Thickened cortical bones in congenital neutropenia

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Abstract. Congenital neutropenia is an uncommon entity which may be familial and has a wide spectrum of clinical expression. Three sisters with the severe form of the disease, that suffered from recurrent infections which lead to their demise, are described. Review of their radiographs revealed the presence of cortical thickening of the bones. Although several syndromes with different bone abnormalities have been reported associated with neutropenia, the radiographic finding of thickened cortex in children with congenital neutropenia has not been previously described.

Children with congenital neutropenia comprise a heterogeneous group of patients with a common feature of a granulocyte count of less than 1500/mm³. There is a wide spectrum of clinical expression, ranging from a benign condition that is often discovered fortuitously to a disorder characterized by recurrent infections resulting in severe morbidity and mortality. The etiology and pathogenic mechanisms of the congenital neutropenias are largely unknown, including abnormalities in marrow development through failure in production, maturation or release. Other mechanisms such as decreased survival of peripheral cells through immune mechanisms, retic-

Fig. 1. a Patient 1. Chest radiograph shows left lobe consolidation and thickening of the ribs. b Patient 1. Cortical thickening involves the diaphysis of both tibiae and fibulae. Similar findings were present in femora and upper extremities.
uloendothelial sequestration or altered margination are also recognized [1-3].

We had the opportunity to study three sisters with severe congenital neutropenia. Their bone marrow evaluation showed adequate myeloid elements, but with maturation arrest at the myelocyte stage with very few metamyelocytes [3]. They all had a poor response to leucocyte stimulation tests and suffered from repeated skin, ear and lung infections, which lead to their demise. Review of the radiographs revealed the presence of thickened cortical bones, a finding not previously known to be associated with congenital neutropenia.

Family study

These three children are the only affected in a Jordanian family of nine. The parents are distantly related and both of their laboratory evaluations showed “in vitro” arrest of regeneration after 4-5 cycles.

All three sisters demonstrated monocytosis and severe neutropenia secondary to maturation arrest, suggesting a defect at the level of the myelocyte.

Case 1

A. Am. presented with skin and ear infections at 2 months of age and was treated with antibiotics. At 5 months she had a very severe reaction to vaccination, with delayed healing. A peripheral smear showed the absence of neutrophils and her IgM was low. During the first 2 years of life she had multiple staphylococcal infections, developed generalized lymphadenopathy and tooth deformities. A CBC always showed neutropenia, such as a total white blood count of 66 000 with 3% polynucleutrophils. Chest X-rays taken during treatment showed the presence of a very thick cortex of bones (Fig. 1a), and a skeletal survey confirmed these findings (Fig. 1b). Follow-up was lost until she was 7 years old, when she had an acute episode of abdominal pain, emesis and fever for 24 h. Her parents brought her to the Emergency Room in a moribund state, with a mottled bluish appearance of the right posterior flank area. Radiographs showed free intraperitoneal air and gas in the soft tissues on autopsy hemorrhage and necrosis of the cecum with a normal appearing appendix, characterizing the presence of typhlitis were present. Bacteroides fragilis was cultured from a blood sample obtained at admission.

Case 2

S. Am. had a history of repeated multiple staphylococcal skin abscesses since birth. At the age of 4 months laboratory workup revealed congenital neutropenia. By 2½ years of age, she had had five episodes of pneumonia. On physical examination, done dur-