Indolent Non-caseating Mycobacterial Tuberculosis

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At the present time, tuberculosis affecting the skin or the small bones of the hands and feet is uncommon in Great Britain. Out of 2500 cases of tuberculosis in children documented by Miller, Seal, and Taylor (1963), 34 had a primary skin infection and 28 had a haematogenous skin infection. Of these 28, only 6 were of the verrucous type. In their entire series they saw only 2 cases of tuberculosis of the phalanges, and these presented as painless, spindle-shaped swelling of the affected phalanx with underlying radiologically detectable bone changes. The child here described embodied clinical features of both these rare types, and the case raises some interesting questions.

Case Report

A 3-year-old girl presented with recurrent boils, mainly situated on arms and legs, which had appeared over the previous 9 months (Fig. 1a, 2). Three in particular kept breaking down and persisting. She had also experienced pain affecting the right ankle and terminal interphalangeal joint of the left index finger. These joints were swollen and there had also been swelling on her left big toe and proximal phalanx of the left middle finger. The child had been a little apathetic but there had been no weight loss. She had received courses of intramuscular and oral penicillin and of oral tetracycline without effect.

Clinical examination on admission revealed areas of inflammation on the right buttock, right thigh, and behind the right knee. There was spindling of the left middle finger. There was no undue lymphadenopathy and no splenomegaly.

Blood count normal. ESR 35 mm. ASO titre 400 units. Total plasma proteins 8.3, albumin 5.5, globulin 2.8 g./100 ml. RA latex test negative. Urinalysis normal. Heaf tuberculin test negative. X-ray film of left hand normal.

Swabs of the lesions grew both a staphylococcus and a β -haemolytic streptococcus. Because of the latter she was given a course of penicillin. It was thought initially that these were staphylococcal lesions, perhaps with a superadded secondary infection, and some corroboration for this view appeared in the form of a

fresh lesion on her left forearm which grew a coagulase positive *Staphylococcus aureus*. Treatment was started with cloxacillin and this lesion cleared. Moreover, the ESR fell to 10 mm. and there was slight improvement in the chronic skin lesions. Skin biopsy taken during this admission showed an infected keratotic papilloma reflecting simple chronic inflammation. No fungus appearances were present.

The improvement in the skin lesions was not maintained and she had further joint pains. Seven weeks after her first admission, both big toes were found to be swollen and painful. Further x-ray pictures now showed cystic medullary changes in the proximal phalanges of both great toes and the middle phalanx of the left index finger, with slight widening of the bones (Fig. 3). The chest x-ray film was normal.

Serum Ca^{++} was estimated three times and the results were: 10.6, 11.5, and 10.3 mg./100 ml.; serum inorganic phosphorus 4.2/100 ml.; alkaline phosphatase 20 KA units/100 ml. A chronic migratory staphylococcal osteomyelitis was thought to be the most likely explanation and about this time a blood culture was reported positive for a coagulase positive staphylococcus after prolonged incubation, though the drug sensitivities were different from those of the organism obtained from direct swabbing of the lesions. A Mantoux 100 TU was negative. A second and deeper skin biopsy was taken and portions were sent for histology and bacteriology. Sections showed inflammatory infiltrate of the dermis and deep to this multiple foci of epithelioid cells and multinucleate giant cells. No fungi or tubercle bacilli were seen in the initial sections. Bacteriological cultures were set up.

Six weeks later, the Mantoux 100 TU had become strongly positive and a chest x-ray film showed two small opacities in the left upper zone. Fresh sections cut from the second biopsy block were examined and acid-alcohol-fast bacilli were found. Gastric washings, CSF, and urine were cultured for *M. tuberculosis* but the organism was not found. The optic fundi were examined for miliary tubercles but these were not present.

These findings were regarded as being sufficiently significant to start antituberculous therapy with PAS and isoniazid. There was no history of contact and none was subsequently revealed. However, the child had played amongst turkeys that dwelt nearby, and there had been some mortality amongst the chicks, though apparently no more than is normally expected by the rearers.

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FIG. 1.—Skin lesions (a) before, and (b) 4 months after, starting antituberculous chemotherapy.

The possibility of avian tuberculosis was therefore entertained, and differential tuberculin testing was carried out. The reaction to the human antigen was notably brisker, viz. 17×18 with 5 mm. induration, as compared with the avian reaction 7×7 with 2 mm. induration. The biopsy specimen eventually grew tubercle bacilli and these were subsequently typed as human strain, sensitive to PAS, INAH, and streptomycin, the degree of sensitivity being similar to that of the H 37 Rv control strain.

One month after starting chemotherapy, the bone lesions were radiologically unchanged, and the ESR had remained at 10 mm./hr. Two weeks later she had a febrile illness and her ESR rose to 34 mm., but this episode settled spontaneously. However, more chest x-ray films were taken at this time and it was noted that the chest lesion had begun to calcify.

After a further $2\frac{1}{2}$ months, the bone lesions showed marked improvement on x-ray picture, and the skin lesions had begun to heal (Fig. 1b).

FIG. 2.—Close-up of tubercle.

Fifteen months after her first attendance her hands were radiologically normal, and the foot lesions had undergone great improvement. The complex in the left upper zone became clearly calcified; the hands were normal, though some cystic changes in the bones of the feet persisted. The skin lesions were still visible, but had undergone considerable healing.

FIG. 3.—X-ray film of left index finger, showing the punched-out areas in the middle phalanx.

Discussion

There is not much doubt that this child had tuberculosis. Not only was a human strain tubercle bacillus isolated, but her tuberculin reaction became positive, and, most significant of all, all the pathology regressed on antituberculous therapy. The temporal evolution of the various features of this case poses the question of which lesion is the primary one. Two of the skin lesions are not on exposed sites, and it is difficult to conceive what mechanism would produce three simultaneous primaries in such a distribution. The chest lesion has the appearance of a primary complex, but the skin lesions had been present for a year before the lung lesion became radiologically evident. The possibility of more than

one primary cannot be entirely ruled out; neither can the possibility that the skin lesions were originally of non-tuberculous aetiology and that dissemination to them had occurred from a pulmonary primary complex. This last possibility could explain the apparently anomalous conversion of the tuberculin reaction after 14 months.

Rich (1951) pointed out that a genuine negative tuberculin response was strong evidence against tuberculosis. Hart (1932) estimated this to be so in 98% of cases and Sweany (1947) in 97% of cases. In a series of 107 cases of tuberculosis, Scadding (1956) found 4 non-reactors, all of whom had an indolent infection with the human strain of the tubercle bacillus.

The sarcoid features of this case (the word 'sarcoid' being used as an adjective) are interesting, i.e. the negative tuberculin response at the outset and the radiological changes in the bones. At one stage it would not have been difficult to call this sarcoidosis—the histology, though not specific to sarcoidosis, was sarcoid. This diagnosis was only disproved by the subsequent developments. Sarcoidosis is very uncommon in childhood. In a review of world literature, McGovern and Merritt (1956) found 113 cases under 15 years and of these only 16 were 4 years or younger, the youngest being a 2-month-old boy (Polland, 1931). The bone lesions in the case described here are almost identical to those described in a 2-year-old boy diagnosed as a case of sarcoidosis by Newns and Hardwick (1939). Unfortunately, it has not been possible to trace this patient to find out if there were subsequent developments. Jüngling (1920) described a tuberculous condition which was characterized by onset during childhood, bone lesions in hands and feet, relative absence of symptoms, and no disturbance of function. The bone lesions comprised characteristic cystic spaces and diffuse enlargement of phalanges without periosteum or joint involvement. He called this 'osteitis tuberculosa multiplex cystica' and it ran an insidious benign course. He noted a frequent association with lupus pernio and 'Böeck's sarcoid'. This description accords well with the case described and it is noteworthy that some of Jüngling's cases were Pirquet-negative. He later amended the term 'cystica' to 'cystoides', as the radiolucent bone areas actually contained tuberculous granulation tissue (Jüngling, 1928).

There is a 10–25% association between sarcoidosis and tuberculosis (Siltzbach, 1958) which may take the form of the one condition merging into the other, the two coexisting or the 'aller et retour' phenomenon (Benda, Orinstein, and Morelec, 1956). The

arguments regarding the aetiology of sarcoidosis continue, but the present case seems to lend weight to the view that at least some of these cases have a basis of indolent non-caseating mycobacterial tuberculosis.

Summary

The case is described of a 3-year-old girl with indolent non-caseating mycobacterial tuberculosis from which a human strain of the organism was eventually isolated. The clinical picture fitted well with that of osteitis tuberculosa multiplex cystoides. The possibility of some of these cases being diagnosed as sarcoidosis is mentioned.

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