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Recurrent oculomotor neuritis related to autoimmune hypothyroidism

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Abstract

Ophthalmopathy related to thyroid disease is due mainly to diffuse periorbital or eye muscle inflammation. It is more common in Grave's hyperthyroidism and rare in Hashimoto's hypothyroidism. Here we report a case of recurrent oculomotor nerve palsy associated with autoimmune hypothyroidism. Brain MRI revealed enhancement of the oculomotor nerves. Despite thyroid hormone replacement therapy, oculomotor nerve palsy recurred at the side contralateral to the initially involved nerve and the autoimmune antibody titer remained high. The symptom was responsive to high-dose steroid therapy.

INTRODUCTION

Recurrent oculomotor neuropathy is extremely rare (Grabau *et al.* 2014). It has been described in ophthalmoplegic migraine, compressive conditions, essential mixed cryoglobulinemia, diabetes mellitus, and as a postvaccinal phenomenon (Grabau *et al.* 2014). Here we present a patient with recurrent oculomotor neuritis documented by magnetic resonance imaging (MRI) that may have been caused by autoimmune hypothyroidism.

CASE REPORT

A 16-year-old girl presented for care at the neurology department with left ptosis. She had no previous history of medical illness and no headache. On neurologic examination, complete ptosis was noticed in the left eye. The left pupil was dilated and the papillary light reflex was preserved. Ocular movement showed limitations in the medial gaze and upward gaze on the left side. In a neutral position, the left eyeball deviated to the lateral side and downward. The remainder of neurologic examination was normal. Brain MRI revealed dense enhancement and enlargement of the left oculomotor nerve (Figure 1A). The right oculomotor nerve was also weakly enhanced, but it was not enlarged. No vascular abnormalities were seen. The patient's complete blood counts and routine chemistry were all normal. The blood tests used to screen for autoimmune diseases were all negative or within normal limits and included the following: erythrocyte sedimentation rate, perinuclear anti-neutrophil cytoplasmic antibody, cytoplasmic anti-neutrophil cytoplasmic antibody, anti-ribonucleoprotein antibody, anti-Smith antigen antibody, anti-Sjögren's syndrome type A antibody, anti-Sjögren's syndrome type B antibody, anti-Ro-53, anti-Scl-70 antibody, anti-Jo1, anti-Jo1 antibody, anti-proliferating cell nuclear antigen antibody, anti-double-stranded DNA antibody, anti-nucleo-

CASE REPORT

some antibody, anti-PM/Scl antibody, anti-histone antibody, anti-ribosomal P protein antibody, and anti-AMA-M2 antibody. The antinuclear antibody showed a dense fine speckled pattern at a dilution of 1:80. The cerebrospinal fluid analysis was normal. The patient was negative for oligoclonal bands, and the immunoglobulin G (IgG) index was within normal range. The thyroid stimulation hormone (TSH) level was elevated at 32.7 mIU/L; the normal range is 0.17–4.05 mIU/L. The level of T3 (101 ng/dl) and free T4 (0.94 ng/dl) were within normal limits. The thyroglobulin antibody level (278 IU/ml; normal range 0–30 IU/ml) and antithyroid microsomal antibody (500 IU/ml; normal range 0–100 IU/ml) were increased. The TSH receptor antibody level was normal (0.6 IU/ml; normal range, 0–1.0 IU/ml). The patient was treated with steroid pulse therapy and thyroid hormone replacement. On the third day of steroid pulse therapy, her symptoms began to resolve, and eye symptoms were resolved completely after the 5-day steroid pulse therapy.

Five months later, the patient came back to the neurology department due to ptosis in the right eye. She had been on thyroid hormone replacement therapy since her last visit. The neurologic examination revealed right ptosis. There was no profound extraocular movement limitation; however, the patient reported subjective vertical diplopia. Brain MRI revealed enhancement of the bilateral oculomotor nerve (Figure 1B). There was less enhancement of the left oculomotor nerve than on the previous MRI. Results of a thyroid function test prior to admission were within normal limits, and the TSH level was 0.17 mIU/L. The levels of the thyroglobulin antibody (1 156 IU/ml) and the antithyroid microsomal antibody (585 IU/ml) remained elevated and were even higher than determined at the patient's first visit. The TSH receptor antibody level was normal (0.6 IU/ml). The blood tests used to screen for other autoimmune diseases were all normal or within normal limits, as at her previous admission. Cerebrospinal fluid analysis was normal, the IgG index was normal, and she was negative for oligoclonal bands. After treatment with high-dose steroid therapy for five days, her symptoms were completely resolved.

A follow-up MRI which was performed five months after symptom resolution, showed no enhancement in the left oculomotor nerve and remaining enhancement in the right oculomotor nerve (Figure 1C). After discharge, the patient had no recurring eye symptoms during the 5-year follow-up period.

DISCUSSION

This patient showed recurrent ophthalmopathy related to having a high titer of autoantibodies against the thyroid. Brain MRI revealed high signal intensity in the involved oculomotor nerves.

The majority of ophthalmopathy-related thyroid disease is due to diffuse periorbital inflammation or eye muscle inflammation, which is usually associated with Grave's hyperthyroidism but not with Hashimoto's

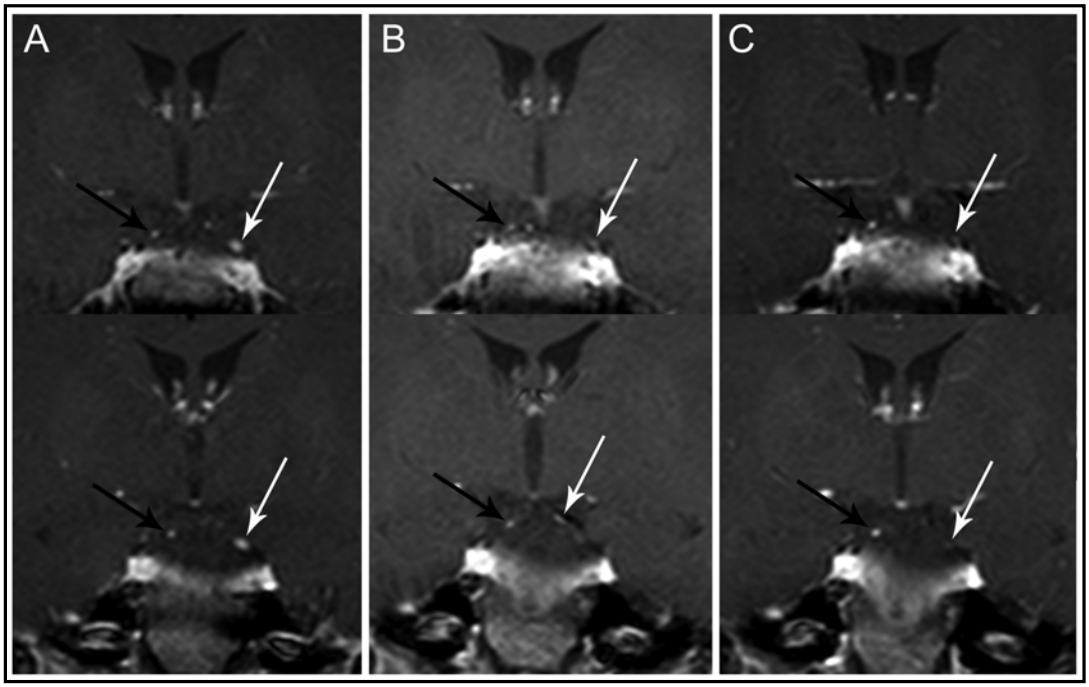

Fig. 1. Gadolinium-enhanced T1 coronal magnetic resonance imaging (MRI). (**A**) The initial MRI. The patient had left oculomotor nerve palsy. The bilateral oculomotor nerves showed high signal intensity, and the density was prominent on the left side. (**B**) The second MRI which was performed when the patient had right oculomotor nerve palsy. The bilateral oculomotor nerves showed high signal intensity; however, the left oculomotor nerve density had decreased since the initial MRI. (**C**) The third MRI performed after patient's recurred symptoms were resolved. The left oculomotor nerve enhancement disappeared. The right oculomotor nerve still showed enhancement. White arrows indicate left oculomotor nerve and black arrows indicate right oculomotor nerve.

hypothyroidism (Cockerham & Chan 2010). Involvement of the cranial nerve itself is rare. Peripheral neuropathy and carpal tunnel syndrome are the most commonly reported neuropathies in hypothyroidism (Nandi-Munshi & Taplin 2015). In this patient, MRI revealed dense enhancement of the oculomotor nerves. MRI enhancement of the cisternal portion of the oculomotor nerve is always an abnormal finding (Bhatti *et al.* 2003). Various insults can disrupt the blood-brain barrier, allowing leakage and accumulation of contrast material with resultant perineural enhancement (Saremi *et al.* 2005). Such disruption may arise secondary to neoplasm, autoimmune disease, inflammation, demyelination, ischemia, trauma, radiation, and axonal degeneration, all of which result in abnormal cranial enhancement (Saremi *et al.* 2005). The clinical course and response to steroid therapy led to a diagnosis of oculomotor neuritis-related autoimmune hypothyroidism in the presented patient. It was suggested previously that hypothyroidism related to cranial nerve palsy could also be due to autoimmunity that affects both the thyroid and cranial nerve or to inflammatory cell infiltration that induces demyelination (Kuroki *et al.* 1985). In the present case, the oculomotor neuritis relapsed despite thyroid hormone replacement therapy. The levels of thyroglobulin antibody and antithyroid microsomal antibody were higher after relapse than at the initial diagnosis. After recovery from the second attack of oculomotor nerve palsy, cranial nerve palsy did not recur, and the level of autoantibodies decreased. These findings suggest that autoimmunity was related to cranial nerve palsy. In the inflammatory process, nerve enhancement can be seen on MRI even up to several months after the symptoms resolved as seen in this patient (Bhatti *et al.* 2003).

Antithyroid microsomal antibody (also known as thyroid peroxidase antibody) is considered the best serological marker for establishing a diagnosis of Hashimoto thyroiditis (Caturegli *et al.* 2014). The titer of the antithyroid microsomal antibody correlates well with the number of autoreactive lymphocytes infiltrating the thyroid (Pandit *et al.* 2003). Notably, antibodies to thyroglobulin are less sensitive and less specific than antithyroid microsomal antibodies (Caturegli *et al.* 2014). Thyroglobulin and antithyroid microsomal antibodies seem to represent two different autoimmune responses to the thyroid gland, because the levels of these two autoantibodies are poorly correlated (Caturegli *et al.* 2014). Thyroglobulin antibodies may represent an initial immune response, whereas antithyroid microsomal antibodies might be characteristic of a later adaptive immune response (Caturegli *et al.* 2014). According to this hypothesis, thyroglobulin antibodies should be present at disease onset. Indeed, in mouse models of spontaneous autoimmune thyroiditis, thyroglobulin antibodies precede the appearance of antithyroid microsomal antibody (Chen *et al.* 2010). In this patient, the increase in the level of the thyroglobulin antibody was much greater than the increase in the antithyroid microsomal antibody. Thus, antithyroglobulin antibodies may have played a role in inducing oculomotor neuritis; alternatively, oculomotor nerve palsy may have been an initial symptom of autoimmune hypothyroidism in this patient.

In summary, this report describes a patient with recurrent oculomotor neuritis documented by MRI and related to autoimmune hypothyroidism.

Conflict of interest

The authors declare that they have no conflict of interest

REFERENCES

1 Grabau O, Leonhardi J, Reimers CD (2014). Recurrent isolated oculomotor nerve palsy after radiation of a mesencephalic metastasis. Case report and mini review. Front Neurol **5**: 123.

2 Cockerham KP, Chan SS (2010). Thyroid eye disease. Neurol Clin **28**: 729–755.

3 Nandi-Munshi D, Taplin CE (2015). Thyroid-related neurological disorders and complications in children. Pediatr Neurol **52**: 373–382.

4 Bhatti MT, Schmalfuss IM, Williams LS, Quisling RG (2003). Peripheral third cranial nerve enhancement in multiple sclerosis. AJNR Am J Neuroradiol **24**: 1390–1395.

5 Saremi F, Helmy M, Farzin S, Zee CS, Go JL (2005). MRI of cranial nerve enhancement. AJR Am J Roentgenol **185**: 1487–1497.

6 Kuroki T, Ruf J, Whelan L, Miller A, Wall JR (1985). Antithyroglobulin monoclonal and autoantibodies cross-react with an orbital connective tissue membrane antigen: A possible mechanism for the association of ophthalmopathy with autoimmune thyroid disorders. Clin Exp Immunol **62**: 361–370.

7 Caturegli P, De Remigis A, Rose NR (2014). Hashimoto thyroiditis: Clinical and diagnostic criteria. Autoimmun Rev **13**: 391–397.

8 Pandit AA, Vijay Warde M, Menon PS (2003). Correlation of number of intrathyroid lymphocytes with antimicrosomal antibody titer in hashimoto's thyroiditis. Diagn Cytopathol **28**: 63–65.

9 Chen CR, Hamidi S, Braley-Mullen H, Nagayama Y, Bresee C, Aliesky HA, Rapoport B, McLachlan SM (2010). Antibodies to thyroid peroxidase arise spontaneously with age in nod.H-2h4 mice and appear after thyroglobulin antibodies. Endocrinology **151**: 4583–4593.