Bone Marrow Dysfunction

In all types of leukemia, the proliferating cells depress bone marrow production of the formed elements of the blood by competing for and depriving the normal cells of the essential nutrients for metabolism. The three main consequences are (1) anemia from decreased erythrocytes, (2) infection from neutropenia, and (3) bleeding from decreased platelet production.

The invasion of the bone marrow with leukemic cells gradually causes a weakening of the bone and a tendency toward fractures. As leukemic cells invade the periosteum, increasing pressure causes severe pain. The most frequent presenting signs and symptoms of leukemia are a result of infiltration of the bone marrow. These include fever, pallor, fatigue, anorexia, hemorrhage (usually petechiae), and bone and joint pain. In the presence of neutropenia, the body's normal bacterial flora can become aggressive pathogens. Any break in the skin is a potential site of infection. Frequently, vague abdominal pain is caused by areas of inflammation from normal flora within the intestinal tract.

Disturbance of Involved Organs

The spleen, liver, and lymph glands demonstrate marked infiltration, enlargement, and eventually fibrosis. Hepatosplenomegaly is typically more common than lymphadenopathy.

The next most important site of involvement is the CNS. Less than 5% of patients with B-cell ALL and 10% to 20% of patients with T-cell ALL have CNS involvement (Rabin, Gramatges, Margolin, et al, 2016). The use of prophylactic CNS intrathecal therapy has dramatically decreased the incidence of CNS relapse in these patients.

Additional sites of involvement may be the cranial nerves (most often cranial nerve VII, or the facial nerve) and spinal nerves, particularly of the lumbosacral plexus, hypothalamus, and cerebellum. Clinical manifestations for these sites are directly related to the area involved. For example, with lumbosacral invasion, the patient has weakness in the lower extremities, pain radiating down the legs to the feet, and difficulty in voiding. Although such signs may suggest a brain tumor, the absence of localized signs often leads to the discovery of CNS involvement in