

Hashimoto's Thyroiditis in a Child with Familial Mediterranean Fever: a Case Report

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Familial Mediterranean Fever (FMF) is an auto inflammatory disease^[1] and also it can occur together with autoimmune disorders, such as Behçet's syndrome and systemic Lupus erythematosus^[2,3]. Here, we present Familial Mediterranean fever and Hashimoto's thyroiditis association in a 10-year-old girl.

This girl was admitted to our hospital with a history of intermittent abdominal pain, fever, headache and chest pain. Her complaints have been recurring two or three times every month lasting 4-5 days for approximately two years. On admission, the physical findings were remarkable for fever and general abdominal tenderness. Laboratory studies revealed elevated levels of C-reactive protein and fibrinogen. Urinalysis and stool were normal. Abdominal ultrasonography and direct abdominal X-rays were unremarkable. So, she was diagnosed as FMF with periodic fever, abdominal and chest pain^[4]. Her complaints resolved with colchicine treatment. DNA amplification analysis revealed a heterozygous E148Q mutation in the *MEFV* (Mediterranean fever) gene. On follow-up, after eight months of colchicine treatment she experienced some symptoms like progressively declining cognitive function, desire to sleep and fatigue. Her physical examination showed a smooth, painless thyroid enlargement. She had no other physical findings of hypothyroidism such as dry skin, hypothermia, decreased systolic blood pressure

and increased diastolic blood pressure and edema of lower extremities.

Complete blood count, glucose, calcium, electrolytes, renal and liver function test results were normal. Blood hormone levels were: TSH 2.03 mIU/mL (0.51-4.94), fT4 0.65 ng/dL (0.8-1.7), and fT3 4.2 pg/mL (2.3-4.2). The titers of thyroid antibodies were: anti-thyroid peroxidase (anti-TPO): >500 (0-60 IU/ml), antithyroglobulin (anti-TG): 370 (0-60 IU/ml). Other auto immune antibodies such as anti-gladiadin antibody (AGA), antiendomysium antibody (EMA), antinuclear antibody (ANA), double-strand DNA antibody (Anti dsDNA) were negative. Ultrasonography of the thyroid gland revealed slight heterogeneity and slightly enlargement of the gland. These findings were compatible with HT^[5]. Although her TSH level was normal, Levothyroxin treatment was started because of declining cognitive function, desire to sleep, fatigue and decreased fT4 level. After three months of treatment symptoms were resolved and the level of fT4 returned to normal. She has been followed for two years and has no additional problem.

Hashimoto's Thyroiditis (HT) is the most common cause of autoimmune thyroid disease in children and adolescents. T cells play a critical role in disease pathogenesis by reacting with thyroid antigens and secreting inflammatory cytokines. Patients with HT thyroiditis have blocking antibodies to thyroid peroxidase, thyroglobulin, and the TSH receptor. These autoantibodies are secondary to thyroid follicular cell damage induced by T cells^[6].

HT can be confirmed as the cause of hypothyroidism by measuring antithyroid antibodies, best done by measuring TPO Ab^[5,7]. The patient with HT shows typical ultrasound changes such as scattered hypo and hyperechogenicity in thyroid gland^[8]. Our patient had higher titers of antithyroid antibodies and revealed slight heterogeneity in thyroid ultrasonography so she was diagnosed as HT.

The thyroid gland may be asymptotically involved in most patients with systemic

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amyloidosis secondary to FMF. However, clinically detectable thyroid goiter is quite rare. The patients with amyloid goiter are clinically euthyroid despite the diffuse involvement of thyroid gland without antithyroid antibodies^[9]. Our patient had antithyroid antibodies and specific ultrasound findings so amyloid goiter was eliminated in the diagnosis.

Many different drugs may affect thyroid function through different ways. Alexander et al^[10] showed that colchicine treatment increased protein content in paraventricular nucleus and median eminence and decreased the plasma TSH of hypothyroid rats. Colchicine treatment of intact rats did not affect plasma TSH. There is no data about the effect of colchicine treatment on thyroid hormones and antithyroid antibodies in humans. Our patient's antithyroid antibodies were positive so we did not think that her findings were associated with colchicine.

Several studies have reported the coexistence of FMF with other autoimmune disorders, such as the Behçet's syndrome, SLE, juvenile idiopathic arthritis and juvenile diabetes mellitus^[2,3,11,12]. Also children with some chromosomal disorders or other autoimmune disorders are at increased risk for chronic autoimmune thyroiditis^[13]. In our patient AGA, EMA, ANA were negative. Clinical and biochemical data for other autoimmune disorders such as hypoparathyroidism, adrenal insufficiency, diabetes mellitus and autoimmune gastritis were negative.

An association of HT thyroiditis and FMF was reported rarely in the medical literature. Gulcan et al^[14] reported a 21-year-old woman who had FMF with HT like our patient. They argued that FMF and HT have similar pathophysiological mechanisms, and cytokine expression in FMF may provoke an autoimmune response^[12]. There is not enough data for this hypothesis but we think that the increased knowledge in this matter of coexistence of FMF and HT will give us more clues regarding the relationship between the two diseases. We report this case to increase awareness for coexistence of FMF and HT.

Key words: Familial Mediterranean Fever; Hashimoto's Thyroiditis; Auto Inflammatory Diseases; Autoimmunity

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