**Case report**

**Knee arthropathy secondary to Mycobacterium scrofulaceum**

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Atypical mycobacteria have been described as long as 36 years ago, but it has only been in the last 10 years that the ability of these organisms to cause disease in man has been recognized. The most common pathological processes with which the atypical mycobacteria are associated occur in the lungs and in the cervical lymph nodes. More rare is joint pathology. We describe here a case of knee arthritis with culture of *Mycobacterium scrofulaceum* from the synovial fluid.

**Case Report**

A 47-year-old nun who had had no significant medical or surgical history up to August, 1970, then noted a tender swelling on both sides of her neck near the angle of the jaw. No definite reason was found for this lymphadenopathy and the swellings subsided spontaneously. In September, 1970, both knees became painful, stiff, and swollen. The arthropathy continued *in status quo* up to June, 1971, when we first saw her.

**Physical examination**

She was a somewhat obese but healthy female in no distress. Nothing abnormal was noted except for bilateral knee joint effusions with mild to moderate limitation of movement and minimal erythema of the overlying skin. All other joints were normal. There was no lymphadenopathy and auscultation of the chest was normal. There was no history of trauma to or injections into either knee. The family history for tuberculosis and arthritis was negative. There was no previous contact with cattle.

**Laboratory investigations**

Haemoglobin, 11.5 g. per cent; haematocrit, 36 per cent; mean corpuscular haemoglobin concentration, 32 per cent; white cell count, 6,300; neutrophils 74 per cent; lymphocytes 24 per cent; monocytes 2 per cent; erythrocyte sedimentation rate, 68 mm/1st hr.; uric acid 5.7 mg. per cent; R.A. factor (Latex), negative; sheep cell agglutination test, negative; tests for *Brucella abortus*, negative; L.E. factor, negative; sputum and urine Ziehl Nielson staining, negative.

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**Radiology**

Chest, normal; knees showed no joint destruction or narrowing.

Both knee joints were aspirated and fluid from the left knee was sent for culture and Ziehl Nielson staining.

**Treatment**

The patient was given indomethacin 25 mg three times a day. This had no effect and was changed after 4 weeks to phenylbutazone 100 mg four times a day.

**Synovial fluid**

This was yellow-green in colour, turbid, and of low viscosity. Mucin clot formation was poor and no crystals were seen. White cell count 16,300/cm. Ziehl Nielson staining showed acid-fast bacilli. Lowenstein-Jenest culture grew atypical chromogenic mycobacteria identified as *M. scrofulaceum*. These were shown to be at least sixteen times more resistant to streptomycin and isonicotinic acid hydrazide (INAH) and at least four times more resistant to para-amino salicylic acid (PAS) than the standard strain. A guinea-pig inoculated with the synovial fluid showed no evidence of infection *post mortem*.

**Course**

When Z-N staining showed atypical mycobacteria the patient was given streptomycin 500 mg. intramuscularly twice daily, sodium aminosalicylate 6 gr. twice daily, and isoniazid 150 mg twice daily, along with phenylbutazone. The *in vitro* sensitivity report showed resistance to these three antibiotics, and they were stopped after 11 days' therapy. At this time there were no signs or symptoms of improvement.

Therapy was started with kanamycin 500 mg twice daily for 14 days, and then 1 gr. every second day plus doxycycline 100 mg daily. This combination of drugs was used for three reasons:

1. There is at present no definitely recommended scheme for treatment of this type of infection in a joint, and it was felt that the patient's condition did not warrant the use of three or more second-line anti-tuberculous drugs at the same time because of the possible toxic effects of this multiple-drug therapy.
2. It has been shown by Manten and Wisse (1961) that kanamycin plus a tetracycline is often synergic.
(3) Tetracyclines have previously been recommended in combination with other drugs for the treatment of tuberculous infections (Miller, Sands, Gregory, Hightower, Weiser, and Tempel, 1954; Stewart, Turnbull, and Crofton, 1954; Goth, 1964).

A second culture of synovial fluid aspirated from the left knee at the start of therapy with kanamycin plus doxycycline confirmed the presence of _Mycobacterium scrofulaceum_.

These drugs were continued for 4 weeks, and during this time there was a moderate improvement, both symptomatically and clinically. However, after 4 weeks the patient developed symptoms of VIII nerve deafness, and the kanamycin and doxycycline were stopped. The blood urea at this time was 54 mg. per cent. Urine analysis was normal. Clinical examination was normal except for mild bilateral knee joint effusions, the patient complaining of mild to moderate pain plus stiffness. The patient was now given rifampicin 600 mg. mane plus ethambutol 400 mg. twice daily. Synovial fluid staining was negative for mycobacteria and culture confirmed the absence of mycobacteria at this stage. Rifampicin plus ethambutol were continued at the above dosage with the development of no side-effects. After 8 weeks the patient had neither signs nor symptoms of arthropathy. We have continued therapy with rifampicin and ethambutol and at the present time, 14 weeks after commencing these drugs, the patient remains asymptomatic.

Discussion

The 'atypical', 'anonymous', or 'unclassified' mycobacteria, thus called to distinguish them from _Mycobacterium tuberculosis_, _Mycobacterium leprae_, and _Mycobacterium lepraemurium_, are ubiquitous and generally saprophytic. They have been found in water, milk, butter, fruit, vegetables, grass, dust, and faeces (Elston, Parrillo, Meiberger, and Kleitsch, 1964). They are also able to cause chronic disease in man. They have little or no virulence when inoculated into the guinea-pig.

A classification of the atypical mycobacteria was proposed in Runyon (1958):

**GROUP I** _Mycobacterium kansasii_ and _Mycobacterium marinum_. These are also termed photochromogens because of the bright yellow to orange colour developed after 6 to 24 hours' exposure of young, actively growing colonies to light. This group is chiefly associated with pulmonary disease in man. In a large series of patients suspected of having tuberculosis, up to 18 per cent. had _Mycobacterium kansasii_ present in their sputum (Youmans, 1963).

**GROUP II** _Mycobacterium scrofulaceum_. Members of this group are also termed scotochromogens because of the development of a yellow-orange pigment when colonies are grown _ab initio_ in the absence of light. This group is associated with cervical adenitis.

**GROUP III** These are termed non-photochromogens because they do not develop a yellow pigment on exposure to light. They may cause cervical adenitis and examples of widespread and sometimes lethal disease to this group have been reported by Lester (1966).

**GROUP IV** These are also termed rapid growers as colonies are seen after 2 to 3 days' growth at 20–25°C.

There is no constant human source of atypical mycobacteria. They have been grown chiefly from sputum, but have also been isolated from skin (Maberry, Mullins, and Stone, 1965), lymph nodes, tonsils (Merckx, Soule, and Karlson, 1964), nasal secretions, and urine (Tinne, 1965). Four patients have died with pancytopenia associated with widespread infection by _Mycobacterium kansasii_ (Kilbridge, Gonnella, and Bolan, 1967; Zamorano and Tomssett, 1968). Twelve cases of infection of tendon sheaths, joints, and bursae have been reported by Kelly, Weed, and Lipscomb (1963). Destructive polyarthritis due to photochromogenic mycobacteria has been described by Klinenberg, Grimley, and Seegmiller (1965) and at various stages of the disease this closely simulated gout and rheumatoid arthritis. _Mycobacterium kansasii_ was grown from synovial tissue obtained from a knee joint affected by arthritis (Godwin, 1965). In most of the reported cases of arthritis associated with atypical mycobacteria photochromogens have been incriminated. In one of the cases reported by Merckx, Karlson, and Carr (1963), scotochromogens were isolated, and in one case both scotochromogens and photochromogens were implicated. No case of arthritis definitely caused by _Mycobacterium scrofulaceum_ has previously been reported as far as we can ascertain.

The origin of joint infection by atypical mycobacteria is uncertain. Three of Kelly's cases (Kelly and others, 1963) had a history of injection into or laceration of the affected joint. Milk has been incriminated (Chapman, Bernard, and Speight, 1965), as has minor trauma (Klinenberg and others 1965). Our patient gave no history of trauma or injection into the knees, and there were no signs of even minor laceration. It is thus likely that the infection was blood-borne. A focus of infection could have been the previously enlarged cervical lymph nodes.

Drug treatment of extrapulmonary disease due to atypical mycobacteria is not well documented because of the paucity of cases so far reported. It was previously stated that these organisms are resistant to the standard first-line anti-tuberculosis drugs, viz. streptomycin, PAS, and INAH. This is now disputed and there are reports of _Mycobacterium kansasii_ responding to drug treatment (Klinenberg and others, 1965; Godwin, 1965). In the case reported here there was no clinical response to these drugs, and sensitivity tests _in vitro_ showed the organism to be resistant to these drugs. When this situation occurs it is difficult to decide what drugs to use. Some workers recommend...
the use of up to five different anti-tuberculous drugs. In other cases surgery to the affected joint has been necessary (Kelly and others, 1963).

In our case it was not felt, as previously stated, that mycin plus doxycycline was the combination with a number of toxic drugs in combination. It is difficult to ascertain exactly which drugs were successful in this patient. It seems likely that kanamycin plus doxycycline was the combination with beneficial effect.

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