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ORIGINAL ARTICLE

Autoimmune encephalitis associated with Graves' disease: a case report

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Abstract Almost all patients who developed autoimmune thyroid disease associated with encephalopathy were diagnosed to have Hashimoto's thyroiditis, but a few patients with Graves' disease who developed encephalopathy have been reported. A 36-year-old female with a 10-year history of Graves' disease had experienced three episodes of tonic–clonic seizure. At admission, the patient's status was confused, and she also developed tactile and visual hallucinations. The cranial MRI confirmed white-matter lesion and showed subcortical high signal lesions on T2-weighted images. In EEG record, diffuse slow activity was noticed in both sides. T3 and TSH were decreased, T4 remained normal and thyroid peroxidase antibody (TPO) was evaluated to be more than 2,000 (T4 = 8.4, T3 = 12/9, TSH = 0/14, TPO >2,000). The diagnosis of autoimmune thyroid disease is probable in all patients with signs of encephalopathy with unknown origin, while they have a previous history of thyroid disease.

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Introduction

Thyrotoxicosis and myxedema are well-known causes of dementia. Furthermore, thyroid-related autoantibodies (TRAb) are able to precipitate in an encephalopathy even in the euthyroid state. This was mentioned previously by Brain et al. [1] as Hashimoto's encephalopathy (HE). In general, thyroiditis and encephalopathy are the clinical manifestations of common underlying immunological disorders [2]. Based on this hypothesis, two probable mechanisms have been suggested for Hashimoto's encephalitis (HE). First, it can be an autoimmune-mediated CNS vasculitis resulting in disruption of microvasculature, which leads to cerebral edema and/or hypoperfusion [2–4]. Next, it can also be a direct reaction of an anti-neuronal autoantibody, specific for a shared antigen in the thyroid gland and in the brain. After the first report of HE, more than 100 cases have been reported [5]. Although, almost all patients who developed autoimmune thyroid disease associated with encephalopathy were diagnosed to have Hashimoto's thyroiditis, but a few patients with Graves' disease who developed encephalopathy have been reported [6]. Through this article, we explain a case with encephalopathy associated with autoimmune thyroid disease (EAATD) who also presented Graves' disease. We should emphasize on the point that the case was euthyroid at the diagnosis.

Case report

A 36-year-old female with a 10-year history of Graves' disease was referred to Noor Hospital, Isfahan, Iran, in

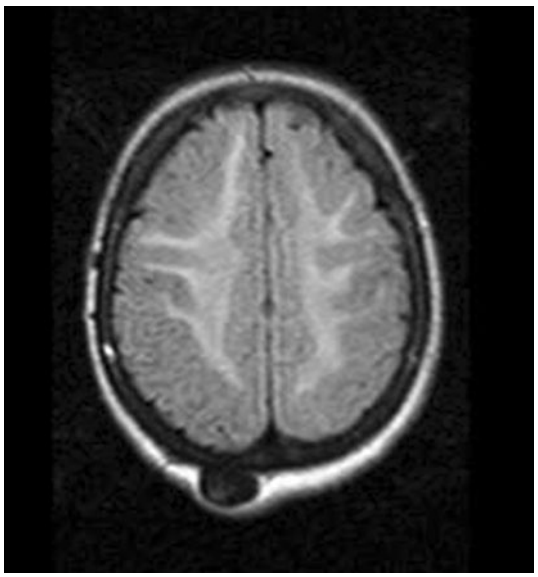

Fig. 1 Cranial MRI with white-matter lesion on T2-weighted image (section1)

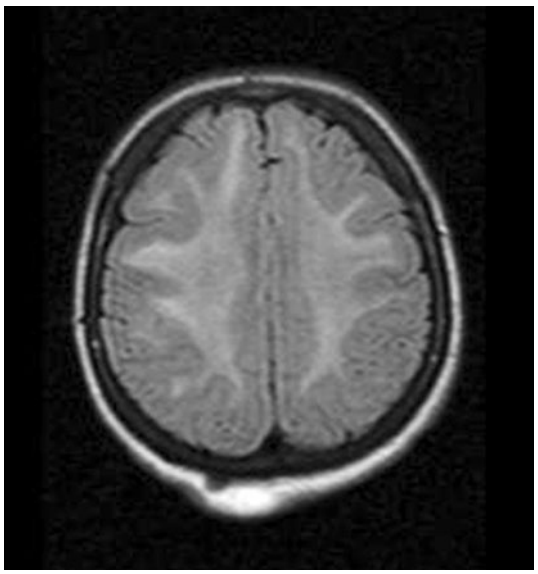

Fig. 2 Cranial MRI with white-matter lesion on T2-weighted image (section2)

August 2007. The referring purpose was evaluation of seizure and loss of consciousness (LOC).

She had experienced three episodes of tonic–clonic seizure in the past 16 days, which had lead to drowsiness 3 days before admission. At admission, the patient's status was confused, and she also developed tactile and visual hallucinations.

In her past medical history, since last year, she had experienced several short episodes of LOC, which had increased in the past 16 days. She was treated with radioactive iodide (in one episode) and propylthiouracil (an antithyroid drug) since last year.

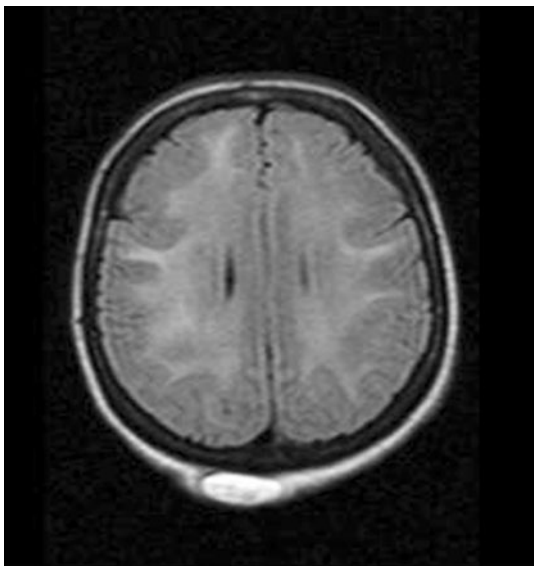

Fig. 3 Cranial MRI with white-matter lesion on T2-weighted image (section3)

On physical examination, she was confused, but there were no evidence of abnormalities in cranial nerves, motor and sensory systems and also she had no meningeal signs. Furthermore, she had bilateral extensor plantar responses.

In laboratory studies, hypochromic microcytic anemia and hyponatremia were detected (Hb = 9/B, MCH = 64/4 MCH = 19/14, Na = 128). Moreover, high CSF protein level without pleocytosis was discovered in LP (RBC = 0, WBC = 0, Pr = 101, COLU = S1). Graves' disease was confirmed by measuring anti-TG, anti-TPO and anti-TSH receptor antibodies. T3 and TSH were decreased, T4 remained normal and thyroid peroxidase antibody (TPO) was evaluated to be more than 2,000 (T4 = 8.4, T3 = 12/9, TSH = 0/14, TPO >2,000). The cranial MRI confirmed white-matter lesion and showed subcortical high signal lesions on T2-weighted images (Figs. 1, 2, 3). In EEG record, diffused slow activity was noticed in both sides.

Following a high dose glucocorticoid therapy (methyl prednisolone) over 3 days, continuing by prednisolone (75 mg/day) for the rest of the week, the patient become oriented and the confusion was diminished.

Discussion

To date, about 14 patients suffering from Graves' disease have developed encephalopathy conditions, associated with autoimmune disease. Seizures, distorted consciousness, involuntary movements, cognitive impairment, focal neurological signs, ataxia, sensorial alterations, language impairment, symptoms of encephalitis and psychiatric alterations reported to be the clinical manifestations of

patients with both Graves' disease and encephalopathy. Graves' disease preserves the background condition essential for EAATD. In almost all aspects, such as the clinical, immunological, radiological, electrophysiological and therapeutic features, of EAATD, Graves' disease does not differ from those patients with Hashimoto thyroiditis. Consequently, the diagnosis of EAATD is probable in all patients with signs of encephalopathy with unknown origin, while they have a previous history of an autoimmune thyroid disease. This condition is independent from the functional status of the thyroid and the nature of the primary autoimmune thyroid disease [7].

The etiology of EAATD is still largely controversial, but there are several arguments suggestive for an autoimmune origin. This includes higher proportion of women, fluctuating course of HE, its association with other autoimmune disorders, as well as the dramatic improvement followed by steroid treatment [8]. Investigations in patients with HE typically showed no pleocytosis with high levels of cerebrospinal fluid (CSF) protein. Even though the hallmark for EAATD is the high titer of anti-thyroid antibodies (especially anti-microsomal antibodies). Generally, EAATD happens when patient has normal, or slightly abnormal, thyroid hormone levels. Accordingly, it does not seem to be correlated with the thyroid function. Anti-thyroperoxidase (TPO) and anti-thyroglobulin (TG) Abs have been identified frequently in the CSF of EAATD patients, but their possible role in the pathogenesis remains to be elucidated [9]. However, neither our patient nor the previously mentioned cases of Graves' disease and encephalopathy were in the thyrotoxicosis phase, while they were all euthyroid while experiencing encephalopathy. So, further measurements of the anti-thyroid antibodies in the serum and CSF, in a larger number of subjects, during the phase of encephalopathy and after recovery, may lead us to discover the importance of the elevated CSF titers of anti-thyroid antibodies in the pathogenesis and prognosis of HE.

Conflict of interest None.

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