A 12 month old female infant born at full term by spontaneous vaginal delivery presented at Sultan Qaboos University Hospital, Oman. Her birth weight was 3.23 kg, length 50 cm and head circumference 34.5 cm, all appropriate for her gestational age. The parents were first cousins and had lost three male children due to repeated severe infections. This infant developed chronic diarrhoea, recurrent chest and skin infections from the age of six months, and subsequently had failed to thrive with a weight, height and head circumference < 3rd centile for age. The physical examination revealed subtle facial dysmorphic features, partial bilateral ptosis, generalized hypotonia, mild hepatomegaly and developmental delay. Investigations revealed hypochromic microcytic anaemia with a haemoglobin range 6-9 g/dl secondary to loss from the gastrointestinal tract. Her liver enzymes were mildly elevated during the time of infectious 

Figure 1: Demonstrates the presence of vacuoles in the bone marrow precursor cells, a characteristic feature seen in the Pearson's marrow-pancreas syndrome
episodes. In the course of time, she developed intermittent severe neutropenia < 0.5/ cumm. Bone marrow examination demonstrated hypercellular marrow with erythroid hyperplasia, the myeloid cell line showed normal maturation, but vacuolations were seen in keeping with a diagnosis of Pearson's marrow-pancreas syndrome. Other investigations revealed normal serum creatinine kinase 17u/l (26-140), and normal motor sensory nerve conduction studies for age. The evaluation of her chronic diarrhea included endoscopy that revealed non-specific superficial inflammation. There was no evidence of coeliac disease or inflammatory bowel disease. Examination of fat in the stool was not feasible. A trial dose of supplemental pancreatic enzymes improved the diarrhoea and the child started to gain weight, while her anaemia required blood transfusion. The neutropenia showed some response to granulocyte colony stimulating factor; however the patient experienced a fulminate sepsis and died of multi-organ dysfunction.

Pearson's marrow-pancreas syndrome was first described by Pearson et al. in 1979. This is a rare multi-system disorder with a poor prognosis. The defining features are marrow failure, anaemia, neutropenia, thrombocytopenia and characteristic vacuolation of haematopoietic precursors. An additional defining feature of Pearson's syndrome is dysfunction of the exocrine pancreas due to fibrosis and acinar atrophy resulting in malabsorption and chronic diarrhoea with fatty stool. Another cardinal feature of Pearson's syndrome is persistent or intermittent lactic acidaemia, which is caused by a defect in oxidative phosphorylation. Variable hepatic, renal, and endocrine failure may also occur. The genetic defect in Pearson's marrow-pancreas syndrome has been found to be a deletion in the mitochondrial DNA. The most common deletion reported is a 4977 base pair deletion identified in > 80% of affected children. In the literature, there is a clear evidence of clinical phenotype homogeneity which has been attributed to genetic variability in the proportion of mt DNA deletions.

References