Comprehensive work-up is required for patients with Pearson syndrome

With interest, we read the article by Martínez de Zabarte Fernández et al., about two pediatric patients with Pearson syndrome (PS) with pancytopenia in both and pancreas insufficiency in the second.[1] We have the following comments and concerns.

Though deletion of mitochondrial DNA (mtDNA) causing PS is usually sporadic there is the possibility that mtDNA deletions are maternally transmitted, as has been reported earlier by Shanske et al. Did either of the two mothers present with phenotypic features of mitochondrial disorder (MID) indicating MID? Were the two mothers investigated for mtDNA deletions?

mtDNA deletions are usually heteroplasmic, with a mixture of mitochondria carrying the wild-type mtDNA and mitochondria carrying the mutant mtDNA. Which were the heteroplasmy rates in the two patients and did they vary between different tissues, such as hair follicles, buccal epithelial cells, fibroblasts, lymphocytes, urine bladder epithelial cells, or muscle?

mtDNA deletions in PS may be associated with partial duplications of the mtDNA. Was mtDNA of the two patients investigated for the presence of partial duplications?

Pearson marrow-pancreas syndrome is a multisystem MID characterised by bone marrow failure and pancreatic insufficiency. Patients who survive the severe bone marrow dysfunction in childhood develop Kearns-Sayre syndrome (KSS) or Leigh syndrome (LS) later in life.[2] Were the two presented patients followed-up and did they develop multisystem MID with features of KSS or LS?

Aseptic pancreatitis is a frequent manifestation of a MID.[3] Pancreatitis may go along with severe abdominal pain, elevated amylase and lipase, and reduced exocrine pancreatic enzymes, but without morphological alterations of the pancreas. Was amylase or lipase elevated in any of the two patients? Patient 1 did not present with pancreas insufficiency.[1] Was the patient prospectively investigated for this gastrointestinal abnormality?

Patients with PS may also present with failure to thrive and organic aciduria with low levels of citrullin and arginine despite low levels of ammonia suggesting insufficiency of the ornithine transcarbamylase.[2] Was there any indication for these abnormalities in any of the two presented patients?

Patients carrying single mtDNA deletions may also present with hypoglycaemia, short stature, sensorineural hearing loss, retinitis pigmentosa, and gastrointestinal dysmotility.[4] Were any of these features present in any of the two patients?

Single patients with PS may develop corneal endothelial dysfunction resulting in corneal edema in addition to other ophthalmologic abnormalities. Did any of the two patients undergo ophthalmologic investigations to investigate if there was corneal epithelial dysfunction or retinitis pigmentosa?

Conversion of PS to a multisystem disease with hypotonia, ataxia, and tremor may take place already one year after birth why these patients should be regularly followed-up for progression of the phenotype.[5] Was there any indication for early conversion to multisystem disease in any of the two?

Overall, the report about these two interesting cases could profit from further investigations of the index cases and their mothers. Maternal inheritance must be excluded to effectively counsel both mothers. Long-term follow-up of these patients is warranted, to see if they survive spontaneously and which phenotypic manifestations they present with after surviving the early stage of the disease.

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References

1. Martínez de Zabarte Fernández JM, Rodríguez-Vigil Iturrate C, Martínez Faci C, et al. Anemia arregenerativa en el lactante: 2 casos de síndrome de Pearson. *Arch Argent Pediatr* 2017;115(1):e24-7.
2. Crippa BL, Leon E, Calhoun A, et al. Biochemical abnormalities in Pearson syndrome. *Am J Med Genet A* 2015;167A(3):621-8.
3. Finsterer J. Pancreatitis as a manifestation of mitochondrial disorder. *Am J Med Genet A* 2007;143A(6):632-3.
4. Liu HM, Tsai LP, Chien YH, et al. A novel 3670-base pair mitochondrial DNA deletion resulting in multi-systemic manifestations in a child. *Pediatr Neonatol* 2012;53(4):264-8.
5. Lee HF, Lee HJ, Chi CS, et al. The neurological evolution of Pearson syndrome: case report and literature review. *Eur J Paediatr Neurol* 2007;11(4):208-14.