CLINICALLY DEMONSTRABLE BONE CHANGES IN LEUKEMIA

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Bone changes in leukemia which are detectable by palpation or radiography are not common, but when present offer some difficulty in interpretation until blood counts are made. Occasionally, also, the pain which may accompany such lesions has been diagnosed as due to osteomyelitis or rheumatic fever. Since many of these cases are associated with an aleukemic blood picture, and occur in children, the immediate diagnosis is not always obvious. The following two cases illustrate one of the several varieties of bone lesions which may be present in leukemia.

CASE REPORTS

CASE I: Aleukemic Lymphatic Leukemia with Gross Bone Changes: A boy of eight entered the University of California Hospital (Pediatric Service), with generalized enlargement of the lymph nodes, spleen, and liver. Blood counts showed 13,850 white cells with 93 per cent lymphocytes or unclassified cells; and again 9,900 white cells with 89 per cent of the lymphocyte series. Roentgenography (Dr. R. S. Stone) showed many lesions involving the long bones, with rarefying processes in the medulla and cortex, and lifting of the periosteum with new bone formation of a very fine lace-work type on the outside. All the bones of the arms and legs and many of the ribs were involved. The skull and pelvis showed a diffuse fine mottling. (Figs. 1 and 2.)

Autopsy (29.106) showed generalized lymph node involvement and an enormous liver (2000 grams) and spleen (1320 grams), the type cell being an immature lymphocyte. The bones (femur and tibia examined) had a raised, roughened periosteum with what appeared to be almost a double cortex: an outer layer of bone separated by tumor cells and a rather friable inner layer (the true cortex) of slightly increased thickness, infiltrated with the cells. The bone marrow was replaced by tumor, parts of which were yellow and necrotic.

CASE II: Leukemia with Marked Bone Changes: A female infant of eleven months was first seen by Dr. C. A. Boehm of the Children's Hospital, San Francisco, on Aug. 4, 1931. She had been well until two months previous when a rash with fever developed, diagnosed as measles. Since that time there had been progressive loss of weight and strength, and the child had become pale and listless. A blood examination (Aug. 4) showed: hemoglobin 25 per cent; red cells 1,460,000, with an occasional nucleated red cell; white cells 40,300; polymorphonuclears 19 per cent; lymphocytes 80 per cent. On Sept. 20, 1931, the child was brought to the hospital because of swelling of the right leg from the knee to the ankle, accompanied by considerable pain. There were also swellings on the forehead, left brow, increasing in size. X-ray pictures (Figs. 3 and 4) showed irregular mottling of femurs, tibiae, and fibulae, with reduplication of the cortices in these bones. The appearance bore a general resemblance to a proliferating periostitis, but of much greater severity than is usually seen, and at the same time with a more regular outline of the bones. A clear line of transparent tissue was evident between the true cortex and the new-formed bone, indicating soft tissue infiltration. A previous roentgenogram of the chest had shown mediastinal masses, assumed to be lymph nodes. Cervical lymph nodes were also enlarged, but it was difficult to determine the size of the liver and spleen because of tenderness and abdominal distention. Later multiple hemorrhages occurred, generalized lymph node enlargement became apparent, and tumors developed in the skull. On Sept. 7, 1931, the blood
count showed 28,900 white cells, 61 per cent of which were large or small lymphocytes, with many immature cells. The peroxidase reaction was negative, the Wassermann reaction negative, and the tuberculin skin test negative.

An axillary lymph node was described as follows: "Most of the architecture of the node is lost, though an occasional germinal center persists. The node is chiefly made up of moderately large, undifferentiated cells with large vesicular nuclei in which many mitoses are seen. There is no invasion of the capsule."

The spleen and liver became palpable, the anemia increased, and purpura became marked. In spite of numerous blood transfusions and x-ray treatments, the course was steadily downhill, and the child died at home, six months after the apparent onset. While no autopsy was permitted, the clinical course, blood picture, lymph node histology, and the x-ray appearance of the bones make the diagnosis certain.
Discussion

These two cases illustrate only one of a number of types of bone changes in leukemia recorded in the literature. Ehrlich and Forer (1), Jacobson (2), Snelling and Brown (3), and Erb and Brown (4) report similar cases, among others, in which subperiosteal infiltration and secondary bony proliferation were the outstanding features. Osteosclerosis or osteoporosis, however, is more frequently mentioned. Craver and Copeland (5) describe such changes as the common ones, with or without "periostitis." According to them these

Fig. 2. Case I: Metacarpals and Phalanges Showing Changes Similar to Those in the Long Bones (Fig. 1)

lesions are most frequent in the pelvic bones, spine, upper ends of the femurs, and humeri. These correspond with the sites in which lymphosarcoma metastases most often occur.

Most of these lesions occur in children. Very few have been seen in adults. Of Snelling and Brown's twelve patients, all were under six years of age. In addition to cortical stratification these writers found rarefaction at the ends of long bones (some of their pictures show changes similar to those of congenital syphilis). One child had a spontaneous fracture at the lower end of the femur. About half of their series had pain in the extremities, and symptoms of rheumatic fever, scurvy, and luetic bone changes were observed. Others have also recorded symptoms of conditions from which it is important that leukemia be differentiated. Sutton and Bosworth (6) mention a girl of two years and eight months with recurrent pain and tenderness, with swelling, of the arm and leg joints. The true nature of the disease was
thus masked for six months. Bonaba and Volpe (7) report a case in which osteomyelitis was suspected because of pain in the long bones. Since the pathologic changes and the x-ray pictures are not always so typical as those shown here, it is quite possible to overlook a leukemia when the presenting signs and symptoms appear to be primary in the bones or joints.

Neumann (8) was one of the first to draw attention to bone changes in leukemia, before the era of roentgen rays, at about the time (1878) that bone marrow proliferation in this disease was being discovered (lit. by Neumann). He described resorption of ribs, ilium, and left trochanter in one case; pain and resorption of bone of the femur in another. Changes described by others may be recorded briefly: Eisenlohr (9), periosteal infiltration of the ribs (1878); Pförringer (10), a large bulky tumor of the upper end of the humerus with fracture; Haenisch and Querner (11), erosion of the skull and femur, associated in one case with an osteolytic lesion of the head of the humerus resembling a myeloma; Lundholm (12), fracture of ulna at the wrist with periosteal stratification in both radius and ulna; Maternowska and Redlich (13), a bone defect demonstrable by x-rays at the proximal epiphyseal line of the left tibia; Trusen (14), a localized rarefaction with spontaneous fracture of the humerus and periosteal infiltration of femur; Jacobson (2), osteosclerosis of vertebrae, ribs, femur, skull, and patella; Stephens and
Bredeck (15), osteosclerosis; Paschlauf (16), rather circumscribed areas of destruction with some calcification of the bones of the hands, upper arms, and pelvis. Thus the outstanding signs of some leukemias may be pain around the joints, resembling rheumatic arthritis; pain in the long bones as in osteomyelitis; periosteal reactions as in scurvy, periostitis, or luetic periostitis; spontaneous fracture in local osteolytic processes; bulky tumors of single bones; osteolytic lesions, as in myeloma or chloroma.1

References

1 Ivanizkaja, for instance, records a case of leukemia in which, after a year, masses developed in the bones of the sacro-iliac region, the fifth metacarpal, and the sternum. He interpreted this as leukemia and multiple myeloma (Ivanizkaja, M. F.: A Case of Myeloblastic Leukemia and Primary Multiple Myeloma, Voprosy Onkologii, Kharkov, 4: 86, 1931. Abst. in Am. J. Cancer 15: 3098, 1931).