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PANCYTOPENIA WITH PROTEINURIA – IMERSLUND GRASBECK SYNDROME

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ABSTRACT
A young girl with progressive generalized weakness and exertional dyspnea found to have pancytopenia and hemolysis due to vitamin B_{12} deficiency and associated with persistent proteinuria. A Case of Imerslund Grasbeck syndrome.
Key Messages: Imerslund Grasbeck syndrome is a rare autosomal disorder presenting as a triad of macrocytosis, proteinuria and vitamin B12 deficiency in an adolescent. Pancytopenia and hemolysis may be associated rare findings. Treatment is lifelong parentral vitamin 12.
Keywords: Imerslund Grasbeck syndrome; pancytopenia; vitamin B_{12} deficiency; proteinuria

1. INTRODUCTION
Imerslund-Gräsbeck syndrome (IGS) is a rare autosomal recessive disorder characterized by vitamin B_{12} deficiency malabsorption and proteinuria. The symptoms of anemia begin from the age of 4 months up to several years after birth. According to the studies the prevalence is about 1:200,000 in Finland and Norway. The etiology being a defect in the receptor of the vitamin B_{12}-intrinsic factor complex of the ileal mucosal cells. To the best of our knowledge around 300 reports have been published worldwide. There are hardly any cases reported with pancytopenia and hemolysis from south India. Hence reporting this unique case of pancytopenia , hemolysis and proteinuria which went undiagnosed for a long time when the treatment was simple parentral administration of vitamin B12 for life long.

2. CASE HISTORY
19 yr old girl from North Kerala presented with history of exertional dyspnea and progressive generalized weakness now for the last 2 months. There was no history suggestive of cardiovascular, renal or hepatic disease. No history of blood loss. However patient gave history of similar complaints in the past since the age of 6 years for which she had frequent admissions and blood transfusion. No other significant history in the past. She was on oral vitamins since then. On general physical examination, she was moderately built and nourished. Mild icterus and gross pallor were the obvious finding. Systemic examination revealed mild hepatosplenomegaly with no other significant systemic findings.

Her investigation (Table 1) showed significant anemia with decreased total leucocyte count and platelet count (pancytopenia). Liver function test showed hemolytic picture and LDH was raised. Serum iron, total iron binding capacity, serum ferritin and folic acid were normal. Peripheral smear showed many macrocytes, tear drop cells, pessary cells, and occasional nucleated red blood cells, white blood cells and platelets were reduced in number- pancytopenia. Vitamin B12 level was very low. Bone marrow aspiration showed megaloblastic hemopoesis.
Her past reports also showed similar picture and the fact that anemia was not corrected by oral vitamins proved that there was defect in absorption of Vitamin B12. Another important finding was persisting proteinuria with a normal renal function and anatomy. A diagnosis of IMERSLUND GRASBECK syndrome was made. She was treated with parentral vitamin B12 and there was increase in hemoglobin, total leucocyte count and platelet.

3. DISCUSSION
IMERSLUND GRASBECK SYNDROME: Imerslund-Gräsbeck syndrome (IGS) is a autosomal recessive disorder due to a defect in the receptor of the vitamin B_{12}-intrinsic factor complex of the ileal enterocyte characterised by vitamin B12 deficiency and persisting proteinuria. Usually the patient presents with symptoms of anemia such as easy fatigability, exertional dyspnea and growth retardation. An investigation usually reveals anemia and/or proteinuria. Investigation showed that the proteinuria was not typical of glomerular or

tubular origin.[1] It is to be noted that in IGS there is no deficiency of intrinsic factor or the vitamin B12- intrinsic factor complex. The defect is in the uptake of the complex by the ileal recetors. This is proved by the classic Schilling's test or the cobalamine absorption tests with radioactive vitamin B12 which demonstrates absorption defect even on supplementing intrinsic factor.[2,3] Certain genes such as cubilin (*CUBN*) gene and the amnionless (*AMN*) gene mutations are associated with IGS.[4] Pancytopenia can be accompaniment of vit B12 deficiency and there have been hardly few IGS cases reported presenting as pancytopenia along with other feature of selective vit B12 deficiency.[5]

The diagnosis of IGS requires the following: young patient with vitamin B12 deficiency which is due to malabsorption , with or without proteinuria and by showing that the condition is reversed by treating with parentral preparations of vitamin B12. Hemolysis and pancytopenia could be a part of ineffective erythropoesis due to vitamin B12 deficiency. However pancytopenia in a young patient could lead us investigating for other causes. Hence in every patient with pancytopenia one should work up for vitamin B12 deficiency which is very much treatable. Once a patient is diagnosed with IGS, all that is required is life-long treatment with vitamin B_{12} . The vitamin B_{12} deficiency is corrected by giving intramuscular injections of cobalamine - 1000mcg/day for first one week and then once a month for the rest of the patient's life.

The prognosis is particularly good with vitamin B12 supplementation. However patient continues to have persistent protenuria. It is to be noted that there is hardly any renal damage and there is no increase in proteinuria even on a long term follow up.

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TABLE 1: INVESTIGATION REPORTS WITH REFERENCE RANGE

INVESTIGATION	VALUES	REFERENCE RANGE
Hemoglobin	4 gm/dl	13- 17 gm/dl
Total leucocye count	3600 cells/mm^3	4000-10000cells/mm^3
Platelet count	1,17000 cells/mm^3	1.5-4 lakhs cells/mm^3
Blood urea	23mg/dl	10- 40 mg/dl
Serum creatine	0.4 mg/dl	< 1.4mg/dl
Total bilirubin	2.5mg/dl	0.2-1mg/dl
Indirect bilirubin	1.9mg/dl	< 0.8 mg/dl
Serum ferritin Serum iron TIBC	152.9ng/dl 138 mcg/dl 238mcg/dl	15- 150 ng/dl 50- 150mcg/dl 240-450mcg/dl
24 hours urinary protein	600mg/day	< 30mg/day
Stool occult blood	Negative	
LDH	12350 units/litre	< 270 units/ litre
SERUM VIT B12	42 .14 pg/ml	200-900pg/ml
SERUM FOLATE	9.19ng/ml	2.7-17ng/ml