Pseudothrombocytopenia in Type 1 Diabetes

A 5-yr-old girl diagnosed with Type 1 diabetes (T1D) since 1½ yr of age, and treated elsewhere with premixed insulins presented to our emergency department with complaints of vomiting, abdominal pain and altered sensorium for 1 day. She was treated for moderate diabetic ketoacidosis based on high blood glucose, positive urine ketones and metabolic acidosis (pH 7.107, HCO3 11.4 mEq/L). Her blood counts showed hemoglobin of 10.7 g/dL, platelet count of 86×10^9/L and total leucocyte count of 6×10^9/L. A repeat platelet count was 64×10^9/L, and peripheral smear suggested clumping of platelets. There were no bleeding manifestations. Suspecting ethylene diamine tetra-acetic acid (EDTA) dependent pseudothrombocytopenia (PTCP), the sample was repeated in EDTA, heparin, and citrate vials which showed platelet counts of 78×10^9/L, 408×10^9/L and 416×10^9/L, respectively. A diagnosis of EDTA - dependent PTCP was made and further workup for etiology of thrombocytopenia was withheld. The child was discharged after switching to basal bolus insulin regimen for a better glycemic control.

PTCP is a relatively uncommon laboratory phenomenon with estimated prevalence of 0.1%-0.3% in adults (1). Of the three types, namely EDTA-, heparin- and citrate-induced, the EDTA-PTCP is the most common [1,2]. The PTCP results from *in vitro* agglutination of platelets caused by IgG or IgM autoantibodies predominantly directed against epitopes on platelet surface glycoprotein (GP) IIb or IIIa [2]. EDTA induces a conformational change in GP IIb/IIIa, exposing these epitopes and resulting in platelet agglutination at low temperature [2]. This phenomenon is probably related to naturally occurring antibodies that cross react with platelet cryptoantigen exposed due to the effects of EDTA [2].

PTCP is an extremely rare condition in children and is described in association with autoimmune, neoplastic, chronic inflammatory and infectious diseases [3]. We could not find any previous reports of its occurrence in children with T1D; although, true thrombocytopenia of autoimmune and viral etiologies has been described in T1D [4]. There is a single report of an adult with T1D who developed PTCP after change in insulin therapy from premixed to basal bolus regimen [5]. However, he showed PCTP in both EDTA and heparinized samples unlike with only EDTA as in our patient [5]. Additionally, there was no recent change in insulin regimen in our patient. Thrombocytopenia without a bleeding diathesis should alert the attending physician to possibility of PTCP.

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Novel Heterozygous *PCCA* Mutations with Fatal Outcome in Propionic Acidemia

Propionic acidemia is an autosomal recessive disorder caused by a defect of propionyl-coenzyme A carboxylase [1]. We report a case of propionic acidemia with fatal outcome and two novel heterozygous *PCCA* mutations.

A male infant presented to us with vomiting and lethargy at 48 hours of life. He showed metabolic acidosis (pH 6.8, HCO3 10.1 mmol/L, base excess -17 mmol/L), and hyperammonemia (761 µM). Analysis of blood acylcarnitine profile indicated an elevated propionylcarnitine level (17 µM, cutoff <6 µM). The analysis of organic acids in urine by using GC-MS indicated an elevated concentration of 3-Hydroxy-propionic acid (153, cutoff: <1.1) and methylcitric acid (23, cutoff: <1.1). Despite restriction of protein supply,

high-caloric nutrition, correction of acidosis, and supplementation of biotin and carnitine, the infant died at 4 days of life. His two elder sisters had died after similar symptoms during the neonatal period. Blood samples from the infant and his parents were tested for genetic- and mutation analysis, after informed consent. Genetic analysis of the infant showed two heterozygous novel missense mutations [*PCCA* NM_000282.3: c.308T>G (p.V103G), *PCCA* NM_000282.3: c.809T>C (p.I270T)], and another heterozygous reported missense mutation [*PCCA* NM_000282.3: c.2002G>A (p.G668A)] in the *PCCA* gene [2]. The father was heterozygous for c.2002G>A (p.G668A). The mother was heterozygous for c.308T>G (p.V103G) and c.809T>C (p.I270T).

In about 80% of cases of propionic acidemia, clinical onset occurs in the neonatal period. In these patients, mortality is much higher than in the late-onset group. Several studies have addressed the possible genotype-phenotype correlations in propionic acidemia [3]. According to the clinical outcome of the patient in this report, there was a certain correlation between the genotype and the phenotype. A deeper insight of the correlation may be obtained by functional studies of the novel mutations in the *PCCA* gene.

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