

Case report

Hemiencephalitis: a hyperaemic presentation of Hashimoto's encephalopathy

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Accepted 16 October 2019

SUMMARY

There are many examples in the literature of Hashimoto's encephalopathy (HE) presenting with heterogeneous manifestations to include stroke-like episodes, seizures, myoclonus and psychiatric symptoms. The pathogenesis is poorly understood but is thought to involve an autoimmune-mediated vasculitis. Here, we present a novel case showing hemispheric hyperaemia which created a diagnostic challenge and insinuated a vascular mechanism for the condition. The patient presented with left-sided stroke-like symptoms and had head CT angiography notable for asymmetric vasculature initially interpreted radiographically as decreased left middle cerebral artery (MCA) flow. An MRI brain demonstrated right-sided holohemispheric fluid-attenuated inversion recovery (FLAIR) hyperintensity with right insula contrast enhancement. She was found to have elevated anti-thyroid peroxidase (TPO) antibodies with an otherwise negative encephalitis workup. The patient was diagnosed with HE and acutely progressed to have focal seizures during a prolonged intensive care unit stay. She ultimately required intravenous Ig and antiepileptic medications to gain control of her disease. This case appears to be the first described presentation of hemiencephalitis with local hyperaemia, and may represent local autoregulatory loss as a result of vasculitis. This supports the existing literature implicating inflammatory microvascular infiltration in the mechanism of the disease. HE must be considered in a broad range of unexplained neurological symptoms.

BACKGROUND

Hashimoto's encephalopathy (HE), commonly referred to as steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT), is a heterogeneous disorder which frequently manifests with stroke-like episodes, seizures, myoclonus and psychiatric symptoms in the setting of high-antithyroid antibody titres.¹ Patients are typically euthyroid at presentation and thus far no aetiological mechanism has been identified that causally relates the antibodies to encephalopathy.² Though still poorly understood, several theories of pathogenesis have been proposed and are generally thought to involve an autoimmune-mediated vasculitis. Multiple case series have characterised the various neuroimaging features of the condition, ranging from normal findings in about 50% to non-specific subcortical abnormalities that typically do not enhance.^{2,3} Here, we describe a case of hemiencephalitis with local hyperaemia, which appears to

be the first such presentation described. This case is thought to be a valuable learning case in light of the broad differential that must be considered with undifferentiated encephalopathy, the challenges of which were especially highlighted by this patient's comorbidities.

CASE PRESENTATION

A 57-year-old woman with history of Sjogren's syndrome and genetically confirmed spinocerebellar ataxia type 10 (SCA10) presented with worsening of her ataxia and dysarthria over a 2-week period, along with new development of blurred vision, progressive right temporal headache and left hemiparesis for 1 week. Her previous baseline included independent ambulation with occasional use of cane for prolonged walking, but over the week preceding her presentation she required more assistance from her husband; this culminated in a minor fall 3 days prior to presenting. For 2 days preceding her presentation, her husband noted that she was holding her left arm in an abnormal flexed position.

INVESTIGATIONS

On examination, she was alert and fully oriented with normal mental status except for ability to follow three-step command. She was found to have left homonymous hemianopia, left lower facial droop, dysarthria, leftward tongue deviation, dense left hemiparesis affecting the upper extremity more than the lower extremity. Upper extremity reflexes were asymmetrically brisker on the left. Standing was difficult and she leaned to the left. Initial head CT was unremarkable but head CT angiography (CTA) on the day of admission was initially read as concerning for decreased left middle cerebral artery (MCA) flow (figure 1A). Brain MRI completed on hospital day 2 demonstrated right holohemispheric increased fluid-attenuated inversion recovery (FLAIR) (figure 1B) and increased diffusion weighted imaging (DWI) (figure 1C) without an apparent diffusion coefficient (ADC) correlate (figure 1D). Contrast enhancement was noted in the right insula (figure 1E–F). An electroencephalogram (EEG) on hospital day 2 demonstrated diffuse slowing of the background consistent with generalised cortical dysfunction suggestive of an encephalopathic process but no epileptiform abnormalities; there was notable asymmetry with increased slowing on the right side.



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To cite: Gregory TA, Jones GN, Loh Y. *BMJ Case Rep* 2019;12:e230011. doi:10.1136/bcr-2019-230011

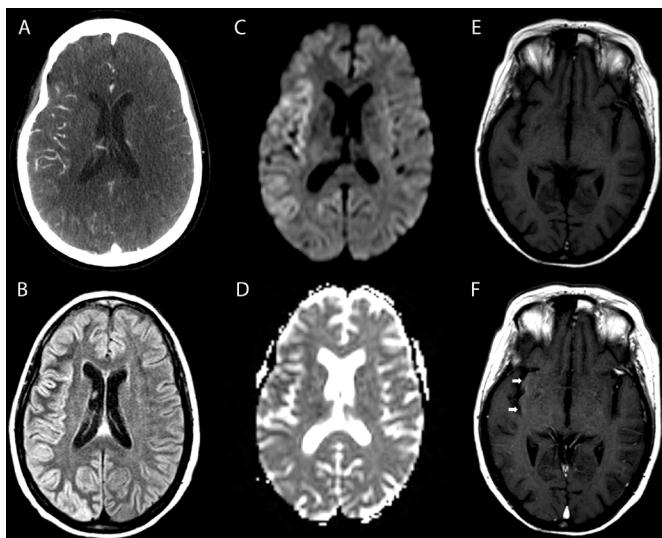


Figure 1 (A) CT angiography showing asymmetry with apparent decrease in size and quantity of left-sided M2 and M3 vessels compared with the contralateral right side, initially thought to be ischaemic in nature and ultimately found to represent right-sided hyperaemia. (B) Axial FLAIR sequence showing right holohemispheric cortical hyperintensity. (C) Axial DWI showing right cortical hyperintensity with no apparent corresponding hypointensity on axial ADC (D). Pre-contrast (E) and post-contrast (F) axial T1-weighted images demonstrating right insular contrast enhancement (arrows).

Laboratory workup was pertinent for leukocytosis to 16 400/ μ L (range 3600–10 000/ μ L) which was 89.7% neutrophilic, erythrocyte sedimentation rate (ESR) 45 mm/hour (range 0–30 mm/hour), C-reactive protein 1.6 mg/dL (range 0–0.5 mg/dL), normal cerebrospinal fluid (CSF) cell count and cytology and CSF protein 240 mg/dL (range 15–45 mg/dL) with elevated IgG synthesis index and two detectable oligoclonal bands that were not present in serum. Notably, thyroid stimulating hormone (TSH) was 1.77 μ IU/mL (range 0.27–4.32 μ IU/mL), but the patient was found to have elevated anti-thyroid peroxidase (TPO) antibody 95.1 IU/mL (range 0–34 IU/mL), elevated thyroglobulin 379 ng/mL (range 1.5–38.5 ng/mL) and normal anti-thyroglobulin (TG) <1 IU/mL (range 0.0–0.9 IU/mL). Normal investigations included Epstein Barr virus (EBV), HIV, Venereal Disease Research Laboratory (VDRL), herpes simplex virus (HSV), varicella zoster virus (VZV), West Nile virus (WNV), *Cryptococcus* and human herpes virus 6 (HHV6), as well as dsDNA, Smith, ribonucleoprotein (RNP), C3/C4, Celiac; the patient had known high-titre antinuclear antibodies (ANA), SS-A and SS-B antibodies in the setting of her Sjogren's syndrome (SS). Serum paraneoplastic and autoimmune encephalitis lab panels were negative, including anti-Hu, anti-NMDA receptor 1 (anti-NR1), anti-glutamic acid decarboxylase 65 (anti-GAD65), anti-leucine-rich glioma-inactivated 1 (anti-LGI1), anti-voltage gated potassium channel (anti-VGKC), anti-contactin-associated protein 2 (anti-CASPR2), anti-Ma1, anti-Ma2, anti-collapsin response mediator protein 5 (anti-CV2/CRMP5) and anti-amphiphysin; the patient had a normal CT of chest, abdomen and pelvis.

TREATMENT

She was subsequently started on high-dose intravenous methylprednisolone for presumed autoimmune encephalitis. Over the first few days of her admission, her mental status declined and

she could no longer follow simple commands, was non-verbal and had global decorticate posturing. On day 5, she developed focal seizures that manifested with versive leftward gaze and rhythmic orofacial movements that ultimately responded to levetiracetam and fosphenytoin while being monitored in the ICU. Given her lack of response to methylprednisolone, a 5-day course of intravenous Ig was started, leading to progressive improvement of her neurological deficits and allowed her to be transferred for acute rehabilitation after a 23-day admission. She was transitioned to mycophenolate mofetil 1500 mg two times per day maintenance therapy.

OUTCOME AND FOLLOW-UP

At interval follow-up, the patient remained on mycophenolate mofetil maintenance therapy and demonstrated baseline dysarthria and ataxia with no recurrence of her left hemiparesis, haemianopia or seizure activity since establishing remission with intravenous Ig. Surveillance MRI brain 2 years after presentation showed slight continued enhancement in the previously encephalitic regions. Given the concern that this may represent incompletely treated persistent inflammation, she has recently been referred to a neuro-immunologist for consideration of advancement of immunosuppression.

DISCUSSION

A broad differential must be explored in cases of encephalopathy of unclear aetiology. In this complex patient with known SCA10, a subtype that is specifically associated with seizures,⁴ an ictal presentation must be considered as this could be phenotypically consistent with the observed diffusion restriction of the cortical ribbon. The EEG performed on hospital day 2 was not compatible with an epileptiform presentation, thus in the absence of clinical seizures at onset, status epilepticus was not felt to explain her presentation or initial MRI brain. The patient's existing diagnosis of SS was another challenging potential contributor to her presentation. MRI changes in SS are most commonly non-specific T2-weighted hyperintensities that are indecipherable from age-related changes and small vessel cerebrovascular disease.⁵ SS does have a variety of recognised neurological manifestations, most commonly including neuropathy and focal optic nerve, brain or cord lesions similar to those seen in multiple sclerosis. Encephalopathy was a reported occurrence in 2 of a retrospective series of 82 SS patients,⁶ however, the causal relationship with SS in these patients was unclear, and the disease was not felt to be a likely contributor to our patient's presentation.

Limbic encephalitis represents another important differential consideration in this patient presenting with altered mentation, elevated CSF protein, and EEG slowing. Serum testing performed on this patient decreased suspicion for common paraneoplastic or autoimmune encephalitides, including anti-N-Methyl-D-Aspartate (NMDA) which was evaluated with anti-NR1. It should be noted that serum testing as in this case only achieves 85.6% sensitivity for anti-NMDA encephalitis versus 100% sensitivity when CSF is tested,⁷ and had we not elicited positive anti-TPO antibodies, further consideration would have been given to testing more sensitively or exploring the possibility of seronegative limbic encephalitis as the diagnosis.

HE is itself a difficult and controversial diagnosis. It is known that antithyroid antibodies are non-specific and can be present in 13% of healthy individuals; prevalence is thought to be even higher in our patient's demographic, as the antibodies can be present in up to 27% of women greater than 60.⁸ An additional

element of complexity is that this presumed case of SREAT was not steroid responsive. Careful review of prior attempts in the literature to quantify steroid responsiveness suggests that only up to 19% will have complete response to steroids alone within the first month.⁹ Analysis of a 251-patient case review shows that though greater than 90% were reported to have at least a partial response to steroids at that interval, 38% required a second-line treatment to achieve adequate therapy. Therefore, despite all competing considerations, HE was ultimately presumed to be the most likely aetiology.

Our patient's lateralised encephalitis confined to the right hemisphere was felt to be a curious feature illustrating the well-described heterogeneity of HE manifestations. Exclusive involvement of a unilateral hemisphere may suggest consideration of Rasmussen syndrome,¹⁰ a possibility that was not entertained in this patient given her age and the acuity of her presentation. From the radiologist's perspective, her initial imaging with CTA appeared to represent a left MCA vaso-occlusive condition; were it not for the discordance with her left-sided clinical deficits, an ischaemic algorithm may have been pursued. Indeed, ischaemia was among the top three initial misdiagnoses along with viral encephalitis and Creutzfeldt-Jakob disease in a series of 20 cases that were later determined to be HE.¹¹ Ultimately, the DWI and FLAIR signal changes with elevated CSF protein prompted the encephalitic workup which indicated that her disease and imaging was representative of a hyperaemic state.

Mechanisms underlying HE remain undefined, but several well-described pathological specimens have implicated inflammatory microvascular infiltration.¹²⁻¹³ The existing literature characterising neuroimaging in HE uniformly reports normal CTA findings.¹⁴⁻¹⁵ Our patient's demonstration of increased blood flow may suggest a local autoregulatory loss. The few existing HE cases documenting cerebral perfusion with

single-photon emission computed tomography (SPECT) demonstrated non-specific patchy uptake heterogeneity in two cases¹⁵ and one case showing global SPECT hypoperfusion in the setting of hypothyroidism.¹⁶ Our case appears to stand in contrast with these but does support that HE has a vascular consequence. It also highlights the importance of considering HE in the setting of a wide variety of unexplained neurological symptoms.

Contributors TAG: primary and corresponding author. GNJ: literature search and editing. YL: staff provider for patient and editing.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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Learning points

- ▶ Hashimoto's encephalopathy presents heterogeneously and can include seizures, myoclonus and psychiatric symptoms in addition to ischaemic presentations.
- ▶ Demonstration of hyperaemia in our case supports the suspected microvascular inflammatory mechanism of the disease, potentially resulting in loss of local autoregulation.
- ▶ Investigation for this condition should be pursued in patients presenting with encephalopathy in whom an autoimmune or inflammatory aetiology is suspected.

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