 1961). Atypical mycobacteria probably account for the majority of cases previously labelled as tuberculin negative tuberculosis (Schachter, 1972). Clinical use has earlier been made of the double Mantoux test (Masters

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and Smyth, 1965), in which skin tests were performed using PPD-S, a tuberculin antigen, and PPD-B, which was derived from a group III, Battey strain. More recently antigens have become available which can be used to differentiate all four groups of atypical mycobacteria from one another. Kendig (1967) recommended that a response not greater than 5–9 mm. with tuberculin should be considered suspicious, and an indication for performing skin tests with atypical mycobacterial antigens. A greater response to the latter would indicate the correct diagnosis (Wolinsky, 1963). Skin tests, may however, be inconclusive, and diagnosis will then depend on culturing and identifying the organisms. Attempts to culture atypical mycobacteria from pus are usually unsuccessful, and the most suitable material for bacteriological studies is excised lymph nodes.

It is generally accepted that the most successful form of treatment is surgical excision of affected tissue, which at the same time provides the best opportunity for bacteriological identification of the infecting strain (Hsu, 1962; Wolinsky, 1963; Mackellar *et al.*, 1967; Llewelyn and Dorman, 1971). Other authors have recommended combined surgery and antituberculosis chemotherapy (Davis and Comstock, 1961; Chapman, 1967; Olson, 1967). Mazzei and Fonkalsrud (1968) reported that initial chemotherapy was unsuccessful, and that cure did not result until surgical excision was performed. Incision and drainage of abscesses is not advisable since permanent sinuses will result (Davis and Comstock, 1961; Hsu, 1962; Mackellar *et al.*, 1967). Our experiences with incision have also been unfortunate, whereas excision of all diseased tissue, performed as a primary procedure, has resulted in clinical cure. All authors agree that atypical mycobacterial lymphadenitis does not require isolation since infection does not occur by human transmission. Isolation and treatment in sanatoria is therefore contraindicated and to be deprecated (Kendig, 1967; Llewelyn and Dorman, 1971).

An early awakening of clinical suspicion, followed by surgical excision of affected lymph nodes prior to formation of abscesses and sinuses is necessary. A generous portion of the excised lymph nodes should be sent to the microbiologist for culture studies, and skin tests should be performed, with antigens against both M. tuberculosis and the atypical mycobacteria.

Summary

Cervical lymphadenitis is the commonest form of mycobacterial infection encountered in otolaryngological practice. A series of seven patients is presented, two with Mycobacterium tuberculosis infection, and five with adenitis due to atypical mycobacteria. The clinical features, diagnosis and treatment of the latter are discussed.

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