OSTEOMYELITIS VARIOLOSA

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Modern travel has now brought smallpox within a day's reach of Europe and America. The acute disease should cause little trouble in diagnosis, but manifestations other than the well known rash are often forgotten or indeed unknown. Clearly radiology has no part to play in the diagnosis of acute smallpox, but the radiographic appearance of bone infection by the virus of smallpox is usually typical and diagnostic. It is important to remember that the clinical signs may be slight; there may be little evidence of smallpox and the patient may even be unaware of any such infection. The purpose of this report is to draw attention to the changes found in osteomyelitis variolosa, and to serve as a reminder that a bone infection which fails to respond to treatment occurring in persons who have recently left a country in which smallpox is endemic may not be pyogenic in origin.

The first reference to such a complication was by Bidder in 1873. Until recently the first and only mention of the disease in British literature was that by Neve in 1887. The whole subject was then reviewed in detail by Cockshott and MacGregor in 1958 and 1959. A recent epidemic of smallpox in Nyasaland gave us the opportunity of studying many patients with this condition, and we made a deliberate attempt to assess its frequency and the clinical findings. Usually between 2 and 5 per cent of young children with smallpox will develop osteomyelitis variolosa (Cockshott and MacGregor 1958, Middlemiss 1962). The largest series so far reported comes from Nigeria where thirty-four cases were found during eighteen months from an estimated 2,500 cases of smallpox (Cockshott and MacGregor 1958). In Nyasaland the total number of patients affected with smallpox under the observation of one of us in the Lilongwe district was 400. Of these a total of 176 were radiographed, antero-posterior films of the elbows and forearms and of the lower limbs from the knees downwards being taken. On the evidence of these films eighty-two patients suffered osteomyelitis. In none of them was there any reason to suppose that this was due to a pyogenic organism. The reasons for ascribing the bone infection to the virus were considered fully by Cockshott and MacGregor and may be briefly summarised as follows: 1) The lesions behave like proven virus infections of bone. 2) Elementary bodies are present in the fluid from affected joints which is usually sterile on culture for pyogenic organisms. 3) The clinical course is quite different from that of acute bacterial osteomyelitis. 4) Antibiotics and chemotherapy fail to prevent the development of these bone changes or to influence their course. We would add to this a fifth reason. The radiological distribution and appearance of the bone infection is unlike that of a simple osteomyelitis and is characteristic in smallpox.

CLINICAL FEATURES

Of the eighty-two patients with osteomyelitis the youngest was nine months and the oldest fourteen years. There were slightly more females than males, unlike the series in Nigeria (Cockshott and MacGregor 1958). The ages of the children are shown in Table I. The majority (80 per cent of those with bone infection) were under six years old, but between six and ten years there was a much higher proportion of children affected than in the older groups. In general, this agrees with previous series (Cockshott and MacGregor 1958).

Some details of this outbreak have already been recorded (Sword 1961), but not with reference to osteomyelitis. The incidence in this series is much higher than in any previously reported, eighty-two cases out of 400 patients with smallpox, for which we have no explanation.
to offer. Malnutrition is prevalent in the Lilongwe district and the state of nutrition of smallpox patients was assessed but no correlation between malnutrition and the incidence of smallpox was found; nevertheless the most severe cases of osteomyelitis occurred in association with anaemia and malnutrition. Because of the high incidence of sickle-cell anaemia and its association with salmonella osteitis in Nigeria, Cockshott and MacGregor (1958) looked for sickling of the red cells in their cases, but did not find it. Although sickle-cell disease occurs in Nyasaland (Davidson 1961) it is not so common as in Nigeria. In five of our severely affected cases it was looked for but not found.

Like Cockshott and MacGregor (1958) we could not find a relationship between the severity of the initial smallpox infection and the occurrence or degree of osteomyelitis. Some of the most extensive bone changes occurred in mild smallpox. In one patient admitted to the General Hospital with pneumonia, the typical radiological appearances of the elbow joint led to an enquiry about a rash which was obviously mild and had left few pock marks. The radiological assessment of the whole series was carried out without knowledge of the clinical state of any patient and the great difference between the clinical and radiological findings is an important feature.

The interval between the onset of the rash and the appearance of clinical bone disease was variable: the shortest in our series was five days (Fig. 1) and the longest twenty-eight days, but as reported by Cockshott and MacGregor (1958), the serious nature of the initial illness tends to obscure the first signs of bone infection. The same authors, from a study of the literature, reported the interval to be between ten days and four weeks.

The onset of bone involvement was usually revealed by swelling around the joint, but occasionally it was possible to detect thickening of a bone, particularly of the fibula. Pain was present but not usually severe, and certainly nothing like that of pyogenic osteomyelitis or arthritis of similar degree. Restricted painful movement of a joint was sometimes observed before periarticular swelling was present. Soft-tissue swelling around the joint was also associated with restricted and painful movement and, in moderate to severe cases, an effusion was present, but detection of fluid was often obscured by the soft-tissue swelling. The elbows were most frequently affected, often both (Fig. 2).

In severely affected joints disorganisation and pathological fractures occurred. Cockshott and MacGregor observed this most often in the elbows, but we found that abnormal mobility occurred most often in the ankles and that in the elbows restricted movement was the main feature. Sinuses occurred in badly affected joints which were not aspirated, or when aspirated late.
The general condition of the patients was not greatly affected by the occurrence of osteomyelitis and many checks were made on the temperatures of these patients at first, as it was difficult to believe that they were not running a high fever. The apparent clinical well-being of the patients with grossly swollen elbows and ankles was very striking. One-third of our patients were afebrile, one-third had a low fever and only three had a swinging temperature. This is similar to the findings by other authors.

Cockshott and MacGregor (1958) were unable to detect radiological abnormalities in any case in which bone infection was not clinically apparent. This has not been our experience: sixteen cases were found to have radiological osteomyelitis in whom there was no clinical evidence of it. This may be in part due to closer medical supervision in the Nigerian series which was not available in Nyasaland due to shortage of staff at that time.

The progress of the condition was slow and we were unable to follow up many of these patients, but in one mildly affected patient the elbows were clinically normal four months later. Another case seen two months later had improved slightly. One of the severely affected patients had improved slightly after one month, but was not seen later. Anyone who has worked in rural Africa will appreciate why our follow-up of these patients is so inadequate.

RADIOLOGICAL FINDINGS

It is not necessary to review these in great detail as they have been described by Cockshott and MacGregor (1959) and Middlemiss (1962). The earliest stage shows soft-tissue swelling around joints with a band of osteoporosis or even bone destruction in the metaphysis, most clearly defined on the epiphysial side (Figs. 3 to 5). Following this the displacement or destruction of an epiphysis can occur, disorganising the joint (Fig. 6). Later there is a marked periosteal reaction with a great deal of new bone forming around the shaft, often extending throughout its whole length. This consolidates leaving the shadow of the old shaft within it.
(Figs. 7 and 8). Remoulding takes place extremely slowly and may require a year or more (Fig. 9) (Middlemiss 1962). We feel it is more important to emphasise the radiological findings which may suggest the true cause of an unsuspected case and distinguish it from a simple pyogenic osteomyelitis, rather than to list all the changes in detail. Osteomyelitis variolosa should be considered for the following reasons: 1) The bone changes are very often symmetrical. The elbow joint is very commonly affected, in some series in as many as 80 per cent of patients. A high proportion of these have bilateral elbow joint infection and all three bones are involved. This finding alone is sufficient to suggest the possibility of a smallpox infection as it is extremely uncommon in any simple pyogenic osteomyelitis. There is also bilateral involvement of the tibia and fibula. These changes are remarkably symmetrical and even if the elbow joints are not affected, bilateral bone infection of each tibia and fibula simultaneously must be unusual, especially in a child who may at this stage be remarkably well. Symmetry follows an unusual pattern in some cases—the left arm and leg being affected and not the right (or vice versa). 2) Separation of an epiphysis, resulting from the transverse metaphysisis, is characteristic of an osteomyelitis resulting from smallpox. The degree of separation and distortion may vary although complete detachment is uncommon. It can be seen in any joint but is common around the elbow, the ankle and the knee. The older the child the more severe the reaction seems to be. 3) A very marked periosteal reaction occurs with this virus infection. It is gross and florid, often smooth in outline but irregular and varying in thickness. It is quite unlike the periosteal reaction seen in scurvy or following trauma and can give the impression that the bone has been dipped into thick creamy paint and then been lifted out again. Although it occurs in the bones of the upper limb it is seen best of all in the tibia and fibula, most frequently in the latter. Again it seems more severe in the older child. Beneath this periosteal reaction the shadow of the cortex remains in its normal position and unlike a simple infection this "sequestrum" does not involute in the normal way but slowly merges with the periosteal reaction as the condition settles. It is usually limited above and below by the capsular

Figure 3—Small areas of destruction of the metaphysis of the humerus and the olecranon, and the head of the radius. Figure 4—The soft-tissue swelling (the pox were still visible on the skin). Figure 5—The same patient as in Figures 3 and 4 one month later. A periosteal reaction has occurred at the lower end of the humerus and metaphysial defects are present in the radius and ulna.
Figure 6—Destruction of the epiphyses and disorganisation of the joint. Figure 7—The left and right forearms. There is a "creamy" periosteal reaction which stops at the capsular attachments. There is extensive metaphyseal involvement of the metacarpal bones and the phalanges.

Figure 8—The same patient as in Figure 7 showing the symmetrical involvement of the tibiae and fibulae. Figure 9—The stage of consolidation with large central "sequestra" and healing of the metaphyses.
attachments (Cockshott and MacGregor 1959), but unlike a true sequestrum its density remains even throughout its length, giving the impression that the whole shaft will form one large sequestrum. In some cases the bone reaction is so severe that the whole shape of the normal shaft is lost, having become expanded and distorted to a considerable degree. In spite of this, and unlike a simple pyogenic infection, the outline is nearly always fairly clear cut, and sharp spicules are not usually seen. 4) In the small bones of the wrists, hands and feet there is often patchy destruction which is unevenly distributed, causing expansion of the bone itself and distortion of the joints. The bone remains expanded and increased in density for a long time and if weight bearing is allowed, deformities develop as these bones are quite soft. As in other series we found that the long bones and small bones were most affected. A patient who has multiple centres of osteomyelitis due to a pyaemia would probably have infection in the ribs, spine or pelvis, but this does not seem to occur in smallpox. One case of a facial bone infection has been described (Cockshott and MacGregor 1959) but this seems an extremely uncommon complication. The calcaneum is often involved.

TREATMENT

As noted by Sword (1961) various antibiotics had been used to treat the smallpox in the hope of reducing the secondary infection. Most patients were given streptomycin and penicillin, and a few chloramphenicol. This did not prevent the occurrence of osteomyelitis. Tetracycline was given in established osteomyelitis, but no beneficial effect could be demonstrated except in patients in whom sinuses were probably associated with secondary infection.

No surgery was carried out as in most cases the extensive nature of the lesion precluded it. Joints were aspirated to try to prevent sinus formation and immobilised in plaster-of-Paris to provide rest and prevent pathological fractures. Attention was also given to the treatment of malaria, malnutrition and anaemia.

As regards mortality, the prognosis of the case of smallpox complicated by osteitis is no worse than in the uncomplicated case. Only one patient in the present series died—from bronchopneumonia.

LATE CHANGES

The late changes are, as would be expected, ankylosis of the joints, malformation of the bones (frequently with an intact joint space), flail joints and ultimately osteoarthritis. Retardation of growth following the disease also occurs and it is quite possible to recognise these changes years after the infection. Deformities of the hands following dactylitis result in short stubby fingers. Ankylosis of one or both elbows is probably the commonest complication (Fig. 10). The hip joints, wrists, knees and ankles do not escape and the changes in the tarsus may result in a severe talipes.

DISCUSSION

Unlike pyogenic infections early surgery has no part to play in this disease and prolonged and expensive courses of antibiotics and chemotherapy do not in any way affect its outcome.
An almost normal white cell count, little or no pyrexia, and very little toxaemia or other physical disability in a patient in whom the radiological changes suggest an extremely severe osteomyelitis should remind the clinician and the radiologist of the possibility of this disease. We agree with Cockshott and MacGregor's (1958) description of the condition as "an uncomfortable interference with function" rather than an illness.

SUMMARY

The purpose of this report is not to describe a new condition but to remind those who seldom see smallpox of one of its most important and easily recognised complications. Bone infection can be late, almost silent and often most unexpected. It is usually symmetrical and almost always multiple. It does not affect the spine, pelvis and ribs, but does affect the arms, hands, legs and feet. It is destructive, unpreventable and untreatable. It ends with deformity but not with loss of life. The recognition of its etiology will prevent a great deal of unnecessary and unrewarding interference with a self-limiting disease.

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REFERENCES


