Salmonella Muenchen Osteomyelitis in a White Boy with Sickle Cell Disease*

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Salmonella osteomyelitis as a localized complication of salmonella infection is rare but when seen is frequently associated with sickle cell disease.[1] A review of the available literature revealed that over 26 cases showing this association have been reported.[2,3,4,5,6,7]

We have recently observed a child whose sickle cell disease has been previously reported[8] and who showed this combination. We feel he is of special interest because he is, so far as we have been able to learn, the first white child to show the combination of salmonella osteomyelitis and sickle cell disease. (One of the cases reported by Silver[9] was white; this was a case of microdrepanocytic anemia). Moreover, the organism isolated, *Salmonella muenchen*, has not previously been observed to cause osteomyelitis. Finally, he showed another interesting complication of sickle cell disease in that the os capitatum of the left wrist had completely disappeared, presumably due to aseptic necrosis with subsequent bony resorption.

Case History : This 10 year old white male, whose home is in southern Turkey (Tarsus), was admitted to the Hacettepe Children's Hospital on May 3, 1958, with complaints of weakness, pallor, fever and chronically draining wounds of the left lower leg.

The past history indicated that this boy had had symptoms of anemia since about one year of age. A diagnosis of sickle cell disease (SS hemoglobin) was made when he was 6 years old and has been reported.[8] Over the years, symptoms have been moderate and treatment sporadic.

Seven and a half months before admission here symptoms became more severe and he was treated with transfusions which were followed a few days later by a series of generalized convulsions which subsided spontaneously. Fifteen days later swelling, erythema, tenderness and local heat developed over the distal portion of the left humerus and

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left lower leg. Over a period of several weeks both lesions progressed and finally began spontaneously to discharge purulent material. These lesions were given no specific treatment; the former finally healed spontaneously, that over the lower leg persisted until admission here. In addition to this, symptoms of anemia became more severe just prior to admission.

The past history was not otherwise remarkable. The family history was interesting in that the parents are first cousins and of Turkish village stock. Our patient is one of 10 children born to these parents of whom 6 are dead. Four of these died of symptoms indicating infectious diseases, the other two of symptoms suggestive of anemia. The three living siblings are in good health as are the parents.

Examination on admission revealed a thin, pallid, jaundiced boy who appeared chronically but not severely ill. The weight was 23.8 kg., height 126 cm., T: 36.6 C., P: 100/min, BP: 110/75 (right arm). In addition to the marked pallor, pertinent physical findings include moderate cardiac enlargement on percussion with a grade II systolic murmur in the apical pulmonary regions, not widely transmitted and unaccompanied by a thrill. There was no significant abdominal organ enlargement nor other abnormalities. A recent well healed cicatrix was noted over the medial aspect of the left humerus and over the antero-medial aspect of the left tibia there was an old unhealed granulating wound from which purulent matter originated from two separate fistulae.

Laboratory Findings. Blood : Hemoglobin 5.77 gm %, red blood cells 2.12 million, hematocrit 21 mm % (MCV 100 gamma, MCH 27 micrograms, MCHC 27.7 %), white blood cells 19,200. Differential: Polymorphonuclear leukocytes, segmented 61, stab 2, eosinophiles 2; monocytes 3; lymphocytes 32. There were 16 nucleated red blood cells per 100 leukocytes. There was marked hypochromia, poikilocytosis and anisocytosis with some sickle cells and a few target cells seen. Reticulocytes were 16.9 %, platelets 339,000. On suspension in sodium metabisulfite solution there was sickling of most of the erythrocytes within one hour. The blood group was A, Rh-negative, and the direct Coombs test negative. The bilirubin level was 0.7 mgm % on direct reading and 1.0 mgm% on indirect, total 1.7 mgm. %. Urinalyses showed a specific gravity between 1.007 and 1.012. A standard urea clearance test was 107 %. Other findings were noncontributory.

Cultures obtained from the blood, stools and urine were sterile. Cultures of the purulent material from the left tibia, as well as from

the sequestra which were subsequently removed surgically, grew out *Salmonella muenchen.*

Radiographic examination of the chest on admission revealed generalized mild cardiac enlargement, normal lung fields, and osteomyelitic changes in the left 4th rib. Films of the left humerus were interpreted as showing healed osteomyelitic changes. The left elbow joint was completely normal to x-ray. Examination of the left tibia revealed an extensive destructive process with marked periosteal reaction and two large sequestra in the proximal and distal metaphyseal regions respectively, surrounded by wide porotic spaces. Films of the skull and spine were interpreted as being within normal limits. Films of the left wrist were not obtained until several weeks after admission, but then revealed complete absence of the os capitatum. Films of this joint taken four months previously were then obtained and revealed that the wrist had been normal at that time.

Hospital Course : On admission erythrosulfa was begun but on the fourth hospital day when the organism had been identified as *Salmonella muenchen* this was changed to chloramphenicol, 50 mgm per kilo per day. He was kept on bed-rest and the anemia was gradually corrected by transfusions of whole blood. On the 33rd hospital day sequestrostomy was done, following which penicillin was added and the left leg was immobilized in plaster for two months. X-rays at this time were consistent with healed osteomyelitis and the fistulae were no longer draining, so antibiotics were discontinued. The findings in the left 4th rib were unchanged and since there had never been any local tenderness in this area they were interpreted as being those of inactive osteomyelitis. After 90 days there were no clinical signs of osteomyelitic activity in the tibia, the hemoglobin was 10.05 gm%, and the patient was considered ready for discharge on August 18, 1958.

Comment. Lambott and Legrand, (as quoted by Silver), were apparently the first to suspect more than coincidence in the occurrence of osteomyelitis caused by Salmonella organisms in patients with sickle cell disease. Shortly thereafter Hughes and Carroll[2] also reported a tendency toward osteomyelitis in patients with sickle cell disease and they pointed out the frequency of Salmonella as a causative organism, a tendency for this complication to occur in children and, finally, they noted that there is a tendency toward involvement of multiple sites. The suggestions of these authors have now been amply confirmed by other reports in the literature.[3,4,9,10]

In attempting to account for this association it may be recalled that with Salmonella infections there frequently is an invasion of the

blood stream by micro-organisms. Bacteria arriving in the marrow cavity are known to remain there for weeks or even months. [3,9] In a normal individual the ordinary body defenses are apparently adequate to restrain the organism and a localized infection such as osteomyelitis rarely occurs.

There are several possible reasons to account for the difference in patients with sickle cell disease. It is suggested, first, that capillary thrombosis, occurring in the gastrointestinal tract as elsewhere in the body, would produce conditions which would enable the Salmonella organisms to invade the vascular compartment more easily and/or in larger numbers. Thus the septicemic phase of Salmonella infection might be more severe in patients with sickle cell disease. Secondly, it has been suggested that the same phenomenon of small local infarcts, thrombosis and necrosis, occurring in the marrow spaces, would markedly impair local defense against infection. The Salmonella organism, arriving at such sites in the septicemic phase of infection, would therefore be relatively less inhibited. Finally, there are the general effects of anemia and "autosplenectomy" in reducing body defenses against infection. These various factors are probably adequate to account for the occurrence of the two processes together, though other factors may also play a role.

Though these predisposing factors seem to increase the incidence, Salmonella osteomyelitis, when it does become established, is usually not severe. Giacci and Idriss [3] have summarized the characteristics as follows: 1: There is a tendency for localization to occur in the epiphyses and diaphyses rather than metaphyses as in ordinary osteomyelitis. 2: There is a tendency for localization to occur simultaneously in multiple sites because of the widespread possibility of infarction. 3: Bony destruction is ordinarily not widespread or severe. They speculate that because localization occurs late in the course of Salmonella infection the body's immune mechanism has time to respond fully and in this respect, at least, body defenses are optimum.

Roberts and Hilburg [4] have discussed the bony changes in sickle cell disease per se and have pointed out that lesions may be seen which resemble the early destructive changes of osteomyelitis generally. It is also established that aseptic necrosis on the basis of localized infarcts is of relatively common occurrence in this disease.

Our patient, who had sickle cell disease of rather marked severity and of long standing, conformed in most respects to cases previously described. We attribute the severity of the tibial lesions to the duration and lack of therapy. That his body defenses were not by any means

totally inadequate is indicated by the fact that the infection in the left humerus and the left fourth rib had apparently healed spontaneously prior to the initiation of antibiotic therapy or correction of the anemia.

The x-ray changes seen in the left wrist were consistent with those of aseptic necrosis and there was no evidence either clinically or by history to suggest that infection had been a factor. While aseptic necrosis is a known complication of sickle cell disease, [11] we have been unable to find any previous report of involvement of the os capitatum.

The particular strain of Salmonella isolated from the lesions of our patient has not been previously isolated from an osteomyelitic lesion as far as we have been able to learn. It had not, in fact, been identified in Turkey under any circumstances prior to this. *Salmonella muenchen* is, however, essentially typical in its behavior and there is no reason to expect it to behave differently from other members of the Salmonella family.

Sickle cell disease occurs in members of the Negro race in the overwhelming majority of cases. However, it is not unknown in patients who have no known genetic relation to that race. In Turkey there have been 19 case reported in patients of non-Negro extraction. Over the centuries there have been Negroes in Turkey and the possibility of racial admixture cannot be denied. In the case of our patient, as indicated, he is, as far as the parents are aware, of purely native Turkish, non-Negro racial derivation. That Salmonella osteomyelitis has not been previously reported in a white patient with sickle cell disease is no doubt due to the infrequent appearance of the latter in white individuals, since, when it does occur, it is typical and one would expect typical complications to occur.

Summary

We have described a patient who presented the now well known combination of sickle cell disease complicated by Salmonella osteomyelitis. He was of interest, we felt, because we have found no previous report of this combination occurring in a white individual. In addition, the particular microorganism, *Salmonella muenchen*, has not previously been isolated under such circumstances. Finally, this child presented another interesting complication of sickle cell disease in that there had apparently been aseptic necrosis of the os capitatum with complete resorption.

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