Shwachman-Diamond Syndrome: Are we Missing Many?

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Shwachman-Diamond Syndrome (SDS) is a rare inherited disorder characterized by pancreatic insufficiency, bone marrow dysfunction and skeletal abnormalities. It is the most common cause of pancreatic insufficiency in children after cystic fibrosis. We report a child with classical SDS who presented to us predominantly with chronic diarrhea along with delayed growth and neutropenia.

Key words: *Lipomatosis, Pancreatic insufficiency, Shwachman syndrome*.

Shwachman-Diamond Syndrome (SDS) is a rare inherited disorder characterized by pancreatic insufficiency, bone marrow dysfunction and skeletal abnormalities [1]. It is the second most common cause of pancreatic insufficiency in children, next to cystic fibrosis, and probably the third most common inherited bone marrow failure syndrome after Fanconi's anemia and Diamond-Blackfan anemia [2]. The estimated incidence in the West is approximately 1: 100,000 to 1: 200,000 live births [3] and till date there are only two case reports of SDS from India [4,5]. Considering the heterogeneity of the disease associated phenotypic manifestations, and lack of awareness, it is likely that we are missing many cases in India. We report a case of classical SDS who is doing reasonably well on pancreatic enzyme supplement for two years.

CASE REPORT

A 11-year-7 month-old boy presented to us with chronic diarrhea (greasy stools, 5 to 10 times a day) and failure to thrive since birth. He also had frequent episodes of fever requiring antibiotics, recurrent oral ulcers, pruritic papular skin rash and dental caries. The child was a product of non-consanguineous marriage with normal birth weight and an apparently healthy elder sister. There was no family history of pancreatic insufficiency or hematological disorders.

His physical examination revealed growth retardation (weight 17.5 kg, height 117 cm; both <5th percentile for age), dental caries, hyperpigmented scar marks of skin lesions, and a just palpable soft liver (span 8cm) without splenomegaly. Investigations done elsewhere 2 years earlier showed hemoglobin 11.4 g/dL, total leukocyte count 3100 per cu.mm and a differential count of 49% polymorphs, 44% lymphocytes, 2% eosinophils and 5% monocytes. Though his anti-tissue transglutaminase antibody (IgA-tTG) was negative and duodenal biopsy showed mild stunting of villi, he was put on gluten free diet (GFD) as his IgA-antigliadin antibody was positive (32.4 U/mL, cut-off: 17). Despite strict adherence to GFD, the child did not show much response and was further investigated at our institution. His absolute neutrophil count was 840 per cu.mm with normal hemoglobin and platelets. Serum amylase, lipase and blood sugar were within normal limits. Stool examination showed high fecal fat excretion (6.3 g/day after fat loading with 50 g butter) and Sudan stain revealed 22 droplets of fat per high power field (normal up to 5 droplets). CT scan abdomen (***Fig.* 1**) showed generalized fatty replacement of pancreas without significant dilatation of main pancreatic duct. Sweat chloride was 31 mEq/L (normal <40 mEq/L). He had normal liver function tests, thyroid profile, serum immunoglobulins, and negative antiendomysial antibody. Duodenal biopsy was normal and bone marrow examination revealed mild marrow hypoplasia.

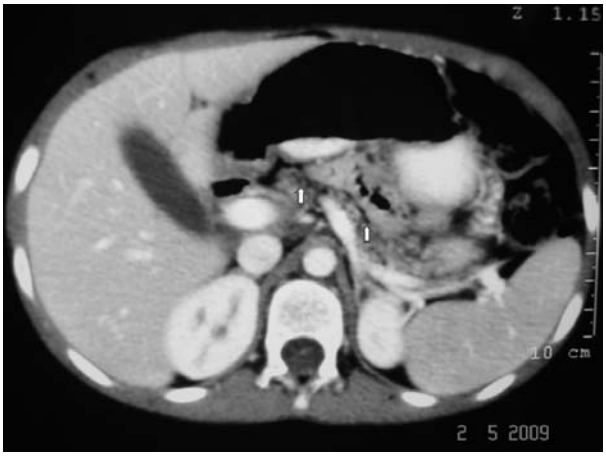

Fig. 1. *Contrast enhanced CT scan abdomen showing generalized fatty replacement of the pancreas* (white arrow).

A diagnosis of Shwachman-Diamond syndrome was made and he was started on pancreatic enzyme and fat soluble vitamin supplementations. On follow-up, steatorrhea settled and growth improved (3.5 kg increase in weight and 6 cm increase in height after 18 months). Intermittent neutropenia continued to occur on follow-up but no evidence of serious infection except one episode of *Herpes labialis* which was treated with acyclovir by the local practitioner.

DISCUSSION

When a patient presents with steatorrhea with recurrent respiratory symptoms, the diagnosis first considered is cystic fibrosis. As infections in our patient were not restricted to lungs, the possibility of immune deficiency was also considered. However, steatorrhea with intermittent nutropenia suggests the diagnosis of SDS. Patients with SDS experience recurrent viral, bacterial and fungal infections, including otitis media, bronchopneumonia, osteomyelitis, skin infection and septicemia. The quantitative and qualitative defects in neutrophils contribute to these infections in SDS [2,6,7]. Failure to thrive is a common manifestation because of malabsorption, recurrent infections and metaphyseal dysostoses. The diagnostic criteria of SDS, as laid down by Dror and Freedman, require documentation of exocrine pancreatic dysfunction and characteristic hematological abnormalities [8]. Although not done in our case, genetic analysis can be performed for confirmation. Shwachman-Bodian-Diamond syndrome (SBDS) gene is located at chromosome 7q11 [6,9]. Ultrasonography shows normal sized pancreas with increased echogenicity of the silhouette but CT and MRI reveal lipomatosis of the pancreas with greater accuracy [6]. Common causes of pancreatic lipomatosis in children besides SDS are cystic fibrosis, diabetes mellitus, obesity, Johanson-Blizzard syndrome, Pearson's marrow pancreas syndrome and agenesis or hypoplasia of pancreas.

For gastrointestinal manifestations, the mainstay of treatment is pancreatic enzyme therapy, medium-chain triglyceride, and fat soluble vitamin supplements. With this treatment, steatorrhea resolves and body weight increases but growth is not generally accelerated [6]. Exocrine pancreatic function tends to improve with time in almost half of the patients but hematological problems deteriorate [6]. Our patient showed response to enzyme supplements but continued to have problems related to neutropenia. For the treatment of hematological abnormalities in SDS, stem cell transplantation [10] and bone marrow transplantation have been reported [3]. The projected median survival of patients with SDS is 35 years and the main reason of untimely death is hematological (bone-marrow failure, myelodysplastic syndrome and acute myeloid leukaemia).

In conclusion, the diagnosis of SDS should be strongly considered in any child who presents with steatorrhea, growth retardation, and intermittent or persistent neutropenia.

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