NEONATAL DIABETES SECONDARY TO ISOLATED PANCREATIC AGENESIS

Sarah Bakhamis MD, Afaf Al-Sagheir MD
Pediatric department, King Faisal Specialist Hospital and Research Centre

ESPE 2021 The 59th Annual Meeting Online 22-26 September 2021

مستشفى الملك فيصل التخصصي ومركز الأبحاث
King Faisal Specialist Hospital & Research Centre
Gen. Org. مؤسسة عامة

BACKGROUND

Pancreatic agenesis has been reported as a cause of neonatal diabetes. Most commonly it was associated with severe neurodevelopmental problems caused by Homozygous mutations in the transcription factor PTF1A. Isolated pancreatic agenesis was related to biallelic mutations in an enhancer located near PTF1A gene, which suggests that the enhancer is tissue specific to the pancreas.

PDX1 is another transcription factor gene in which biallelic mutation resulted in neonatal diabetes in the absence of exocrine pancreatic insufficiency.

THE PATIENTS

2 siblings (Currently, 18 years old boy and 15 years old girl) from consanguineous parent diagnosed with early onset neonatal diabetes. They delivered at term by normal spontaneous vaginal delivery, with normal birth weight. Clinically, there were no dysmorphic features or impaired neurological manifestations.

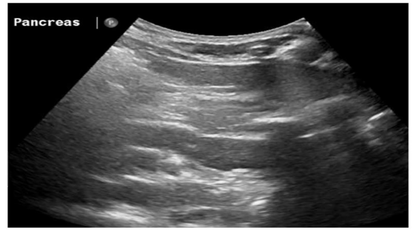
They presented on the first 3 days of life with high blood glucose not related to stress or medications and started on Insulin during the first week. Insulin doses were adjusted based on their need.

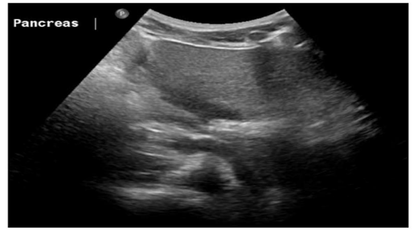
Throughout their clinical course, they were evaluated for short stature and failure to thrive. Celiac screening was positive in the older boy but negative for the girl. They were complaining of recurrent foul-smelling diarrhea, which was greasy and hard to flush, diagnosed with malabsorption and ADEK vitamins deficiency and started on replacement therapy.

INVESTIGATIONS

	Patient 1 (Boy)		Patient 2 (Girl)	
	Before Treatment	**After Treatment**	**Before Treatment**	**After Treatment**
Vitamin A (343-838 ug /L)	265	620	<95	342
Vitamin D (50 – 75 nmol /L)	15	43	23	73
Vitamin E (5.5 - 15.5 mg /L)	4.3	6.1	5.2	8.2
Vitamin K (0.1 – 2.2 ng /ml)	0.04	0.27	0.06	0.41

- MRI Abdomen of both patients showed no visualization of the pancreas within its expected location compatible with pancreatic agenesis.
- Brain MRI was normal in both patients.



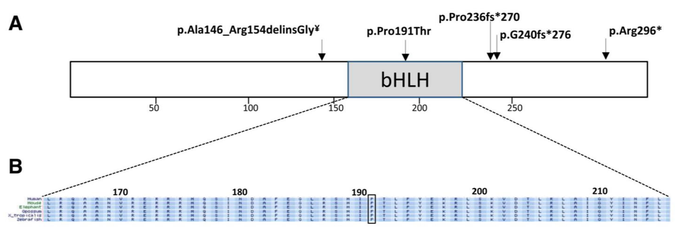


US abdomen showed pancreatic agenesis in patient-1, and partially seen small pancreases (body) in patient-2

GENETIC TEST

Whole exome sequencing of both patients showed homozygous missense mutation (PTF1A, exon1: c.571C>A: p.(Pro191Thr)), classified as variant of unknown significant causing isolated pancreatic agenesis.

This variant had been reported once by Houghton et al., 2016 as hypomorphic PTF1A mutation in four individuals from two separate families from Saudi Arabia and Kuwait with same presentation. They described this variant as founder mutation with 75% reduction of DNA binding and transactivation activity.



CONCLUSIONS

Hypomorphic PTF1A missense mutations can cause isolated pancreatic agenesis. This mutation should be considered in patients presenting with neonatal diabetes without neurological manifestations especially in a child with consanguineous parent. Patients with this mutation has been reported in our region which could be a founder mutation.

REFERENCE

Houghton J, Swift G, Shaw-Smith C, Flanagan S, de Franco E, Caswell R, Hussain K, Mohamed S, Abdulrasoul M, Hattersley A, MacDonald R, and Ellard S. Isolated Pancreatic Aplasia Due to a Hypomorphic PTF1A Mutation. Diabetes 2016;65:2810–281.