Exocrine pancreatic insufficiency and vitamin K deficiency associated to Octreotide therapy in congenital hyperinsulinism: An under-recognized potential adverse effect.

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The authors have nothing to declare

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BACKGROUND

- Congenital hyperinsulinism (CH) is the most frequent cause of persistent hypoglycemia in the newborn.
- Octreotide, a long-acting somatostatin analogue (SSA), is a second line treatment for diazoxide unresponsive CH patients.
  - Although it has been found to be a safe and effective treatment, long-term benefits and side effects have not been thoroughly evaluated.
  - Furthermore, some authors have emphasized that exocrine pancreatic insufficiency is a common but under-recognized adverse reaction in adults treated with octreotide.
- To our knowledge, no pediatric patient with somatostatin analogue-induced pancreatic exocrine insufficiency has been reported to date.

OBJECTIVE

Our aim is to report the first case of an infant with CH and exocrine pancreatic insufficiency and secondary vitamin K deficiency, associated to Octreotide therapy.

CASE REPORT

- A 7 month and 3 week old male with diazoxide unresponsive diffuse CH (heterozygous autosomal dominantly mutation in the *ABCC8* gene; NM_000352.4:c.357del) was found with bruising of legs, back and forearms after two months of SSA treatment onset (8.9 mcg/kg/day divided into 4 daily doses)(Fig. 1 a,b,c). Bruises and bleeding remnants were also observed at the puncture points of the sensor (Fig. 1 a).
- In addition to intermittent capillary blood glucose measurement, Real-time subcutaneous continuous glucose monitoring was used for glycemic control (Guardian ™ Sensor 3; Medtronic Diabetes, Northridge, CA, USA)(Fig. 2).

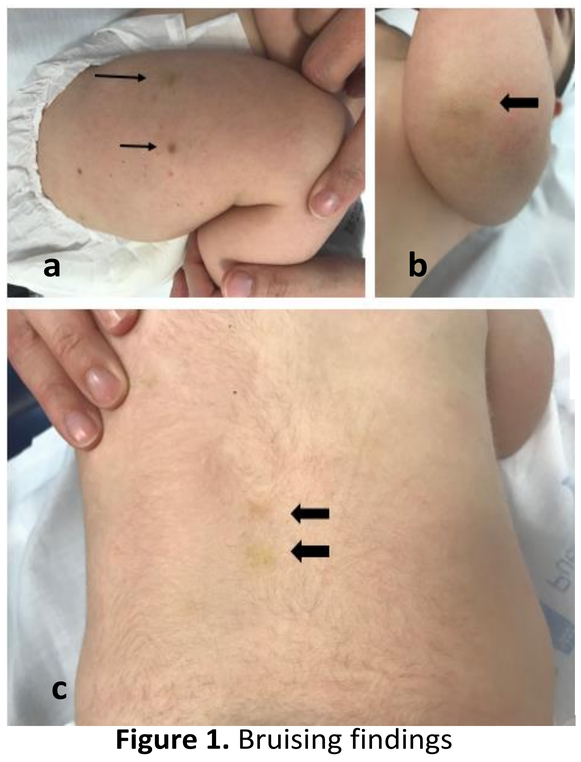

Figure 1. Bruising findings

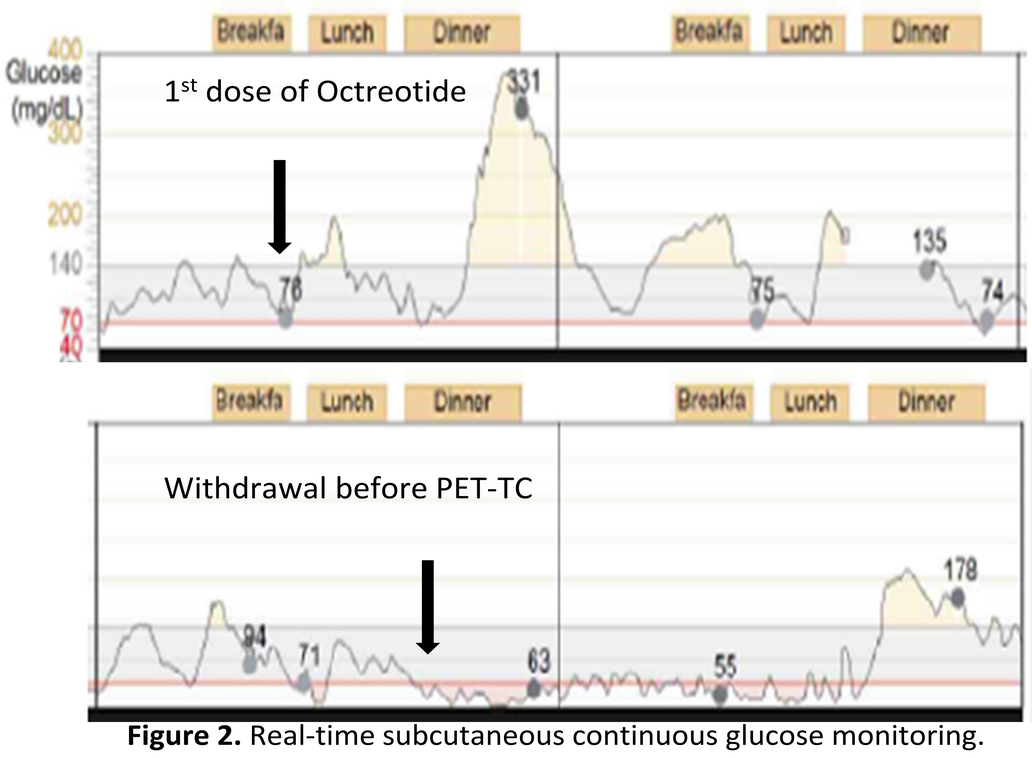

Figure 2. Real-time subcutaneous continuous glucose monitoring.

Table 1. Laboratory findings	Initial sample	After vitamin K	RR*
Blood analysis			
Prothrombin Activity	**7%**	**77%**	70-120%
Prothrombin Time	**117.4s**	**15.3s**	11.5-15.3s
International Normalized Ratio	**9.1**	**1.18**	0.8-1.2
Activated Partial Thromboplastin Time	**88.4s**	**36.7**	35-46s
Coagulation factors			
Factor II	**4%**	**45%**	7-120%
Factor VII	**10%**	**99%**	55-170%
Factor IX	**8%**	**55%**	60-150%
Factor X	**3%**	**60%**	70-120%

*RR: Reference range

Table 2. Fecal analysis	Initial samples	After enzyme replacement		NV*
Fat fecal quantification (g/24h)	19.1/18.2	8.1	2.9	< 6
Elastase-1 enzyme (mcg/g)	125	-	155	>200

*NV: normal values

- Laboratory findings identified vitamin K deficiency as the cause of the cutaneous hemorrhagic syndrome with an abnormal coagulation values and a decrease in all vitamin K-dependent proteins (Table 1).
- Coagulopathy was resolved with vitamin K treatment (5 mg/day intravenous; 3 days). The patient was discharged without incidents.
- Further investigations revealed association of steatorrhea and decreased fecal elastase-1 levels, both markers of malabsorption. Fecal Elastase-1 enzyme levels confirmed the exocrine pancreatic insufficiency, which was resolved after the pancreatic enzymes replacement (Table 2). Cystic fibrosis and bacterial overgrowth syndrome were excluded.

- Outcome: The patient is now 11 months old. He has adequate neurodevelopment, normal growth and weight pattern (Figures 3 and 4).
- He has also developed cholelithiasis requiring ursodeoxycholic acid therapy, with favorable outcome.
- He has required up to 11 mcg/kg/day of Octreotide .

Figure 3.

Figure 4. Weight and length chart

CONCLUSION

To emphasize the potential adverse effects and clinical relevance of the exocrine pancreatic insufficiency associated to Octreotide treatment I congenital hyperinsulinism.

1. Hosokawa Y et. al. Endocr J. 2017 Sep 30;64(9):867-880 2. Lamarca A et al. Expert Rev Gastroenterol Hepatol. 2018 Jul;12(7):723-731. 3. Saif MW, et al. Expert Opin Drug Saf. 2010 Nov;9(6):867-73.