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Case Report

A rare Presentation of Imerslund-Grassbeck Syndrome with Bicytopenia and Recurrent Respiratory Infections Since Neonatal period.

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Abstract

Background: Imerslund-Gräsbeck syndrome (IGS) is a rare autosomal recessive disorder characterized by vitamin B12 deficiency which results in megaloblastic anemia, failure to thrive, infections and neurological damage. Mild proteinuria is present in about half of the patients. The molecular basis of the selective malabsorption and proteinuria involves a mutation in one of two genes, cubilin (CUBN) on chromosome 10 or amnionless (AMN) on chromosome 14.

Case report: We report here the case of a 14 months old child, she had problems since neonatal age with frequent respiratory infections, fever, anemia, neutropenia and physical and developmental delay. Whole genome sequencing revealed a homozygous variant in AMN gene: AMN, c.1006+34_1007-32del, compatible with Imerslund-Grassbeck syndrome.

Discussion: Vary rarely Imerslund-Grassbeck syndrome can present with important symptoms since neonatal period. If the patients are not diagnosed and treated correctly, they may develop life threatening infections and severe neurologic abnormalities including seizures and developmental delay. Treatment with the right dose of vitamin B12 helps immune reconstitution and the patient recovers completely.

Case report

The patient VS, date of birth 24.09.2012, female, of Egyptian ethnicity, by normal delivery, birth weight 3600 gr. The child suffered frequent episodes with high temperature since she was 3 days old. Almost every month had episodes of fever and respiratory infections treated with iv antibiotics, frequent hospitalizations at the local hospital. She was vaccinated regularly according to our calendar of immunizations.

First presentation at Hematology Unit, UHCT, Tirana when she was 13 months old, because of severe anemia. She was diagnosed with Megaloblastic anemia, treated with iv antibiotics and RBC transfusions. On discharge it was prescribed oral drops of vitamin B12.

Second presentation at Pulmonology Unit, UHCT, Tirana: 14 months old admitted again because of severe anemia, bilateral pneumonia and respiratory insufficiency. She got treatment with Oxygen therapy, blood transfusion and antibiotics and then discharged home.

Third presentation at UHCT, Tirana: one week after discharge the child presents again at Pulmonology unit with high temperature, coughing, respiratory insufficiency, bilateral pneumonia, Sat O2= 75% in room air.

The problems observed:

1. Recurrent fever since neonatal age
2. Failure to thrive
3. Poor weight gain (the weight is 8.5 kg and the child is 15 months old)
4. Anorexia
5. Delayed growth
6. Physical and mental development delay: the child is 18 months, she can sit down without pillows but she doesn't walk, her legs look flaccid. Doesn't speak, she is aggressive and quite fretful.
7. Seizures several times, Epilepsy, treated with Depakine
8. Recurrent severe anemia, recurrent leucopenia, recurrent neutropenia
9. Recurrent pneumonia
10. Constipation since she was six months old, painful evacuation of normal stools (the child cries loudly), the mother refers that the child several times had bloody and mucoid stools, she uses regularly enema and lactulose solution.
11. Recurrent aphthae of the tongue
12. Recurrent palpebral oedema and distal oedema (hypoproteinemia during fever episodes)
13. Usually inflammatory syndrome is present (PCR 70, 100mg/dl)

Lab test results:

The Chest X ray shows bilateral hyper aeration, bilateral pneumonia. On Lung CT is evidenced Bilateral bronchial infiltrates, ground-glass opacities at the left lung. Heart ultrasound reveals DIA ostium secundum and a septum aneurism about 1cm. Normal abdominal ultrasound.

CBC (first admission): Entry WBC 5.300/mm^3, RBC 1.800.000/mm^3, HB 6.1g/dl, PLT 251000/mm^3, GRANULOCYTES 1000/microl, Reticulocytes 14%. At discharge after blood transfusions WBC 2.700/mm^3, RBC 3.300.000/mm^3, HB 10.1 g/dl, PLT 214.000/mm^3, GRANULOCYTES 500/microl.

CBC (second admission): Entry WBC 3.800/mm^3, RBC 1.700.000/mm^3, HB 4.9 g/dl, PLT 351000/mm^3, GRANULOCYTES 0/microl. At discharge after blood transfusions WBC 5.700/mm^3, RBC 4.300.000/mm^3, HB 11.1g/dl, PLT 214.000/mm^3, GRANULOCYTES 900/microl.

CBC (third admission): Entry WBC 2.200/mm^3, RBC2.200.000/mm^3, HB 8.6 g/dl, PLT 146000/mm^3, GRANULOCYTES 0/microl. At discharge after blood transfusions WBC 5.700/mm^3, RBC 4.300.000/mm^3, HB 11.1 g/dl, PLT 214.000/mm^3, GRANULOCYTES 1400/microl.

PCR was respectively 70 and 100mg/dl (in first admission and second admission). Total protein 4.5-5g/dl (low); B12 vitamin: 80.18pg/ml (low), LDH 2680 U/l- 2958 U/l- 2490U/l in three admissions. Urine complete: proteinuria 75mg/dl.

Sputum culture, Sweat test, Protein electrophoresis, IgG, IgM, IgA, Lymphocyte immunophenotype, C3, C4, IgA antibodies to tissue transglutaminase, Rheumatoid factor, Hb electrophoresis, G6PHD, Folic acid, Bilirubin were normal.

ANA, ANCA, Anti ds-AND/ IgG Human immunodeficiency virus serology, Coombs test (direct & indirect), Occult blood in feces were negative. Bone marrow aspiration: Active bone marrow. The erythroid series predominates, some of the erythroid elements are megalo. Bone marrow leucocyte immunophenotype: normal Contrast enema of the colon: revealed a slow movement of the contrast, but no transition zone as for Hirschsprung. Biopsy of the rectum: thickening of submucosa, a lot of inflammatory cells: neutrophils, monocytes, eosinophiles, lymphocytes. The aspect goes for chronic inflammation of the gut with signs of acute inflammation also.

EEG reveals diffuse paroxystic anomalies and on the MRI of the brain is seen Cerebral sub atrophy. ENG: electrophysiologic parameters of the lower limbs are normal. The family history: the parents are consanguineous, first child and the only one is the patient, no history of child death or abort.

According the history of the disease and lab test results we thought the child may have an immune-genetic disorder manifested with neutropenia and extra- hematopoietic multisystemic manifestations. It was suspected for interferonopathies and the child got checked for Aicardi goutier syndrome which came negative. During exacerbations the child was treated in hospital with iv antibiotics, RBC transfusions, Granulocyte Colony Stimulating Factor, human albumin. At home was prescribed to use GCSF2µgr/kg, s/c, every day; prophylactic dosage of Trimetoprime-sulphamethozasole, oral vitamin B12, Valproic Acid and lactulose.

Even on maintenance therapy the patient continued to have the same episodes of fever, neutropenia, recurrent pneumonias with respiratory insufficiency and no neurologic and somatic progress. Then we began treatment with intramuscular Vitamin B12. Everything changed, after one month the child came to the ward walking, she began to speak, the CBC normalized, no more infections and hospitalizations, no more seizures, she began to eat, the gastrointestinal transit got better. The follow up was spectacular after introduction of intramuscular VitB12.

Only 8 years latter (2021) we had the possibility to do whole genome sequencing which resulted a homozygous variant in AMN gene: AMN, c.1006+34_1007-32del, compatible with Imerslund-Grassbeck syndrome.

Discussion

Imerslund-Gräsbeck syndrome (IGS) is a rare autosomal recessive disease characterized by megaloblastic anemia, persistent proteinuria, failure to thrive, gastrointestinal and respiratory infections, and neurological abnormalities [1].

IGS is considered an orphan disease because of the low prevalence <6:1000000 inhabitants, about 300 cases are described in the literature [2].

IGS is caused by mutations in cubilin (CUBN) or amnionless (AMN) gene, which encode for the cubam receptor, which is responsible for the absorption of cobalamin in the small intestine and in renal proximal tubules [3].

We describe here an unusual case of a 14-month-old baby girl with recurrent respiratory infections and bicitopenia: megaloblastic anemia and neutropenia, which began since neonatal period. The age of onset was rather atypical because usually, symptoms begin between 1-5 years old, time when the level of fetal hepatic VitB12 decreases [4]. The most predominant complaint of our patient was recurrent respiratory infections, in the literature only 3% of the patients have respiratory symptoms [1]. Megaloblastic anemia, leucopenia and neutropenia are very frequent clinical findings in IGS, but are reversible after adequate therapy [5] Our patient had very interesting neurological phenotype: she had seizures which happen only in 6% of the patients, she had a physical and mental retardation, and on MRI was noticed Cerebral subatrophy which happens only in 3.8% of the patients with IGS [6].

Based on the age of the patient and respiratory symptoms we suspected for a congenital form of immunodeficiency. Our patient had gastrointestinal symptoms as constipation, failure to thrive, which happen in 32% of the cases [6]. She had also recurrent lesions of the mouth, in the literature we found that recurrent aftae of the mouth happen in 17% of patients [6].

The child had proteinuria, but normal renal function, which very characteristic of IGS. It is reported in the literature that 15% of the cases have comorbidities, but our patient had different comorbidity from the ones described in the literature [6]. She had DIA os and septal aneurism, hemodynamically important and she did a cardiac intervention to correct it.

We tried to correct the low levels of VitB12 by oral route but resulted ineffective, probably because we didn't try high oral dosages. We suspected a genetic problem, related to the genes that code Cobalamin, but had no possibility to exclude it. After introduction of intramuscular Vit B12 we saw a real success and continued the therapy in order to keep the level of VitB12 in the normal range. It was 8 years later that the genetic test confirmed the diagnosis of IGS. Whole genome sequencing is the gold standard to confirm the diagnosis and of course to improve patient management.

Lifelong vitamin B12 supplementation is the only available treatment for IGS. The prognosis of IGS is very good after supplementation of VitB12, [7], proteinuria persists all life long but it doesn't affect kidneys function [1,7].

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Authors' contributions

SB made the diagnosis, followed the diagnostic work-up, wrote the manuscript.

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Competing Interest

The author declares no competing interests.

References

1. Gräsbeck R (2006) Imerslund-Gräsbeck syndrome (selective vitamin B12 malabsorption with proteinuria). Orphanet J Rare Dis 1: 17.
2. Grasbeck R, Gordin R, Kantero I, Kuhlback B (1960) Selective vitamin B12 malabsorption and proteinuria in young people. A syndrome. Acta Med Scand 167: 289-296.
3. Imerslund O (1960) Idiopathic chronic megaloblastic anemia in children. Acta Paediatr 49(Suppl): 208-9.
4. Watkins D, Rosenblatt DS, Fowler B (2016) Disorders of Cobalamin and Folate Transport and Metabolism. In: Saudubray J-M, Baumgartner MR, Walter JH, editors. Inborn Metabolic Diseases. 6th editio. Springer pp. 385-399
5. Rasmussen SA, Fernhoff PM, Scanlon KS (2001) Vitamin B12 deficiency in children and adolescents. J Pediatr 138(1): 10-17.
6. Kingma SDK, Neven J, Bael A, Meuwissen MEC, van den Akker M (2023) Imerslund-Gräsbeck syndrome: a comprehensive review of reported cases. Orphanet J Rare Dis 14(1): 291.
7. Broch H, Imerslund O, Monn E, Hovig T, Seip M (1984) Imerslund-Gräsbeck anemia. A long-term follow-up study. Acta Paediatr Scand 73(2): 248-253.
8. Eslamiyeh H (2021) Acute cerebellar ataxia as the first manifestation of Imerslund-Gräsbeck. Iran J Child Neurol 15(4): 105-108.