CASE REPORTS

Neurofibromatosis Type 1 Associated with Hashimoto's Thyroiditis

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Abstract

Hashimoto's thyroiditis is a common form of chronic autoimmune thyroid disease (AITD) and it often coexists with other autoimmune diseases, but Hashimoto's thyroiditis associated with an autosomal dominant neurofibromatosis type 1 is exceedingly rare. A 30-year-old woman presented with complaints of headache for 1 year on and off. Physical examination revealed nodular swelling in the neck, cafe-au-lait spots, and neurofibromas covering the entire surface of her body. Her thyroid hormones were within normal limits. Thyroid ultrasound revealed mild altered heterogeneous echo texture, multiple nodules of varying sizes, with hyper vascularity and ultrasound-guided fine needle aspiration cytology revealed lymphocytic infiltration of the gland, suggesting Hashimoto's thyroiditis. High levels of autoimmune antibodies such as antithyroglobulin and antimicrosomal antibodies confirmed the diagnosis. When encountering a patient with Neurofibromatosis type 1, the possibility of associated autoimmune diseases should be considered. So further studies of such patients having combination of neurofibromatosis type 1 and autoimmune thyroiditis will certainly provide better understanding of this link in the near future.

Introduction

Hashimoto's thyroiditis or goitrous autoimmune thyroiditis is a common form of chronic autoimmune thyroid disease (AITD). It occurs in 2% of the general population and is ten times more frequent in women than in men especially older women.[1] Neurofibromatosis type 1 (NF1) is an autosomal dominant neurocutaneous disorder, characterized by neurofibromas, cafea-au-lait spots, axillary and inguinal freckling, and Lisch nodules in the eye. NF1 is caused by mutation of the NF1 gene on chromosome 17q11.2. The NF1 gene encodes for neurofibromin, which acts as a tumor suppressor protein. NF1 associated with autoimmune diseases is rare. A review of the literature reveals that Hashimoto's thyroiditis associated with NF1 is extremely rare, and only few cases have been reported so far. 2,3 we present a case of Hashimoto's thyroiditis incidentally detected in a patient with neurofibromatosis type.

Case Report

A 30-year-old woman presented with complaints of headache for one year on and off associated with neck pain. She also complained of feeling lethargic with occasional breathlessness, weight gain and unable to tolerate cold places. Her family history revealed consanguineous marriage of her parents, and her father also had similar skin lesions all over the body. Physical examination revealed a large firm swelling with multi-nodular appearance in the front of the neck which moved with deglutition (Figure 1). Neurofibromas over the entire surface of her body, cafe-au-lait macules and axillary skin fold freckling were found.

Complete blood count, serum biochemistry, and urine analysis were normal. Our patient had serum levels of total thyroxine (T4) at 2.5 ug/dL (normal 4.5-12 ug/dl), triiodothyronine (T3) at 66.3 ng/mL (normal 80-180 ng/dL), and thyroid stimulating hormone (TSH) levels of 7.8 IU/mL (normal 0.35 to 5.5 ^U/mL). Thyroid ultrasound (US) revealed both lobes of thyroid showing mild altered heterogeneous echo texture with multiple nodules of varying sizes, largest being 0.8*0.6cm in right lobe and 0.7*0.6 cm noted in left lobe, with hyper vascularity not associated with lymphadenopathy. An ultrasound-guided fine needle aspiration cytology (FNAC) was carried out which showed follicular epithelial cells in singles and few cohesive clusters in acinar pattern with some of the follicular cells showing Hurtle cell change with plenty of lymphocytes and occasional plasma cells in a background

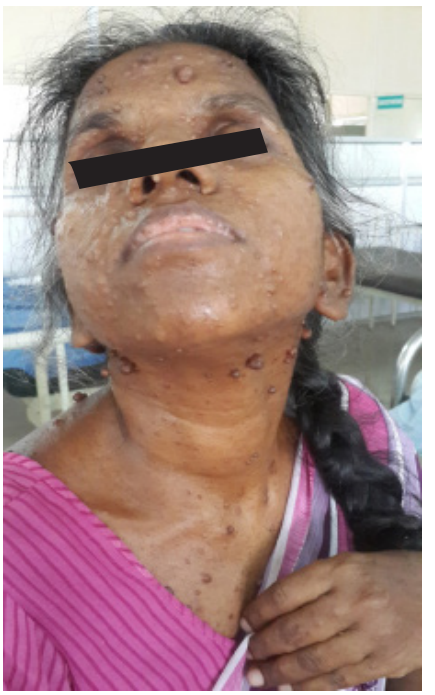

Fig. 1: Neurofibromas and swelling over neck

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of abundant colloid. The findings suggested the diagnosis of Hashimoto's thyroiditis. Antithyroglobulin levels were 618 IU/mL (normal range < 100 IU/mL), and anti-microsomal antibodies were >900 IU/mL (normal range was <35 IU/mL), confirming the diagnosis. US abdomen, ECG, Echocardiographic findings were normal.

Discussion

Hashimoto's thyroiditis has been shown to coexist with other autoimmune diseases such as type 1 diabetes, celiac disease, rheumatoid arthritis, multiple sclerosis, and vitiligo and with autoimmune polyendocrine syndrome type 2 (APS-2), which has two or more of following: Addison's disease (always present), AITD, and/or type 1 diabetes,[4] in the same patient.

However, association of Hashimoto's thyroiditis with neurofibromatosis 1 is very rare, since each of them follows a different pathophysiology. A comprehensive search of published literature revealed two more instances where NF1 was associated with autoimmune diseases, especially with vitiligo and autoimmune thyroiditis.[2,3]

NF1 (von Recklinghausen disease) is an autosomal dominant multisystem disorder, which affects approximately 1 in 3500 people. In 1987, seven cardinal diagnostic criteria for NF1 were established.5 If any two of the following seven criteria are met, a diagnosis of NF1 is made: (a) two or more neurofibromas on or under the skin or one plexiform neurofibroma, (b) freckling of the groin or the axilla (arm pit), (c) six or more cafe-au-lait spots measuring 5 mm in the greatest diameter in prepubescent individuals and over 15 mm in the greatest diameter in post pubescent individuals, (d) skeletal abnormalities such as sphenoid dysplasia or thinning of the cortex of the long bones of the body, (e) two or more Lisch nodules (hamartomas of the iris), (f) optic glioma, or (g) a first-degree relative with NF1. These diagnostic criteria are highly specific to adults with NF1.

Clinical presentation of neurofibromatosis and Noonan syndrome often overlaps and recent studies have implicated a mutation in NF1 gene in the etiology of NFNS.

Our patient presented with neurofibromas all over the surface of her body, multiple large cafe-au-lait spots, and axillary freckling along with a positive family history. The pathophysiology involves a mutation in NF1 gene, which encodes for a tumor suppressor protein neurofibromin, located on chromosome 17q11.2. Abnormal production of neurofibromin suppresses expression of fas-ligand, preventing apoptosis of CD4+ T-cells, which may contribute to the development of autoimmunity.6 It is hypothesized that such a mechanism may have led to Hashimoto's in our patient.

A growing number of cases reporting an association between neurofibromatosis type 1 and autoimmune thyroiditis point to a possible link between these etiologically different diseases. A comprehensive study using the published data from the reported cases may elucidate a veritable connection.

Conclusion

Neurofibromatosis type 1 is a common heritable neurocutaneous disorder and is rarely associated with Hashimoto's thyroiditis. It is pertinent for a physician diagnosing neurofibromatosis type 1 to be aware of the possibility of coexisting autoimmune diseases owing to increased reports of such association. More extensive studies are required to establish whether this association with neurofibromatosis type 1 is coincidental or a link in pathogenesis does exist.

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