

Shwachman-Diamond Syndrome

Disease Information

First described in 1964, Shwachman-Diamond Syndrome is a rare disease which mainly involves the pancreas, bone marrow and skeleton, but other organs may also be affected.

Next to Cystic Fibrosis, it is the most common cause of pancreatic insufficiency in children. For that reason, it is sometimes confused with Cystic Fibrosis; but in children with Shwachman-Diamond Syndrome the sweat test is normal.

People with Shwachman-Diamond Syndrome usually have a decreased ability to digest food because the cells of the pancreas, in which digestive enzymes are produced, do not work properly.

Additionally, there is usually a decreased number of at least one kind of blood cells. In some patients, there is a decrease in all kinds of blood cells. Most frequently, this decrease occurs in the number of neutrophils, the blood cell that is necessary to fight bacteria infections.

Cause

Shwachman-Diamond syndrome is genetic, most likely an autosomal recessive condition. The inheritance is supported by the presence of more than one affected patient in a family. Males and females are affected with equal frequency. However, the factors which lead to multi-system diseases are unknown.

General Features

Infants often become ill with symptoms by the age of four or six months old. Early problems include failure to thrive, feeding

problems and recurrent infections. Growth soon slows and remains below normal; only a few children show growth beyond the third percentile. Infections are present early in at least 85% of children. These occasionally lead to death. Diagnosis is generally made in the first few years of life, although occasionally diagnosis is delayed.

Specific Features

Digestive

Diarrhea is almost always present in infancy. Stools contain an excessive amount of fat and are foul smelling and greasy in appearance. Improvement in stools is seen after enzymes replacement therapy is begun. Although weight gain is noted, growth does not seem to improve. Some older patients are able to discontinue enzyme replacement with no clinical consequences.

Bone Marrow

As a result of dysfunction of the bone marrow, patients may have a decrease in any or all types of blood cells. There may be decreased numbers of neutrophils (the white blood cell that helps fight infection), platelets (the blood cell that helps clot the blood), or red blood cells. Blood cell counts should be monitored regularly. Shwachman-Diamond Syndrome patients have a propensity to myelodysplasia or leukemic transformation, for this reason bone marrow aspirates and biopsies are recommended.

Neutropenia

Neutropenia is present when the counts are lower than 1500 per microliter. Neutrophils are a type of white blood cell important in fighting bacteria infections. Neutropenia is seen, at sometime during the course of the disease, in virtually all patients. Many patients are prone to repeated bacterial infection. Some of these infections may

be life threatening. Close attention should be paid to infection, with appropriate treatment instituted as quickly as possible.

Thrombocytopenia

The blood also contains cells called platelets. It is their function to clot the blood when bleeding occurs. Normally, platelet counts are above 150,000 per microliter. In about 35% of patients with Shwachman-Diamond syndrome this count is below that number; this is called thrombocytopenia. Easy bruisability is one indication of thrombocytopenia, but severe bleeding is unusual. Precautions may be required before dental work or surgery, and platelet transfusions or medications may be necessary to diminish the risk of abnormal bleeding.

Anemia

Anemia occurs when the hemoglobin level is under 10gm/dl, and has been observed in up to 40% of patients with Shwachman-Diamond Syndrome. Anemia is usually mild and does not respond well to treatment with iron, folic acid and vitamin B-12.

Skeleton

Bone lesions have been reported in 10 to 15% of patients. The bone abnormalities are called metaphyseal chondrodysplasia. X-ray changes are most commonly seen in the hip, femur, tibia (leg bone) and ribs. These changes can be severe enough to require surgical correction.

Liver

Abnormalities in the structure of the liver and in function are not uncommon. Hepatomegaly (enlarged liver) occurs in about 2/3 of patients under the age of five years of age, but is less frequent in older children. Serum liver enzymes are elevated in 50 to 75% of

cases, again most often in young children and tending to fall with age. Chronic liver disease has been reported.

Other Involvements

Less frequently reported conditions include cardiac lesions, developmental and intellectual delays, behavior and eating problems, lung disease, renal tubular malfunction, abnormal pulmonary function tests, testicular fibrosis, dental problems, diabetes mellitus and pubertal delays.

Prognosis

Mortalities have been reported. Full growth may not be obtained despite aggressive therapy, particularly if hip disease is severe. The other features of the disease may persist into adulthood.

Treatment

If the pancreas is not working properly, enzyme replacement should be begun immediately. Guidelines for enzyme use are similar to those for Cystic Fibrosis. Enzyme replacement should decrease diarrhea and foul, greasy stools. This may not, however, improve growth.

Multivitamins and supplemental fat-soluble vitamins (vitamins A, D, E, and K) should be given daily. The diet should provide protein and energy adequate for nutritional needs and may require supplementation with high calorie foods or prepared supplements.

Infections should be treated vigorously with appropriate antibiotics. Bleeding problems and anemia may require blood and platelet transfusions or other intervention (such as DDAVP). Hip disease should be monitored closely and may require surgical intervention. Developmental delays may be helped by physical and speech therapy.