Organ Specific Autoimmunity in Thyroid Disorders; A Case Presentation of Thyroid Eye Disease and Monophasic CNS Manifestation

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ABSTRACT

Idiopathic inflammatory diseases (IIDs) of the central nervous system (CNS) comprise a broad spectrum of disorders which may be differentiated according to the clinical presentation, neuroimaging and pathological findings. Systemic autoimmune diseases including vasculitis, Behçet’s disease, antiphospholipid syndrome and thyroiditis may also present with CNS manifestations and MRI findings of hyperintense lesions in the CNS. Graves’ disease is an autoimmune thyroid disease that might involve CNS and orbits in the setting of hyperthyroid, hypothyroid or euthyroid state. Findings of orbital involvement are proptosis, dry eyes, strabismus, and optic neuropathy. Recent literature has also proposed that altered thyroid function homeostasis might trigger subsequent demyelination. Here, we report a patient who presented with a hyperintense pontine lesion and oculary findings in the setting of hyperthyroid state. We aim to further discuss the underlying mechanisms leading to this presentation.

KEYwords: Autoimmune disorders, hyperthyroidism, Graves’ disease, multiple sclerosis

ÖZET

Merkezi sinir sisteminin (MSS) idiopatik inflamatuar hastalık çıklığı çok geniş bir spektrumu kapsar ve birbirlerinden klinik prezentasyon, nöro-görüntüleme bulguları ve lezyon patolojisine göre ayırt edilir. Vaskülitler, Behçet hastalığı, antifosfolipid sendromu ve tiroidit gibi sistemik otoimmun hastalıklar, ilk olarak MSS tutulum bulgularıyla ortaya çıkabilir ve manyetik rezonans görüntülemede (MRT) MSS’de hiperintens lezyon saptanabilir. Graves hastalığı MSS ve orbita etkileyebilen otoimmün bir tiroid hastalığıdır, klinik prezentasyon hipertiroid, hipotiroid veya ötiriod durumlarında da gözlenebilir. Göz bulguları arasında proptoz, strabismus, kuru göz ve optik nöropati bulunmaktadır. Son zamanlarda, tiroid işlevlerindeki değişimlerin demiyelinizasyonu tetikleyebileceği ileri sürülmüştür. Bu bildiride diplopiyle başvuran, MRG’sinde ponsa hiperintens lezyon gözlenen ve hipertiroidi olan bir hastayı sunarak, tiroid bozukluklarında MSS etkilenimini ve altta yatan mekanizmaları tartışmak istiyoruz.

Anahtar kelimeler: Otoimmün hastalıklar, hipertiroidi, Graves hastalığı, multipl skleroz

Introduction

Idiopathic inflammatory diseases (IIDs) of the central nervous system (CNS) comprise a broad spectrum of disorders which may be differentiated according to the clinical presentation, neuroimaging and pathological findings (1,2). Central pontine myelinolysis (CPM), steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT), Bickerstaff’s brainstem encephalitis (BBE) are some of the disorders that might present with a localized lesion that specifically involves the pontine area (3). Systemic autoimmune diseases including vasculitis, Behçet’s disease, and antiphospholipid syndrome may also present with neurological signs and hyperintense lesions in the CNS and these conditions should be considered in the differential diagnosis. Autoimmune thyroid diseases may initially present with SREAT which is a relatively rare condition. The clinical presentation consists of a subacute, sometimes relapsing-remitting, steroid-responsive encephalopathy with diffuse or focal neurologic signs, headache, altered cognitive function, neuropsychiatric symptoms, diffuse electroencephalographic abnormalities and elevated levels of antithyroid antibodies. Recent literature has reported the pathological features of SREAT as a complication of autoimmune thyroid disease. Biopsy showed primary CNS demyelination and neuroimaging revealed responsiveness to steroid treatment. The histopathological features included...
vasculitis involving venules and arterioles, lymphocytic perivascular cuffs and microglial activation (4). The pathogenesis of CNS manifestations of autoimmune thyroid disorders remains to be unknown; however, vasculitis and autoimmunity directed against common brain-thyroid antigens seem to be the most probable responsible pathways (5). Recent literature has also proposed that altered thyroid function homeostasis might be responsible for triggering a subsequent demyelination process (6). The clinical presentation has been attributed mostly to Hashimoto’s thyroiditis (HT) and less frequently to Graves’ disease (GD) (5). GD is also an autoimmune thyroid disease and the clinical presentation might involve the orbits leading to proptosis, dry eyes, strabismus, and optic neuropathy in the setting of hyperthyroid, hypothyroid or euthyroid state (7). Altered consciousness, involuntary movements, seizures, cognitive impairment, focal neurological signs, sensorial alterations, headache and psychiatric alterations have been reported in GD patients. Hyperintense white matter changes might be detected on MRI and appear to be reversible as previously reported also in case of HT (8,9).

In this article, we report a patient who presented with a monophasic hyperintense pontine lesion and ocular findings in the setting of a hyperthyroid state, and further discuss the underlying mechanisms.

Case Report

A 47-year-old female presented with primary complaint of oblique diplopia. The past medical and family history was nonremarkable. Her neurological examination revealed right lower extremity weakness (medical research council score of +4/5), however, cerebellar and sensory findings were normal, plantar reflexes, deep tendon reflexes were normoactive. Neuro-ophthalmological evaluation of the patient showed normal visual acuity (VA: 20/20 OD (right) and 20/20 OS (left)) and color vision (ISH 11/11 OU), fundus exam did not show any abnormality. However, further exam showed mild proptosis with Hertel exophthalmometric measures as: 20 OS, 22 OD. At the 6-month follow-up, thyroid function tests normalized (T3: 2.5, T4: 1.2, TSH: 2.44). The neuro-ophthalmological evaluation still revealed mild limitation in adduction and supraduction OD and, proptosis remained to be improved (Hertel exophthalmometric exam: 20 OS, 22 OD). No additional changes in extra-ocular eye movements were observed and the follow-up cranial MRI revealed that the hyperintense pontine lesion observed on T2 and FLAIR images on previous evaluations completely alleviated (Figure 1).

Discussion

Idiopathic inflammatory diseases of the CNS represent a wide spectrum of disorders with relatively specific clinical, laboratory and imaging findings. Here, we report a patient with a monophasic CNS lesion and a hyperthyroid state. Different entities might lead to localized pontine lesions including multiple sclerosis (MS), variants of MS, clinically isolated syndrome (isolated brainstem syndrome) or CNS lymphoma. In our case, the clinical picture was not compatible with the proposed diagnostic criteria for MS. The patient did not have any previous signs and symptoms that could be attributed to MS. The CSF evaluation was normal with no oligoclonal bands (OCB) and with normal IgG index. Follow-up MRI of the patient did not reveal any dissemination in space or time.

The clinical and MRI findings also precluded other possible diagnosis for IIDs (acute disseminated encephalomyelitis or neuromyelitis optica). A hyperintense lesion in the central pons treatments were initiated. After completion of the pulse therapy, the patient was on oral prednisolone that was gradually tapered. At discharge, 2 weeks after initiation of therapy, the patient’s complaints mostly resolved. The final neurological examination revealed mild supraduction and restriction of adduction OD as well as improved proptosis (Hertel exophthalmometric exam: 20 OS, 22 OD). At the 6-month follow-up, thyroid function tests normalized (T3: 2.5, T4: 1.2, TSH: 2.44). The neuro-ophthalmological evaluation still revealed mild limitation in adduction and supraduction OD and, proptosis remained to be improved (Hertel exophthalmometric exam: 20 OS, 22 OD). No additional changes in extra-ocular eye movements were observed and the follow-up cranial MRI revealed that the hyperintense pontine lesion observed on T2 and FLAIR images on previous evaluations completely alleviated (Figure 1).

Figure 1. A) Axial FLAIR MRI images reveal a hyperintense lesion in pontine area. B) The 12th month follow-up axial T2 weighted images reveal that the hyperintense pontine lesion resolved.
is the typical finding of CPM, which most commonly develops due to rapid correction of hyponatremia. The other disorders that might lead to CPM include malnutrition, chronic alcoholism, liver disease and organ transplantation, however, our patient did not have any previous history of the above mentioned disorders and the metabolic and hepatic panels were all within normal limits. Lymphoma also responds rapidly to corticosteroid treatment, however, a possible lymphoma was ruled out in our patient with the lack of systemic findings and with normal hematological evaluations. Differential diagnosis also included neuro-Behçet’s disease, CNS vasculitis and neurosarcoidosis, however the immunological and serological evaluations, chest X-ray and ACE levels were all within normal levels and these entities were ruled out.

Previous reports have suggested a possible relationship between autoimmune thyroid diseases and neurological involvement. GD is a thyroid disorder caused by an antibody-mediated autoimmune reaction with unknown etiology. Shared auto-antigens against the extraocular muscles and thyroid trigger a cascade of events leading to involvement of extraocular muscles and hyperthyroidism. Here, we present a patient with hyperthyroidism and extraocular findings compatible with GD. GD presents with lid retraction, exophthalmos, myopathy with muscle involvement that can be detected by MRI and optic neuropathy (7). Some evidence suggests that IgG plays an etiological role in the development of hyperthyroidism in GD and thyroid stimulating immunoglobulin (TSI) seems to aid in predicting relapse and identification of ophthalmic GD. Here, we present a patient with GD based on high thyroid hormone and low TSH levels as well as TSI level in the upper normal range (12%).

A recent study reported a patient with GD and Miller-Fisher syndrome and discussed the presentation of peripheral nervous system demyelination in the presence of thyroid disorders (11). Additionally, a recent report presented a case of concomitant GD and clinically isolated demyelinating disease in childhood linking thyroid and CNS dysfunction (12). In our case, the patient had a hyperintense lesion in the pontine area and the presenting symptom, subacute diplopia, might result from brainstem involvement due to the localization of the lesion. However, proptosis and eye movement dysfunctions seem to be more related to GD. It might also be speculated whether the MRI finding was due to a metabolic dysfunction secondary to the thyroid condition or was the expression of a concomitant disease. Thyroid disorders should be considered in patients with neurological dysfunction of unknown origin independent of the functional status of the thyroid and the nature of the underlying autoimmune thyroid disease itself.

It is important to consider the wide spectrum of symptoms that might present with thyroid diseases in order to reach an accurate diagnosis for prognostic and treatment implications.

References