

Pancytopenia secondary to hypothyroidism in a 13-year-old male child

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Abstract

Thyroid hormones have a crucial role in erythropoiesis and metabolism. They enhance erythropoiesis through hyper proliferation of immature erythroid progenitors and increase secretion of erythropoietin by inducing erythropoietin gene expression. Thyroid dysfunction has various effects on blood cells such as anaemia, erythrocytosis leukopenia, thrombocytopenia, and in rare cases pancytopenia. The exact pathogenesis of anaemia secondary to hypothyroidism is not precisely explained but appears to reflect an adaptation to decreased tissue oxygen requirements resulting from a decrease in the basal metabolic rate. In reviewing the literature, there have been few previously reported cases of hematological abnormalities due to hypothyroidism, all of them concerning adults. In this article, we describe a rare case of pancytopenia secondary to hypothyroidism in a 13-year-old male child and its partial reversal after thyroid hormone replacement. Hypothyroidism should be considered in patients with unexplained pancytopenia. Further studies are needed to determine the exact underlying disease mechanism.

Introduction

The thyroid gland synthesizes and secretes two major hormones, known as 3, 5, 3'-triiodothyronine (T3) and 3, 5, 3', 5'-tetraiodothyronine (T4) or thyroxine, which have critical role in early brain development, somatic growth, bone maturation, protein synthesis and regulate production of red blood cells. Thyroid hormones also involve in hemoglobin production and maturation of hemoglobin in fetus [1].

In hypothyroidism anaemia of a mild degree is commonly present. Characteristically, the anaemia of hypothyroidism is normochromic and normocytic and is not correlated with the severity of the hypothyroidism. Less commonly it can be macrocytic or microcytic. Hypothyroidism also causes thrombocytopenia, leukopenia and in rare cases pancytopenia [2].

In this article, we describe a rare case of pancytopenia secondary to hypothyroidism in a 13-year-old male child.

Case report

A 13-year-old male child admitted to our department with a 24 hours history of febrile illness, headache and fatigue. One hour before the arrival he experienced an episode of loss of consciousness lasting 15 seconds. He had no significant past medical history and an unremarkable perinatal history (he was born full term, weighting 3.500 gr, with Apgar score 1¹⁰ and 5¹⁰). He was not taking any medication and there was a family history of Hashimoto's thyroiditis.

On physical examination he was in good general condition with a temperature of 36.4 °C, blood pressure 95/53 mm Hg, heart rate 92 beats per minute, and SpO₂ 99%. On examination, he appeared with dry skin, alopecia areata, myxedema, typical hypothyroid facial features and delayed relaxation of deep tendon reflexes. The rest clinical examination was unremarkable.

Laboratory analysis revealed the following: WBC: 3×10³/ μL (normal 5-18×10³/ μL), NEU: 65.4%, LYM: 20.9%, RBC: 3.55×10⁶/ μL (normal 2.8-5.3×10⁶/ μL), HGB: 11.5 g/dl (normal 10-17 g/dl), HCT: 34.4% (normal 37-52%), MCV: 96.9 fl, MCH 32.4 pg, PLT: 98×10³/ μL (normal 150-400×10³/ μL), ferritin: 318.7 ng/ml, Erythrocyte Sedimentation Rate: 37 mm/1 h, SGOT: 144 U/L (normal<80 U/L), SGPT: 184 U/L (normal<52 U/L), K⁺: 4.3 mEq/L, Na⁺:136 mEq/L, Ca⁺²: 9.19 mg/dl, P: 3.6 mg/dl, urea: 33 mg/dl, creatinine: 1.89 mg/dl, glucose: 83 g/dl, IgA: 93 mg/dl, IgG: 895 mg/dl, IgM: 96 mg/dl, IgE: 79.8 IU/L, C3: 74.3 mg/dl, C4: 15.3 mg/dl, CRP: 1.130 mg/dl, PT: 14.8 sec, APTT: 38 sec, INR: 1.22, Lactate Dehydrogenase: 450 U/L, creatine phosphokinase: 3690 U/L, Vitamin B12: 441 pmol/L, cortisol: 245 nmol/L.

To exclude any neoplastic disease, we performed a bone marrow biopsy which revealed a hypocellular bone marrow and was not indicative of any hematological or neoplastic disease.

Further investigations revealed normal autoimmune profile (ANA, dsDNA, ANCA, Ro/SS – A, Ro/SS – B, Sm, RNP, Scl 70, Jo1). The patient's thyroid function was abnormal with thyroid stimulating hormone (TSH) 100 μIU/ml (normal, 0.3–3.0 μIU/ml) and free T4 of 0.3 pmol/L (normal, 10 -25 pmol/L). Antithyroid peroxidase antibodies (Anti-TPO: 5 IU/ml, normal<35 IU/mL) and thyroglobulin antibodies (Anti-TG: 42 IU/ml, normal<20 IU/mL) were detectable. In evaluation of the thyroid gland, ultrasonography demonstrated a diffusely enlarged thyroid gland with a heterogeneous echotexture with the

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presence of hypoechoic micronodules. Colour Doppler study showed normal flow. The radiologic appearance was most consistent with Hashimoto thyroiditis. The patient had normal response to the ACTH test (Synacthen test).

A diagnosis of hypothyroidism was made based on the thyroid hormone production levels and thyroid gland ultrasonography. The patient received intravenously fluid resuscitation and treatment with levothyroxine sodium, administered orally, was initiated. The patient's symptoms of fatigue, as well as his hematologic abnormalities, resolved rapidly.

On subsequent endocrine outpatient follow-up 3 months later, the patient's repeat blood counts (RBC, PLT) and also thyroid function hormones had normalized showing resolution of pancytopenia. However, WBC remain below normal levels (approximately $3-4 \times 10^3/\mu\text{L}$) within 3 months of thyroid hormone replacement. The informed consent was signed by patient's parents.

Discussion

Thyroid hormones have a crucial role in erythropoiesis and metabolism. They enhance erythropoiesis through hyper proliferation of immature erythroid progenitors and increase secretion of erythropoietin (EPO) by inducing EPO gene expression. Thyroid hormones also augment repletion of hypoxia inducible factor1 (HIF-1) and then motivate growth of erythroid colonies (BFU-E, CFU-E) [3].

Thyroid dysfunction has various effects on blood cells such as anaemia (normochromic-normocytic, hypochromic-microcytic or macrocytic), erythrocytosis leukopenia, thrombocytopenia, and in rare cases pancytopenia. Hypothyroidism can cause anaemia through reducing the oxygen metabolism. The exact pathogenesis of anaemia secondary to hypothyroidism is not precisely explained but appears to reflect an adaptation to decreased tissue oxygen requirements resulting from a decrease in the basal metabolic rate. Hypothyroid individuals with anaemia and normal serum iron, B12, and folate levels, have an increase in haemoglobin soon after thyroid hormone replacement [4].

Alteration in other hematological parameters such as hemoglobin (HG), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), white blood cell count (WBC) and platelet count has also been associated with thyroid dysfunction. Pancytopenia is a rare side effect of hypothyroidism and its cause is not well understood. Immunological mechanisms have been associated with decline of erythrocytes' and platelets' life-span. Pancytopenia due to bone marrow hypoplasia has been reported in patients with myxoedema coma. Autoimmune reaction against bone marrow has

been suggested as the underlying cause. Acton et al. [5] reported pancytopenia in a patient with hypopituitarism and autoimmune hypothyroidism which immediately resolved with initiation of corticosteroid and thyroid replacement therapy. The association between hypothyroidism and raised levels of hepatic transaminases, especially when muscle weakness is a symptom, in the blood has been described and possibly attributed to highly variable release of enzymes from cells resulting presumably from individual metabolic set-point [6]. These abnormalities of liver function were normalized in all published cases after hormone replacement therapy.

Conclusion

In reviewing the literature, there have been few previously reported cases of hematological abnormalities due to hypothyroidism, all of them concerning adults. There is one published report of an 11-year-old girl who developed hypothyroidism and prolonged pancytopenia after radiotherapy. The pancytopenia resolved after thyroxine replacement [7]. We describe a rare complication of hypothyroidism, pancytopenia, and its reversal after thyroid hormone replacement. Hypothyroidism should be considered in patients with unexplained pancytopenia. Further studies are needed to determine the exact underlying disease mechanism.

Conflicts of interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. The authors received no financial support for the research, authorship, and/or publication of this article. The participation involved informed consent.

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