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Brief Report

Dilated cardiomyopathy in a case of Shwachman–Diamond syndrome

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Abstract The Shwachman–Diamond syndrome is an autosomal recessive bone marrow failure syndrome with exocrine pancreatic insufficiency. Additional organ systems, such as the liver, heart and bone, may also be affected. We report a patient with a long history of cardiac failure and diagnosis of dilated cardiomyopathy with intermittent neutropenia. Periodic follow-up revealed progressive cardiac failure and pulmonary hypertension. A diagnosis of Shwachman–Diamond syndrome was made at the autopsy.

Keywords: Shwachman–Diamond syndrome; cardiac failure; dilated cardiomyopathy; neutropenia

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Case report

A 15-year-old girl was admitted to the intensive care unit with cardiogenic shock. She was diagnosed with dilated cardiomyopathy and cardiac failure at the age of 2 years at our hospital. At that time, routine laboratory investigation revealed neutropenia. Chest X-ray showed marked cardiomegaly and radionuclide angiocardiography demonstrated left ventricular ejection fraction of 24%. Radionuclide scanning after the administration of gallium was negative for inflammatory changes characteristic of myocarditis. During the 6 months before her first evaluation, she had episodes of pulmonary infection, otitis media, and flu. The patient lost follow-up until the age of 10 years, when she was readmitted to the hospital with decompensated cardiac failure. During that period, intermittent neutropenia was observed with the lowest neutrophil count of 559 cubic metres. Endomyocardial biopsy was performed which showed few scattered mononuclear inflammatory cells, but myocarditis was absent according to the histopathological Dallas criteria. At the age of 14 years, she was admitted for the first time to the intensive care unit with low cardiac output symptoms and diffuse abdominal pain. Routine liver and pancreas laboratory investigations – liver enzymes, bilirubins, and amylase – were normal. Abdominal ultrasound showed signs of congestive liver. An evaluation of pulmonary vascular resistance was performed which revealed pulmonary hypertension that excluded her for possible heart transplantation. During her last intensive care unit stay, despite high doses of IV inotropic agents, the patient had a complicated hospital course with acute renal failure. Cardiac arrest non-responsive to resuscitative efforts occurred 2 days after admission. Autopsy was performed and the heart showed typical features of dilated cardiomyopathy (Fig 1), such as global dilation, increased weight (478 grams), thinning of fibres, and extensive areas of interstitial fibrosis. Death was caused by the occlusion of the right pulmonary artery due to thromboembolism. An important finding was the extensive fatty replacement of the exocrine pancreatic tissue (Fig 2). At the bone marrow, mild hypoplasia, mostly from white series, was noted. Another pathological finding was lung fibrosis at both inferior lobes, with irregular but well-delineated boundaries. At these areas, vessels

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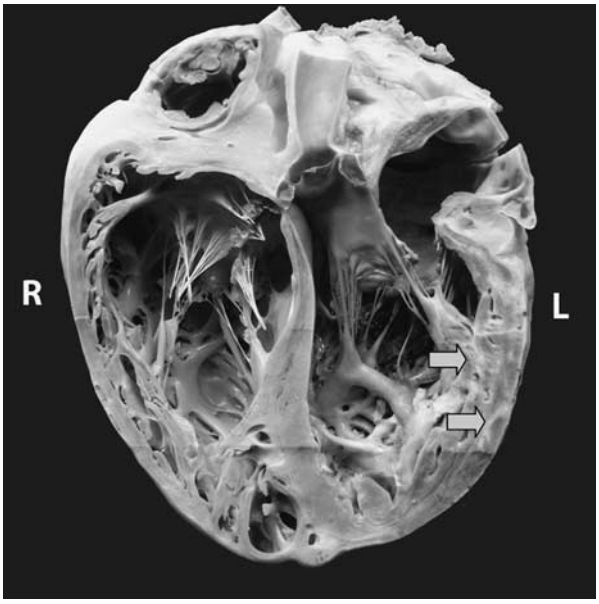

Figure 1.
Sagittal section of the heart, which is dilated and presents areas of fibrosis, as those pointed by arrows. L – left side; R – right side.

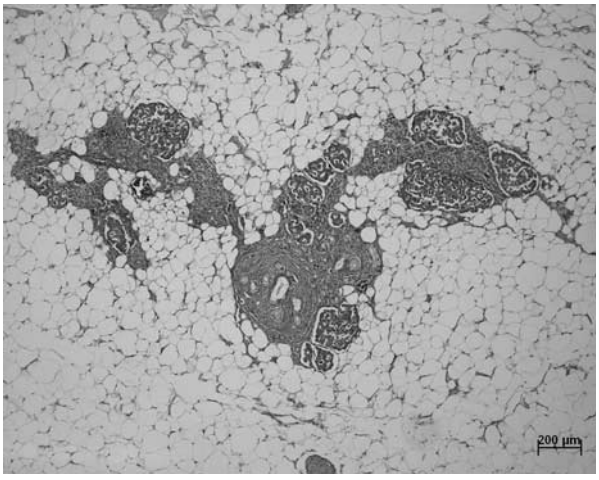

Figure 2.
Histological section of the pancreas showing fat replacement of the exocrine glandular tissue. The remaining parenchyma is composed mostly of islets of Langerhans (haematoxylin and eosin staining; objective magnification ×5).

presented features of pulmonary hypertension and organised thrombus.

Discussion

The Shwachman–Diamond syndrome is a rare autosomal recessive multi-system disorder, first described in 1964,[1] in which the principal manifestations include bone marrow dysfunction, exocrine pancreatic insufficiency, and skeletal abnormalities with failure to thrive. This genetic disorder is also related to the involvement of other organ systems such as the liver and heart. The Shwachman–Bodian–Diamond syndrome gene, located on chromosome 7, was identified as a causative gene for Shwachman–Diamond syndrome in 2003.[2] Since then, a number of different mutations affecting the Shwachman–Bodian–Diamond syndrome gene are described, expanding the molecular diagnosis now available.[3] Haematologically, Shwachman–Diamond syndrome is characterised by varying degrees of intermittent or persistent neutropenia and an increased risk of myelodysplastic syndrome and leukaemia.[4] Anaemia and thrombocytopenia may also be present. The clinical phenotype of Shwachman–Diamond syndrome is highly variable, showing a wide range of abnormalities making the diagnosis challenging in some patients, particularly in the older ones, when symptoms such as steatorrhoea had resolved and neutropenia was intermittent.[5] Our patient never had a complaint that suggested steatorrhoea and always showed intermittent neutropenia with normal levels of haemoglobin and platelets. Patients with Shwachman–Diamond syndrome are susceptible to recurrent bacterial, viral, and fungal infections, including sinusitis, otitis media, bronchopneumonia, osteomyelitis, septicaemia, and skin infections. Primary causes of death in Shwachman–Diamond syndrome during infancy are related to malabsorption, severe bacterial infections, and thoracic dystrophy. In older patients, major causes of morbidity and mortality are associated with haematologic abnormalities, such as bone marrow aplasia, myelodysplastic syndrome, or acute leukaemia.[4] Despite their infrequency, cardiac manifestations of Shwachman–Diamond syndrome were described such as myocardial necrosis or fibrosis seen on histopathology and increased risk of fatal cardiac failure in infants.[6] In our patient, death was related to cardiac disease. As viral and other infections are frequent during the first years of life in Shwachman–Diamond syndrome patients, the aetiology of cardiac disorder could be attributed to a myocardial complication of an infection, like viral myocarditis. However, since no signs of inflammatory process were found in our patient, either at the non-invasive radionuclide study or at the myocardial biopsy, it seems more likely that her cardiomyopathy was associated with the syndrome. Lung fibrosis could be related to previous infarctions, even though this morphological pattern is not common, or be secondary to an abnormal healing process of repeated infectious episodes in a potentially immunocompromised host. These lung alterations possibly contributed to the hypertrophy and dilation of the right side of the heart. Some patients with Shwachman–Diamond syndrome-associated bone marrow dysfunction may require bone marrow transplantation. Cardiac complications

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were described in this population, specifically cardiac failure during induction chemotherapy and long-term cardiac dysfunction after the procedure. As a result, investigation of the anatomical and function features of the heart should be done carefully because of the prognostic and therapeutic implications.[7]

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