

A RARE CAUSE OF DIABETES INSIPIDUS: CONGENITAL PROPROTEIN CONVERTASE 1/3 DEFICIENCY

Gülay Karagüzel¹ Murat Çakır² Ulaş E Akbulut² Andreas Janecke³
Ayşenur Ökten¹

¹Department of Pediatric Endocrinology, ²Gastroenterology, Karadeniz Technical University, School of Medicine, Trabzon, Turkey, ³Division of Human Genetics, Innsbruck Medical University, Innsbruck, Austria

INTRODUCTION

Proprotein convertase 1/3 (PC1/3) deficiency, an autosomal-recessive disorder caused by rare mutations in the proprotein convertase subtilisin/kexin type 1 (PCSK1) gene, has been associated with severe malabsorptive diarrhea and certain endocrine abnormalities.

To date, only 13 subjects with PC1/3 deficiency have been reported, now we want to report a new patient who was diagnosed PC1/3 deficiency with novel PCSK1 mutation and diabetes insipidus.

CASE REPORT

A 3-month-old girl was referred to our clinic for the investigation of severe intractable diarrhea. She was the first child of non-consanguineous parents. She suffered from watery diarrhea started on the 9th postnatal day and persisted despite oral feeding with a variety of whole protein, hydrolysate, and amino acid-based infant formula feeds. There was no improvement on a therapeutic trial of pancreatic enzyme supplements.

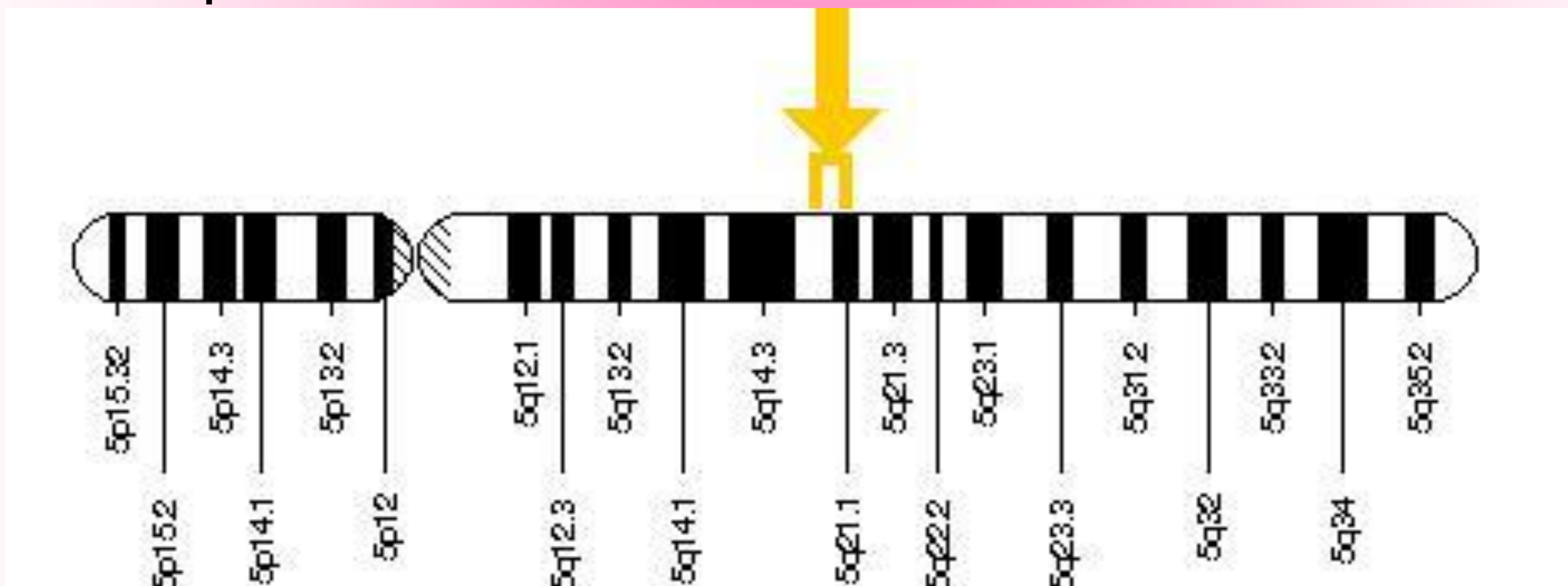


Figure 1 : Cytogenetic location of *PCSK1* gene (5q15-q21).

She required long-term parenteral nutrition while establishing her on a hydrolyzed feed. She also had hypernatremic dehydration and polyuria at the presentation. Urine density was low and diabetes insipidus was diagnosed by DDAVP test. Serum levels of corticotropine, cortisol, growth hormone, and free thyroxine were normal, proinsulin was high (81.07 pmol/L). We clinically diagnosed of the patient as PC1/3 deficiency and confirmed the diagnosis by demonstration of a novel homozygous PCSK1 mutation.

CONCLUSIONS

PC1/3 is expressed richly in endocrine cells in the gut, in the arcuate and paraventricular nuclei of the hypothalamus, and beta cells of the pancreas, where it has a well-defined role in processing proinsulin.

Diabetes insipidus was also reported the previous 8 patients. PC1/3 deficiency should be considered in patients presenting with intractable neonatal onset diarrhea and endocrinopathy like diabetes insipidus. Our case extends the clinical and molecular spectrum of human congenital PC1/3 deficiency.