Pathological Case of the Month

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A 3-MONTH-OLD BOY was seen for pallor and oily stools. Findings revealed a hemoglobin level of 46 g/L; platelet count, 442×10^9/L; and total lymphocyte count (TLC), 4.6×10^9/L with polymorphs at 0.26×10^9/L; lymphocytes, 0.72×10^9/L; and monocytes, 0.02×10^9/L. Moderate anisocytosis, mild poikilocytosis, hypochromia, microcytes, macrocytes, and teardrop and crenated cells were seen on peripheral blood film. Stool fat estimation at age 5 months was 14.75 g in a 3-day collection. Results of a sweat chloride test were normal. He was treated with oral iron and folic acid preparations and pancreatic enzymes and given 1 blood transfusion; his hemoglobin level improved initially (91 g/L).

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The TLC and absolute neutrophil count decreased, and at age 5 months the TLC was 1.8×10^9/L with an absolute neutrophil count of 0.36×10^9/L. The child had repeated infections with loose oily stools and diarrhea for 2 years and 9 months. He developed septic shock and died at age 3 years, at which time hemoglobin levels were 82 g/L with decreased platelet count, and the TLC was 1×10^9/L. A blood culture grew *Pseudomonas aeruginosa*. Cut section of the pancreas revealed loss of normal pancreatic architecture (**Figure 1**). Microscopy shows the bulk of the pancreatic tissue replaced by fatty tissue (**Figure 2**). Pancreatic ducts are preserved, and islets of Langerhans are relatively prominent and composed of large cells (**Figure 3**). Atrophic and shrunken acinar tissue is seen with cells having a pink cytoplasm and pyknotic nuclei (**Figure 4**). A section of bone marrow showed maturation arrest of the myeloid series of cells with normal erythroid and megakaryocytic series.

Figure 1.

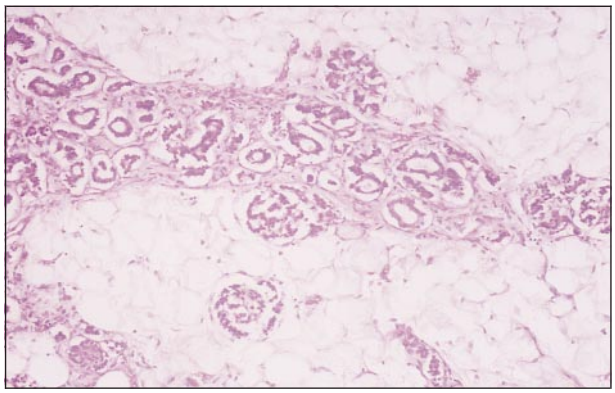

Figure 3.

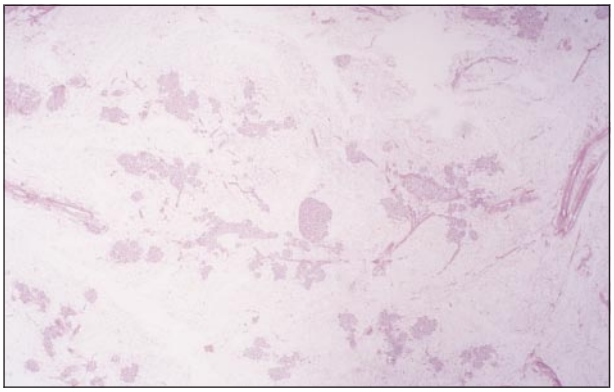

Figure 2.

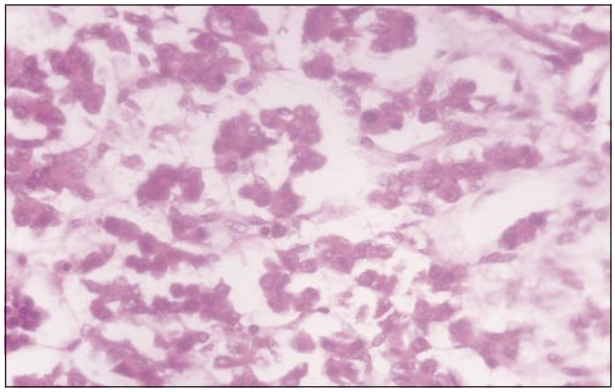

Figure 4.

Diagnosis and Discussion

Shwachman-Diamond Syndrome: A Syndrome of Pancreatic Insufficiency and Bone Marrow Dysfunction

Figure 1. *Normal architecture of the pancreas is lost. It is soft and mucinous to the touch.*

Figure 2. *Extensive replacement of pancreatic tissue by adipose tissue and few scattered remnants of the pancreatic tissue (hematoxylin-eosin, original magnification ×55).*

Figure 3. *Remnants of pancreatic tissue composed of proliferated ducts and relative increase of islets of Langerhans (hematoxylin-eosin, original magnification ×140).*

Figure 4. *Atrophic and shrunken acinar tissue with cells having a pink cytoplasm and pyknotic nuclei (hematoxylin-eosin, original magnification ×280).*

Shwachman-Diamond syndrome[1-4] is the second most common cause of pancreatic insufficiency in early life after cystic fibrosis. Pancreatic exocrine insufficiency is accompanied by growth retardation, bone marrow dysfunction with neutropenia, and skeletal changes, predominantly metaphyseal dysostosis. Sweat chloride test findings are normal. Cases have been associated with anal atresia,[4,5] Hirschsprung disease,[6] and asphyxiating thoracic dystrophy.[7] The bone marrow dysfunction is associated with the eventual appearance in some cases of leukemia, usually nonlymphocytic.[8-10] Cases have been reported in which the clinical onset of pancreatic insufficiency occurred soon after birth[2,7] and includes malabsorption, steatorrhea, and failure to thrive. More than 25 families had at least 2 affected children, and the inheritance is presumed to be autosomal recessive. Many patients develop anemia (15%) or thrombocytopenia (7%) or both (20%). Occasionally, anemia and thrombocytopenia precede neutropenia. In this condition the neutrophils may not be totally normal. There may be a defect in neutrophil mobility, which may explain infection even when the neutrophil count is not extremely low. Histopathologic analysis reveals the bulk of the pancreas to be replaced by fatty tissue.[3] Pancreatic ducts and endocrine elements are preserved.[11] Usually the acinar is absent,[11] but occasionally some acinar cells are present and are large and devoid of secretary granules.[1] Occasionally, atrophic acinar tissue is seen with pink cytoplasm and pyknotic nuclei.

The relationship of the pancreatic insufficiency to the hematologic abnormalities remains unknown. Pancreatic insufficiency from other causes such as cystic fibrosis is not associated with neutropenia. Pancreatic replacement therapy does not improve the neutropenia in Shwachman-Diamond syndrome. An injury or insult during the fifth fetal month, when development of both the pancreatic exocrine tissue and the myeloid population in the bone marrow occurs, may explain this association. However, familial cases suggest that the disorder is inherited as an autosomal recessive trait.

In this index case, the clinical onset of pancreatic insufficiency occurred soon after birth. The pancreatic replacement therapy did not improve the neutropenia. Anemia responded to therapy and blood transfusion. Repeated infections occurred, but growth and weight gain were within normal limits.

Patients with pancreatic insufficiency with normal sweat electrolytes and lack of respiratory disease should be evaluated for Shwachman-Diamond syndrome. These patients seem to have a better prognosis than those with cystic fibrosis.

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