CASE REPORT

Focal neurological presentation in Hashimoto's encephalopathy mimicking a vascular occlusion of the middle cerebral artery

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SUMMARY

Hashimoto's encephalopathy is a rare form of autoimmune encephalopathy. It is likely an underdiagnosed entity especially in the setting of focal neurological defects. We report a case of a 49-year-old man who presented with "strange behavior" of a day's duration. Examination was significant only for lethargy, poor attention span and agitation. Routine labs revealed leucocytosis. Head CT scan was unremarkable. Lumbar puncture showed high white blood cells with lymphocytosis and elevated protein level. The patient was empirically treated for meningitis without improvement. His symptoms progressed to sudden right-sided weakness, ataxia and right facial droop. The MRI and magnetic resonance angiogram (MRA) were normal. The patientâ€™s focal neurological signs improved spontaneously. Encephalopathy work-up was negative except for positive anti-Thyroid Peroxidaseand antithyroglobulin. The patient was treated as Hashimoto encephalopathy with steroids and azathioprine with marked improvement. Our case highlights how focal neurological findings can potentially mislead the provider to consider vascular aetiologies in Hashimoto's encephalopathy.

BACKGROUND

In this case report we describe some novel features of Hashimoto's encephalopathy. The focal neurological features in our patient consistent with middle cerebral artery (MCA) occlusive disease almost resulted in the administration of thrombolytic therapy, which could have adversely affected this patient. We believe this case report will be of interest to your readership, and to our knowledge is the first such report that highlights the range of focal neurological defects and risk associated with failure to diagnose Hashimoto's encephalopathy.

CASE PRESENTATION

A 49-year-old white man presented to the emergency department with 'strange behavior' of a day's duration. His illness had begun 2 weeks prior to his presentation to the emergency room (ER) department as he presented to the outpatient clinic with sinus pressure, nasal congestion and discharge. He was diagnosed with acute bacterial sinusitis and was treated with a course of amoxicillin. He failed to improve and his symptoms progressed over 2 weeks to neck stiffness, vomiting and confusion. The patient had a medical history significant for essential tremor, restless leg syndrome, hypertension and dyslipidemia. He lived with his wife, who was healthy and reported no recent illness. He had no recent exposure to anyone who was ill. He did not smoke, drink alcohol or use illicit drugs. He did not have a family history of autoimmune disease. His medications were lisinopril 40 mg once daily, ropinirole 1 mg once daily and simvastatin 20 mg once daily.

In the ER on examination he appeared unwell. His blood pressure was 134/78 mm Hg, pulse was 88 beats per minute, respiratory rate was 22 per minute and his temperature was 98.8°F. He was awake but very lethargic. He was unable to follow commands and had waning poor attention span and agitation. A funduscopic examination revealed no evidence of papilloedema. There was no facial asymmetry or tongue deviation. Kernig's sign and Brudzinski's sign were negative. His disorientation prevented him from following commands for a full neurological exam, but his strength and deep tendon reflexes were intact and symmetric, with bilateral flexor plantar responses. The rest of his physical exam including cardiac, respiratory, abdominal, thyroid and neck examination was unremarkable.

INVESTIGATIONS

Routine labs revealed leucocytosis with white blood cells (WBC) of 13 000 per microlitre (normal range 4000–11 000 per microlitre) and with a normal differential, mildly elevated liver enzymes: alanine aminotransferase 75 IU/L (normal range 20–60 IU/L) and aspartate aminotransferase 45 IU/L (normal range 6–34 IU/L). The rest of liver and renal function tests, urine drug screen, thiamine level, alcohol level and vitamin B_{12} level were otherwise unremarkable. Head CT scan with and without contrast was unremarkable. Lumbar puncture done under fluoroscopy showed 388 WBC/μL (normal range 0–5 cells/μL) with 99% lymphocytes, normal opening pressure and normal glucose, but significant elevation of protein at 272 mg/dL (normal range <45 mg/dL).

DIFFERENTIAL DIAGNOSIS

At early stages of admission the differential diagnosis was viral or bacterial meningitis, encephalitis and metabolic encephalopathy.

After the acute onset of neurological deficit, the differential diagnosis was acute ischaemic or

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Table 1 Focal neurological presentations in Hashimoto's encephalopathy

Article	Author/year	Age/gender	Presenting focal neurological deficit	Disease course	CT or MRI findings	Response to steroids/alternate treatment
Autoimmune thyroid encephalopathy presenting with epilepsia partialis continua	Aydin-Ozemir *et al*/2006[4]	37/F	Multifocal motor seizures	Asymmetrical quadriparesis, truncal ataxia and continuous semirhythmical jerks	Pathological signal alterations detected in both precentral cortices	Seizures stopped
Alternating hemiplegia of childhood or Hashimoto's encephalopathy?	Balestri *et al*/1999[5]	14/M	Aphasia lasting 5 hours	Three separate alternating hemiplegic episodes lasting 8–10 hours	Mild reduction of volume of the left nucleus caudatus	Treated with flunarizine with no clinical relapses
Unusual presentation of Hashimoto's encephalopathy: trigeminal neuralgiform headache, skew deviation, hypomania	Beckmann *et al*/2011[6]	51/M	Right medial rectus muscle palsy lasting 5 days	Left haemiparesis and skew deviation presenting 3 months later	Hyperintense lesions on right midbrain and bilateral thalamus	Initially recovered spontaneously over 5 days, treated for relapse and improved with minimal vertical gaze palsy
Hashimoto's thyroiditis — a rare but treatable cause of encephalopathy in children	Byrne *et al*/2000[7]	14/F	Generalised tonic and clonic seizure	Acute hemiplegia and aphasia	Normal	Full recovery over 72 hours within ongoing neuropsychological difficulties (one relapse treated)
		12/F	Generalised tonic and clonic seizure	Right-sided facial weakness, mild right haemiparesis, significant expressive dysphagia	Normal	Improvement after a week with persistent subtle right-sided weakness (one relapse treated)
A case of Hashimoto's encephalopathy: association with sensory ganglionopathy	Cao *et al*/2005[8]	54/F	Left-sided clumsiness lasting 20 min and transient left-sided numbness	Abnormalities in sensory nerve conduction	Mild non-specific pattern of diffusely increased signal intensity within the periventricular white matter bilaterally	Dramatic improvement within 2 days (two future relapses treated)
Time course of Hashimoto's encephalopathy revealed by MRI: report of two cases	Chen *et al*/2011[9]	27/M	Sudden weakness of both lower limbs	He was experiencing memory loss and seizures that continued to get progressively worse with time	Oval ischaemic lesion at middle splenium of corpus callosum, pre-existing lesion in right hippocampus	Symptoms of lower limb weakness relieved within 5 days, no other clinical symptoms showed improvement
Hashimoto's encephalopathy presenting with stroke-like episodes in an adolescent female: a case report and literature review	Graham *et al*/2016[10]	15/F	Sudden-onset right haemiparesis and slurred speech resolved within 35 min	Acute bilateral lower extremity weakness 2 weeks later	Normal	No further stroke-like episodes after initiation of steroids, normal neuropsychological functioning by 4 months
Seizures, psychosis and coma: severe course of Hashimoto encephalopathy in a 6 year old girl	Hoffmann *et al*/2007[11]	6/F	Generalised seizure	Haemiparesis	Normal	Dramatic improvement within a day after therapy was initiated with later occasional focal seizures
Central nervous system lymphoma in a patient with Sjogren's syndrome and autoimmune thyroiditis	Kinikli *et al*/2007[12]	60/F	Muscle weakness, sudden visual loss on right eye 3 months before admission, presented with minimal paresis of left side	Development of visual loss in left eye	Hyperintense areas of right temporal basal white matter and brainstem	No improvement in right eye vision, still bedridden after therapy with developing visual loss of left eye
Subacute cerebellar syndrome or Hashimoto's thyroiditis. Association or simple coincidence?	Mouzak *et al*/2002[13]	47/F	Left leg weakness	Ataxia, dysarthria, paraplegia	Non-contrast enhancing long-standing lesion in left lateral medullary area and mild cerebellar atrophy	Slight improvement after given human normal immunoglobulin for 6 days, further improvement after steroids added to treatment plan 3 months later
Autoimmune thyroiditis and acquired demyelinating polyradiculoneuropathy	Polizzi *et al*/2001[14]	7.5/F	Flaccid paraplegia	Did not develop any other neurological symptoms	Normal	Gradually improved with intravenous immunoglobulin, no motor or sensory defects on follow-up
		70/F	Unsteady gait, bilateral ophthalmoplegia, pain and paraesthesia in upper and lower extremities	Did not develop any other neurological symptom	Normal	Improved with intravenous immunoglobulins, complete remission after weeks
Rarity of encephalopathy associated with autoimmune thyroiditis	Sawka *et al*/2002[15]	58/M	Unilateral weakness	Ataxia, aphasia, grand mal seizure	Diffuse white matter changes	Dramatic improvement (four relapses treated)
		63/F	Unilateral weakness	Ataxia, tremor, grand mal seizure	Normal	Improved (final relapse treated)
Ataxia associated with Hashimoto's disease: progressive non-familial adult onset cerebellar degeneration with autoimmune thyroiditis	Selim and Drachman/2000[16]	46/F	Diplopia, dysarthria and dysmetria of all limbs	Progressively deteriorated and became wheelchair users in the next 8 months	Diffuse cerebellar atrophy	Able to ambulate with walker after intravenous immunoglobulins, no improvement in cerebellar deficits or neurological exam
MR Findings in Hashimoto's encephalopathy	Song *et al*/2004[17]	35/F	Transient weakness of left arm	Development of left-sided clumsiness and eventual wheelchair-bound status	Left hippocampal mass and right medullary lesions, unilateral cerebellar atrophy	Marked improvement after several weeks of treatment, can ambulate without assistance
Hashimoto encephalopathy: a case report with proton MR spectroscopic findings	Su *et al*/2011[18]	52/F	Disorientation, amnesia	Numbness in the right hand, blurred vision in the right eye and tonic-clonic seizures	Multiple patchy abnormal hyperintensities in bilateral cerebral hemispheres	Improved after 9 days, relapsed intermittently, follow-up MRI showed remarkable residual cerebral atrophy
A case of autoimmune thyroid disease presenting posterior reversible encephalopathy syndrome	Tateishi *et al*/2008[19]	40/F	Transient loss of sensation in right arm and face 2 months before admission	Incomplete right haemiparesis lasting 2 days	Normal CT, diffusion-weighted imaging showed patchy hyperintense lesions in left occipitotemporal grey and white matter	Lesions disappeared completely after 11 days, given mercaptomethylimidazole and sensory disturbance of right arm resolved within 30 days
Rapid progression and brain atrophy in anti-AMPA receptor encephalitis	Wei *et al*/2013[20]	30/F	Short-term memory impairment	Quadriparesis and quadriplegia	Hyperintensity bilaterally in insula, mesial temporal lobe and caudate nucleus with follow-up 5 days later showing bilateral diffuse cortical atrophy	Spontaneous movement of all limbs 8 weeks following onset, regained consciousness 4 months after onset, persistent irritable mood and impaired learning
Two patients with Hashimoto's encephalopathy and uncontrolled diabetes successfully treated with levetiracetam	Wong *et al*/2015[21]	56/F	Subacute aphasia and unilateral leg weakness	Did not develop any other neurological symptoms	Normal	Steroids contraindicated, given levetiracetam and returned to baseline at 6 months with mild cognitive slowing
Steroid-responsive encephalopathy associated with Hashimoto thyroiditis	Zimmermann and Stranzinger/2012[22]	11/F	Sudden sensory disturbance and left-sided weakness	—	Hyperintensity in right lateral thalamus and internal capsule	Symptoms resolved after 5 days, persistent small hyperintense lesion in right thalamus interpreted as gliosis

haemorrhagic stroke, multiple sclerosis, cerebral vasculitis, brain abscess, chronic inflammatory demyelinating polyneuropathy, epilepsy, brain tumour, epidural abscess, Guillain-Barré syndrome and Lambert Eaton syndrome.

TREATMENT

The patient was admitted to the intensive care unit and was started empirically on vancomycin, ceftriaxone and acyclovir.

OUTCOME AND FOLLOW-UP

The patient failed to improve and had persistent confusion and lethargy. Day 3 after admission he had an episode of sudden right-sided weakness, ataxia, right lateral drift, right facial droop and slurred speech. A stat MRI and MRA was reported as normal. The patient improved spontaneously, and in less than an hour he regained power to his right side, and his ataxia, facial droop and his slurred speech resolved. Electroencephalogram was performed and showed non-specific slowing of background activity consistent with mild to moderate encephalopathy. A repeat lumbar puncture continued to show leucocytosis with lymphocyte predominance, normal opening pressure and significant elevation in protein at 251 mg/dL (normal range <45 mg/dL). Infectious disease work-up including Rapid plasma reagin (RPR), M tuberculosis PCR, Human T-lypmphotropic virus type 1&2(HTLV I/II Ab), antifungal Ab, Epstein-Barr virus (EBV) titres, Bartonella Ab, and blood and cerebrospinal fluid bacterial, viral and fungal cultures were negative. A full autoimmune and paraneoplastic disease work-up ensued and included anti nuclear antibody(ANA), anti-neutrophilic cytoplasmic antibody (ANCA), anti-Saccharomyces cerevisiae Antibody (ASCA), anti-Hu Ab, anti-Yo Ab, neuromyelitis optica (NMO) IgG Ab, anti-Ma1,2, antineuronal nuclear Ab, Purkinje cell cytoplasm Ab, acetylcholine (Ach) receptor Ab and striatal muscle Ab, and were negative except for anti-TPO Ab and antithyroglobulin Ab, which were positive; TPO antibody was 124 IU/mL (normal range <35 IU/mL), and antithyroglobulin Ab was 98 IU/mL (normal range <20 IU/mL). TSH and free T4 were both normal. The patient was diagnosed with Hashimoto's encephalopathy and started on 1 g intravenous methylprednisolone once daily, which was given for 3 days only as the patient improved. Azathioprine 100 mg daily was added per recommendation from neurology since the patient's neurological status had improved but not returned to baseline.

The patient stayed 10 days in the hospital and was discharged home to continue azathioprine 100 mg daily and was put on prednisone 20 mg daily for 3 months. The patient continues to have mild degree of ataxia, but no other residual neurological deficit. He did not have any relapses, but he never went back to baseline neurological status.

DISCUSSION

Autoimmune processes account for at least 20% of all cases of encephalitis.[1 2] One under-recognised cause is Hashimoto's encephalopathy or steroid-responsive encephalopathy. Despite the increased number of reported cases and the growing interest of the medical and scientific community in this condition, we still need a better understanding of its pathology, diagnosis and treatment.

The most reported clinical picture of Hashimoto's encephalopathy is a relapsing-remitting encephalopathy characterised by seizures, headache and psychosis.[1–3] In some patients stroke-like episodes may also occur. In a few reported cases diffusion-weighted imaging (DWI) MRI was able to detect focal or diffuse non-enhancing abnormalities during acute and subacute

Patient's perspective

- 'When ask to write about my emotions when my husband was diagnosed with Hashimoto's encephalopathy. I really did not know to begin to explain how I felt . There was fear of not knowing what the results would be. I was discouraged after stays in the hospital and many tests being done and there was still no diagnosis. The doctors really tried to find a diagnosis but all the tests were negative and that was alarming to me. I prayed that the doctors would find out what was going on with him. I was scared that it might be something that was very rare and it was.'
- 'The future was so very uncertain at this time and we just lived on day at a time. After diagnosis I have tried to understand the diagnosis but I still feel scared that the symptoms will come back. The diagnosis has changed our lives financially and emotionally. Before he got sick he worked out of town and worked sixty to seventy hours a week but now he is disabled. It was overwhelming when the diagnosis came because I never heard of Hashimoto's encephalopathy. I knew Hashimoto's was duo to the thyroid but his levels were normal. That was confusing to understand. But the doctors gave me copies of cases and I was able to understand it better. I'm still having trouble understanding why this happened to him and why it was not caught earlier. I wonder did I miss some signs of something being wrong. It has put a lot more pressure on me to take care of him and to watch for symptoms of the auto immune returning. It is hard to explain to him what Hashimoto encephalopathy is. For me the emotions that I had are hard to explain because there were times I was numb to any emotions. But I am thankful that the doctors found out and he is being treated for it. I guess you could say fear, anger, worried, frustrated, scared, discouraged and I cried and prayed a lot. The thought of him dying was a fear that was always there. But since he is being treated I understand it better and therefore I am able to cope with the changes that we face in our daily routine.'

Learning points

- The diagnosis of Hashimoto's or steroid responsive encephalopathy should be suspected in cases of encephalopathy without obvious cause.
- Early diagnosis and treatment are associated with improved outcomes, which makes prompt recognition of the disease paramount.
- We recommend clinicians consider delaying treatment with thrombolytics for patients with stroke-like symptoms unless there is radiological evidence of ischaemic stroke. However, the possible presence of encephalopathic focal changes in the cortex may complicate interpretation and management.
- We also recommend evaluating antithyroid antibodies in cases of unexplained neurological symptoms and presentations not responding to conventional therapies.
- In case there is uncertainty in the diagnosis, more specific markers like cerebrospinal fluid (CSF) thyroid antibodies and antibodies to NH2-terminal of α-enolase could be used for confirmation.

exacerbations of the disease. These DWI changes are also seen in central nervous system(CNS) vasculitis but different from the ones seen in ischaemia as it resolves completely with treatment.[4] Delay in diagnosis can lead to progression of the neurological signs and symptoms, which makes the picture more complex. In this case, the rapid onset of illness, history of recent sinusitis and features that suggested diffuse brain involvement led to immediate concern regarding a primary infectious cause. The sudden onset of right-sided weakness, ataxia, right lateral drift, right facial droop and slurred speech, and symptoms mimicking acute ischaemic stroke following the distribution of MCA directed the attention towards a primary neurological process. Failure to improve with conventional treatment and the relapsing remitting course of the symptoms led to the suspicion of autoimmune aetiology.

We reviewed more than a hundred reported cases of diagnosed Hashimoto's encephalopathy from 2010 to 2016.[4–22] We compared the clinical presentation, the evolution of symptoms and the disease course. As shown in table 1, 22 patients developed some sort of focal neurological deficit at presentation or later on during the course of their illness, yet none of them showed stroke-like symptoms that follow a typical arterial distribution, as demonstrated in our case. We also noticed that in all of these cases, the diagnosis and treatment were delayed and patients retained residual neurological deficits and/or had multiple relapses.

In most of the reported cases, the diagnosis was made based on positive anti-TPO and/or antithyroglobulin abs. Some cases used more specific markers for diagnosis like CSF thyroid antibodies and antibodies to NH2-terminal of α-enolase. To our knowledge this is the first case to report a focal neurological deficit secondary to Hashimoto's encephalopathy, mimicking the neurological deficit found in ischaemic stroke caused by MCA occlusion.

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Competing interests None declared.

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