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Case Report

A puzzle unravelled: pancytopenia and hepatosplenomegaly in juvenile autoimmune hypothyroidism

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ABSTRACT

Autoimmune thyroiditis is a common cause of hypothyroidism in adolescent females. While normocytic normochromic anemia is a recognized association with hypothyroidism, pancytopenia is seldom reported. This case report discusses a young adolescent girl with autoimmune hypothyroidism presenting with severe pancytopenia and hepatosplenomegaly. After extensive evaluation, hypoproliferative marrow with extramedullary hematopoiesis secondary to uncontrolled hypothyroidism was considered to be the most likely cause. Swift recovery following appropriate levothyroxine replacement further supports this hypothesis. Thus, hypothyroidism can be a potential cause of pancytopenia with hepatosplenomegaly. Early recognition and appropriate management can lead to prompt resolution and prevent unnecessary invasive procedures.

Keywords: Hashimoto's thyroiditis, Levothyroxine, Anemia, Hypoproliferative marrow, Extramedullary hematopoiesis, Endocrine disorders, Hematological manifestations

INTRODUCTION

Hypothyroidism is a well-known endocrine disorder characterized by decreased thyroid hormone production, which can lead to a wide array of symptoms affecting various organ systems. Autoimmune thyroiditis is a common cause of hypothyroidism in children.[1] While normocytic normochromic anemia is a recognized association with hypothyroidism, pancytopenia is seldom reported. This case report details the presentation of a young adolescent girl with poorly controlled hypothyroidism leading to pancytopenia and hepatosplenomegaly, which responded to appropriate levothyroxine replacement.

CASE REPORT

A 14-year-old girl, receiving sub-therapeutic levothyroxine for hypothyroidism for 7 years, presented with a 1-week history of progressive easy fatiguability, facial puffiness, and leg swelling. She denied any history of fever, jaundice, blood loss, dark-colored urine, oliguria, dyspnoea, chest pain, palpitations, syncope, pain abdomen, or paraesthesia. There was no history of malar rash, oral ulcers, alopecia, dry eyes, photosensitivity, joint swelling, bone pain, night sweats, or recurrent infections. She had a good appetite, without any recent significant weight loss or gain. There was no history of hot or cold intolerance, chronic diarrhea or constipation, or hoarseness of voice. She consumed a mixed diet, and her menstrual cycles were regular without excessive bleeding. Her psychomotor development was normal. There was no history of hospitalizations, blood transfusions, or surgeries, and no history of any drug intake apart from irregular levothyroxine consumption. There was a family history of hypothyroidism in maternal grandmother and uncle. On examination, she was conscious, oriented, and normally built. She had a temperature of 98.6˚F, pulse rate of 124 beats/minute, respiratory rate of 24 breaths/minute, blood pressure of 120/68 mmHg, and pulse oximetry

saturation of 99% on room air. Her weight (48.6 kg, 25-50th centile), height (154 cm, 25th centile), and body mass index (20.39 kg/m^2, 50th centile) were within the normal range. She had severe pallor, mild peri-orbital puffiness with bilateral pitting pedal edema and grade 2 thyromegaly without tenderness; there was no icterus, clubbing, lymphadenopathy, or hyperpigmentation. She did not have hemolytic facies or thyroid facies; teeth and oral cavity were normal. She had generalized dry and coarse skin; a focal hypopigmented patch over her left foot, and an eczematous patch over her left shin were noted. The abdomen was mildly distended and non-tender. There was soft, non-tender hepatosplenomegaly with liver palpable 4 cm below the right costal margin and span of 16 cm, spleen palpable 3 cm below left costal margin. Examination demonstrated bilaterally symmetrical normal vesicular breath sounds without any added sounds, normal jugular venous distension, and normal S_1 and S_2 heart sounds with a grade 3 ejection systolic murmur in the right and left second intercostal space. Neurological examination was unremarkable.

The patient's laboratory tests (Table 1) revealed pancytopenia with a hemoglobin of 2.6 g/dl with peripheral smear showing anisopoikilocytosis, predominantly microcytic hypochromic cells with pencil cells and tear drop cells without any hemoparasites or blasts; the corrected reticulocyte count was 1%. The total leucocyte count (TLC) was 2440/mm^3 with an absolute neutrophil count of 1430/mm^3 and an absolute lymphocyte count of 780/mm^3; the platelet count was 77,000/mm^3. She had a low serum iron (27 µg/dl, normal 50-170 µg/dl) and ferritin (0.9 ng/mL, normal 10-120 ng/ml), with an increased total iron binding capacity (429 µg/dl, normal 250-400 µg/dl), suggestive of iron deficiency. Serum vitamin B12 (193.5 pg/ml, normal 180-914 pg/ml) and folate (5.43 ng/ml, normal 3.1-19.9 ng/ml) levels were normal. Direct Coomb's test was negative, and lactate dehydrogenase and serum bilirubin levels were normal ruling out hemolysis. Haemoglobin electrophoresis did not reveal any abnormal variant. The serum electrolytes, and liver and renal function tests were within normal limits. Chest x-ray showed normal lung parenchyma and normal cardiac shadow without any mediastinal mass. Abdominal ultrasonogram (USG) confirmed hepatosplenomegaly with increased echotexture of the liver, without any evidence of hepatic fibrosis or portal hypertension. The human immunodeficiency virus antibody test was negative. Her thyroid stimulating hormone (TSH) level was 41.39 µIU/ml (reference range, 0.38-5.33 µIU/ml), with total triiodothyronine (T3) 0.8 ng/ml (reference range 0.87-1.78 ng/ml) and total thyroxine (T4) 3.9 µg/dl (reference range, 6.09-12.23 µg/dl), suggestive of uncontrolled hypothyroidism. USG thyroid demonstrated an altered echotexture, without any nodules, suggestive of thyroiditis; and she had elevated serum anti-thyroid peroxidase antibodies (anti-TPO, 212.2 IU/ml, reference range, <9.0 IU/ml) with a normal level of anti-thyroglobulin antibodies (anti-Tg, 1.9 IU/ml, reference range <4 IU/ml), thus confirming the diagnosis of autoimmune hypothyroidism. Bone age based on the X-ray imaging of the left wrist was reported to be 14-19 years. Anti-nuclear antibody (ANA) titers by indirect immunofluorescence, immunoglobulin-A tissue transglutaminase (IgA tTG) titers, glycated hemoglobin (HbA1c), intact parathyroid hormone (iPTH), serum cortisol and vitamin D levels were normal.

Table 1: Hematological and biochemical parameters of the index patient.

Parameter	Normal value	Index patient at admission	After 4 weeks
Hemoglobin (g/dl)	11.5-15.2	2.6	11.6
Mean corpuscular volume (µm^3)	77- 97	57.3	80.7
Mean corpuscular hemoglobin (pg)	26-32	16.4	32.8
Mean corpuscular hemoglobin concentration (g/dl)	32-35	28.6	33.2
Red-cell distribution width (%)	11-17	24.7	16.4
Total leucocyte count (/µl)	3500-10000	2440	5070
Absolute neutrophil count (/µl)	3000-5800	1430	3052
Absolute lymphocyte count (/µl)	1500-3000	780	1520
Platelet count (×10^3/µl)	150-400	77	269
Serum sodium (mEq/l)	136-145	139	
Serum potassium (mEq/l)	3.5-5	3.9	
Creatinine (mg/dl)	0.7-1.3	0.3	
Total bilirubin (mg/dl)	0-1	0.4	
Total protein (g/dl)	6.4-8.3	6.9	
Serum albumin (g/dl)	3.5-5.2	3.9	
Aspartate transaminase (U/l)	<35	15	
Alanine transaminase (U/l)	<45	10	
Alkaline phosphatase (U/l)	42-128	218	
Lactate dehydrogenase (IU/l)	225-450	287	

For severe anemia, she was transfused 3 units of packed red blood cells on 3 consecutive days, following which her hemoglobin improved to 6.5 g/dl. Levothyroxine was initiated at 100 mcg/day (previously she was on irregular treatment with 75 mcg/day thyroxine) for hypothyroidism. Iron-folic acid tablets were prescribed for the co-existent iron deficiency anemia. Bone marrow evaluation was planned if cytopenias and hepatosplenomegaly persisted after this treatment. Topical steroid application was advised for focal vitiligo with eczema. The patient's condition gradually improved with the resolution of pallor, edema, and regression of hepatosplenomegaly. Repeat blood counts done after 4 weeks of treatment showed resolution of cytopenias with hemoglobin 11.6 g/dl, TLC 5070/mm^3, and platelet count 260000/mm^3(Table 1). By the 3-month follow-up visit, TSH levels normalized, hepatosplenomegaly resolved, and she continued to have normal blood counts.

DISCUSSION

Autoimmune hypothyroidism is the most common cause of acquired hypothyroidism in non-iodine deficient populations, with the juvenile variant presenting before 18 years and being commoner in females.[1] Thyroid hormones increase the secretion of erythropoietin by inducing its gene expression and enhance erythropoiesis through the proliferation and differentiation of immature erythroid progenitors.[2,3] While mild anemia is seen in nearly 30% with hypothyroidism, pancytopenia is rarely reported. Anemia in hypothyroidism may be normocytic normochromic (due to a reduction in the renal secretion of erythropoietin or a physiologic adaptation to the decreased tissue oxygen requirements resulting from a decrease in the basal metabolic rate), hypochromic and microcytic (due to a defect in iron absorption), or megaloblastic (due to gastric atrophy with vitamin B12 malabsorption).[1]

Our patient had pancytopenia and hepatosplenomegaly with uncontrolled hypothyroidism. Initial possibilities of nutritional anemia, and hemolytic anemia were considered. Though she had iron deficiency, it cannot fully explain pancytopenia and hepatosplenomegaly. Serum B12 and folate levels were normal, ruling out megaloblastic anemia. The possibility of thalassemia and autoimmune hemolytic anemias were ruled out on evaluation. Pancytopenia and hepatosplenomegaly are commonly associated with leukemias and myeloproliferative disorders, however, there was no fever, bone pains, or lymphadenopathy; though confirmation would require a bone marrow examination. After extensive evaluation, the most plausible cause for the observed pancytopenia and hepatosplenomegaly was considered to be hypoproliferative marrow with extramedullary hematopoiesis secondary to uncontrolled hypothyroidism. An autoimmune reaction against the bone marrow could be a contributing factor. The patient's swift temporal recovery of pancytopenia and hepatosplenomegaly with appropriate levothyroxine supplementation further supports the likely cause. However, a concomitant infectious etiology like an atypical viral infection causing transient bone marrow suppression could not be ruled out with certainty.[4] Though few cases of pancytopenia in association with hypothyroidism have been reported in the literature, most were in adults, none were as severe as in our patient, and none of the cases reported hepatosplenomegaly.[5] Most reported resolution of pancytopenia in 4-8 weeks with levothyroxine with or without steroids and B12 supplementation. Laway et al reported pancytopenia with hypocellular marrow in three post-partum women with Sheehan syndrome and panhypopituitarism, wherein thyroxine and glucocorticoid supplementation led to full hematological recovery.[6] However, another report suggested that pancytopenia secondary to hypopituitarism may just be due to hypothyroidism alone.[7]

Additionally, the presence of focal vitiligo with autoimmune hypothyroidism in our patient prompted consideration of autoimmune polyglandular syndromes with a combination of endocrine and nonendocrine autoimmune diseases.[8] Vitiligo, a chronic autoimmune pigmentation disorder, is often associated with other autoimmune diseases; Hashimoto's thyroiditis is the most prevalent co-morbidity with 34% having positive thyroid antibodies. With tyrosine being the primordial parent molecule for both melanin and thyroxine, an oxidative stress-mediated toxicity may affect both skin and thyroid gland to produce vitiligo and autoimmune thyroid disease respectively.[9]

CONCLUSION

This case highlights the importance of considering hypothyroidism as a potential cause of pancytopenia and hepatosplenomegaly, particularly in patients with uncontrolled or undertreated disease. Early recognition and appropriate management with levothyroxine supplementation can lead to prompt resolution and prevent unnecessary invasive procedures. Further research is needed to elucidate the underlying mechanisms linking hypothyroidism, hematological abnormalities, and autoimmune disorders.

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