CASE REPORT

An unusual cause of cerebellovestibular symptoms

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SUMMARY

Hashimoto encephalopathy (HE) is a controversial autoimmune disorder, probably underdiagnosed, that causes a wide variety of neurological manifestations. Symptoms differ among patients and may be very severe in some cases. However, it can be treated, with a very good prognosis. In our case, a teenaged girl with a family history of migraine, vitiligo and benign paroxysmal positional vertigo presented with severe ataxia, vomiting and hypotension. She had a history of similar, but milder, symptoms and was misdiagnosed several times. She had subclinical hypothyroidism, and high levels of antithyroid antibodies. There were abnormal MRI and visual evoked potential findings. After excluding other more common causes, we diagnosed her as having 'Hashimoto Encephalopathy', and started treatment with corticosteroids, on which she showed dramatic improvement. After about 2 years of presentation, the patient is able to continue her life independently.

BACKGROUND

Hashimoto encephalopathy (HE) is a rare and controversial autoimmune disease associated with a high titre of antithyroid antibodies. Patients differ in presentation, with a wide variety of neurological symptoms. HE is probably underdiagnosed, but can be treated, with a very good prognosis. Although many cases—in almost all age groups—have been reported in the literature, many authors have mentioned the need to report more cases about this condition, especially in adolescents, as there are very few reported. We report a case of a teenaged girl with cerebellovestibular symptoms.

CASE PRESENTATION

We report a case of a 17-year-old Egyptian girl with a first-degree family history of migraine, vitiligo and benign paroxysmal positional vertigo. Her menstruation started at 14 years of age, and continued irregularly since then; her mother had a similar history.

Three years prior, she had sought medical advice for dizziness and vomiting. She was misdiagnosed as having otitis media; the physician prescribed antibiotics, then added a 2-week course of oral corticosteroids, on which she showed improvement for about 2 years.

Several months prior to the current presentation, she had sought medical advice for attacks of headache, nystagmus, hypotension, vertigo, nausea and, sometimes, vomiting. She had an impaired vestibulo-ocular response. Her MRI and EEG findings were normal. She was diagnosed with Meniere's disease, and started treatment with ondansetron and oral corticosteroids, on which she

showed minimal improvement. Two weeks later, the physician stopped the treatment of Meniere's disease, and put her on topiramate (100 mg) for vestibular migraine, with no improvement. Subsequently, cerebellar symptoms (gait ataxia, limb ataxia, intentional tremors) appeared and slowly progressed over the course of 2 months until she presented to our hospital. Two weeks prior to presentation, she was discovered to have subclinical hypothyroidism; she had elevated thyroid-stimulating hormone (TSH) levels with normal T3 and T4. She started treatment with thyroxine.

She presented to our hospital, 1 year prior, with severe vertigo, vomiting, dehydration, hypotension (70/40 mm Hg), severe bilateral more-to-left limb and gait ataxia, horizontal nystagmus, marked intentional tremors, dysmetria on finger to nose on left side, photopsia and bilateral diminution of vision. She was oriented to time, place and person. She gave a history of insomnia. She had no fever and no signs of infection.

INVESTIGATIONS

Full blood count, lipid profile, liver and renal functions tests were within normal ranges. Erythrocyte sedimentation rate was 3 mm/h (lower than normal according to lab reference). C reactive protein was negative. The patient was euthyroid with high levels of antithyroglobulin antibodies (62.903 IU/mL). Her testing for antinuclear antibodies (ANA), antineutrophilic cytoplasmic antibodies (ANCA), antimitochondrial antibodies (AMA), antidouble-stranded-DNA and anticardiolipin antibodies (IgG, IgM), were all negative.

Figure 1 MRI showing a small bright oval fluid-attenuated inversion recovery signal area (black arrow) at the right lower temporal lobe.

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Brain MRI showed a small bright oval fluid-attenuated inversion recovery (FLAIR) signal area at the right lower temporal lobe. The posterior fossa structures were normal (figure 1).

The patient's routine digital EEG showed no detectable abnormalities. Visual evoked potential (VEP) test showed marked demyelination of both retinocortical pathways, more on the left side (167.5 on the right and 178 on the left). A nerve conduction study was carried out for the right median, common peroneal, left ulnar and tibial nerves—the results were normal.

Although cerebrospinal fluid analysis could have provided meaningful data, it was not performed, as the parents of the patient refused it.

DIFFERENTIAL DIAGNOSIS

Clinically, the patient reported similar attacks of cerebellovestibular symptoms in the preceding year. At presentation, she had

optic neuritis for the first time in addition to the earlier symptoms. This arose our suspicion for multiple sclerosis (MS). However, MRI was performed and was atypical, as we found only one lesion in an atypical site for MS. No lesions were found in subsequent MRIs including those with contrast. Usually in MS, the lesions are disseminated; that means more than one anatomical site should be involved. Notably, in our case there was one single site (cerebellovestibular connections) repeatedly involved. Also, our case presented with bilateral simultaneous optic neuritis, which is atypical for MS.

Based on the patient's clinical course (recurrence and chronicity of symptom), absence of fever and viral prodrome, non-suggestive levels of acute phase reactants, MRI findings and history of improvement on corticosteroids, we thought infectious causes were unlikely.

Metabolic ataxias such as vitamin B₁₂ deficiency and hypobetalipoproteinaemia were also unlikely, as there were no

Figure 2 Follow-up contrast MRI film showing no detectable abnormalities.

neuropathies, and there was no retinal degeneration and no altered mental status or rash.

MRI showed a small bright FLAIR signal area at the right temporal lobe (suggestive of vasculitis) and the patient also experienced joint pain, but serum markers such as ANA and ANCA were negative. So lupus and other connective tissue disease vasculitides were unlikely.

After discussing the differential diagnoses, and based on the concurrent presence of the aforementioned symptoms, high antithyroid antibodies titre and history of this patient's improvement on corticosteroids, we considered HE as being the most probable diagnosis. Our diagnosis was later supported after dramatic improvement on corticosteroids.

TREATMENT

The patient's optic neuritis was so severe that the ophthalmologist could not wait for further investigations and decided to start her on methylprednisolone 5 g to save her vision; the dose started at 1 g/day, which led to marked improvement of all symptoms but caused hyperglycaemia (500 mg/dL); so the dose was lowered to 0.5 g/day. After completion of the full dose, we

decided—based on the patient's history of relapsing after stopping corticosteroids—to continue oral therapy (prednisolone 40 mg/day), on which she was discharged.

OUTCOME AND FOLLOW-UP

The patient showed marked improvement on corticosteroids. The dose was decreased gradually. A month after discharge, we started the patient on mycophenolate mofetil 500 mg (every 8 h) to decrease the dose of the corticosteroid and to prevent long-term adverse effects. The symptoms were gradually relieved and she was able to continue her life independently. We have continued to carry out monthly routine follow-up.

At the first follow-up, contrast brain MRI was performed—it was completely normal (figure 2). We also discovered that the patient had high levels of antithyroid antibodies (422.9 IU/mL), another reason for continuing monthly follow-up. Her levels kept fluctuating, at one point reaching 1000 IU/mL.

The patient had two relapses (after 4 months and after 20 months). In both attacks, the symptoms relapsed again but were much less severe than at initial presentation. In the first

Figure 3 Contrast MRI film at the last attack (20 months after presentation) showing no detectable abnormalities.

attack, she received an intravenous corticosteroid bolus, whereas in the second, she only had to adjust her corticosteroids dose. In both attacks, the symptoms were again relieved, and she returned to her baseline level. In the last attack (after 20 months), contrast MRI was carried out and was normal (figure 3).

Between the two attacks, the patient showed no neurological symptoms except for stress-induced mild intentional tremors (after about 10 min of handwriting). Her MRI, blood tests and VEP were all normal. She was euthyroid with low antithyroglobulin antibodies, but antithyroperoxidase antibodies were still high.

The patient is currently on corticosteroids (20 mg/day), mycophenolate mofetil (1500 mg/day), thyroxin and propranolol (20 mg/day).

DISCUSSION

The term HE was first introduced to the literature in 1966,¹ and since then there has been controversy over this rare condition, its nomenclature, defining criteria and aetiology, even its existence has been questioned.² Many authors prefer to call it steroid responsive encephalitis with autoimmune thyroiditis. The disease's estimated prevalence is about 2.1/100 000; it affects all ages, females more than males.³ The exact underlying mechanism of the disease pathology is still unknown, but it is thought to be autoimmune as it is fluctuant, highly prevalent in females, and responsive to corticosteroids and other autoimmune therapies such as plasmapheresis.⁴ Although all reported cases mention increased levels of antithyroid antibodies—especially antithyroglobulin antibodies—there is no evidence of a correlation between the titre of the antibodies and the severity of symptoms, so it is still unknown if the antibodies play a direct role.³ Some authors suggest that the titre of antibodies may be a marker for prognosis of the disease.⁵ There is little evidence on direct central nervous system autoimmunity. A recent study found that antithyroperoxidase antibodies bind specifically to primates' cerebellar astrocytes. This mechanism may explain the symptoms as we noticed that our patient had a high level of antithyroperoxidase (the increase was significantly more than it was in antithyroglobulin antibodies).⁶ Another study suggested the presence of immunoreactive TSH receptors in the cerebral cortex, which may play a role in the pathogenicity.⁷

Patients show a wide variety of clinical features, including cognitive impairment, seizures, behavioural disorders, myoclonus, gait ataxia, dysphasia, confusion, tremors and psychosis and, less commonly, headache, sleep disorders, hyper-reflexia, depression and visual changes.³ Our patient only had vertigo, nausea, vomiting, visual disturbances, hyper-reflexia and symptoms of cerebellar ataxia.

Some previous studies showed multifocal high signal intensity lesions on T2-weighted and FLAIR areas at different regions of the brain. All these findings were reversible.^{8–9} In our case, MRI findings showed a small oval bright FLAIR signal area at the right temporal lobe. This finding may have been clinically silent, but it might have indicated the presence of a pathology and was reversible after corticosteroid treatment.

The diagnosis of HE is made after excluding other more common possible causes of encephalopathy such as infectious and metabolic disorders, with the existence of neurological symptoms and detection of antithyroid antibodies. Improvement on steroids is also supportive of the diagnosis. Most patients show improvement on steroids, but a few patients need other immunomodulating interventions such as plasmapheresis, intravenous immunoglobulins and other immunosuppressant drugs such as mycophenolate mofetil.¹⁰ In our case, the patient showed dramatic improvement on steroids. Later, we started her on mycophenolate mofetil in order to reduce the steroid dose and prevent its long-term adverse effects.

Learning points

- ▶ After exclusion of more common causes, Hashimoto encephalopathy should be considered in presentation with cerebellovestibular symptoms, especially when there is a history of hypothyroidism.
- ▶ Although altered mental status is present in most reported cases, Hashimoto encephalopathy may present with no obvious cognitive impairments or psychiatric disorders.
- ▶ Abnormal findings in MRI and visual evoked potential are reversible and resolve completely after treatment.

Contributors MAA, AMS and MJA-H were involved in writing the manuscript, collecting information and writing the discussion. MAN was the mentor and supervised the work during the whole process, she revised it critically and gave final approval for the manuscript.

Competing interests None declared.

Patient consent Obtained.

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