Case report

A 51-year-old physician was found in a taxi unable to tell the driver her address. At the emergency room, she was barely able to speak, disoriented and incontinent with mild left hemiparesis. Her history included transient left hemiparesis 8 years before when primary antiphospholipid syndrome (APS) as well as autoimmune hepatitis and Hashimoto’s thyroiditis were diagnosed. She was on warfarin, azathioprine, eltroxin and olanzapine/valproic acid for an undefined psychosis that developed since. Brain CT was normal and she apparently recovered within 12h and was discharged.

Two days later, sudden aphasia, unresponsiveness and right hemiparesis appeared, followed by rigors, vomiting and fever with 40.6°C. Heart rate was 117/min (normal electrocardiogram, normal chest X-ray) and BP 135/60 mmHg. No signs of meningeal irritation were found. She was aphatic, unresponsive and rigid with mild gaze deviation to the left, 4/5 right hemiparesis and an extensor plantar response. Fundoscopy and the remainder of the examination were normal except for a known mitral systolic murmur. Laboratory tests showed Hb 12 g/dl, white blood cells 3.2×10³/µl (neutrophils 2.4, lymphocytes 0.5) and platelets 98×10³/µl. International normalized ratio was 1.5. Urinalysis and serum chemistry including CPK were normal. Thyroid stimulating hormone, free T4 and T3 were normal. Plasma ammonia was normal and Valproate levels were 63 mg/l (N=50–100). These results were similar to her previous tests over the past years.

Head CT, cerebral CT angiography and later MRI revealed no pathology. Cerebrospinal fluid protein was 87 mg/dl (N<45) with no other abnormality including negative tests for viruses and syphilis. The electroencephalogram (EEG) revealed diffuse slowing, more prominent over the left hemisphere (Figure 1). All drugs except for warfarin and eltroxin were discontinued.

The patient remained somnolent, unresponsive and febrile. ESR was 61 mm/h, C-reactive protein 5 mg/dl. Extensive cultures and serology tests were negative. Transthoracic echocardiography showed no vegetations. Anticardiolipin and anti-β2 glycoprotein antibodies were positive, associated with low-titer antinuclear antibodies (ANAs; 1:80)—unchanged over the past years. Antibodies to double-stranded DNA, Sm, RNP, ribosomal P protein, histone, antibodies to Ro antigen (SS-A), antibodies to La antigen (SS-B), RF and antineutrophil cytoplasmic antibodies remained negative, and serum complement was normal. An assay for serum thyroperoxidase (TPO) antibodies yielded a titer of <1:1000. With a presumptive diagnosis of Hashimoto’s encephalopathy, pulse therapy with methylprednisolone 1g IV for 5 days was started. The patient slowly responded, though initially generalized convulsions developed, controlled with phenytoin. Within 7 days she was responding to her name. Over the next 24 days, steady improvement continued until she could be discharged home on tapering prednisone treatment. A week after her discharge she was walking independently, and talking coherently without cognitive impairment.
Discussion

The patient’s initial wide differential diagnosis (Table 1) was soon exhausted by the negative tests and incompatible clinical features. Her unique fluctuating presentation with severe generalized and focal neurological signs and fever in the absence of any demonstrable anatomical or biochemical abnormalities, or evidence of infection, prompted a consideration of an unusual encephalopathy. Her many previous autoimmune conditions strongly suggested a similar pathogenesis. ‘When you have ruled out the impossible, whatever remains, however improbable – must be the truth . . .’, advised Sherlock Holmes. In Hashimoto’s encephalopathy, this is highly important since no test is specific and other compatible entities must be carefully excluded. First reported by Brain et al.,¹ Hashimoto’s encephalopathy, albeit rare, fits our patient’s illness. Although fever is not typical, fluctuating cognitive impairment and behavioral changes, aphasia, seizures, somnolence, myoclonus and sometimes focal neurological deficits commonly occur.² Normal imaging results were reported for most patients, but the EEG reveals a generalized slowing. Patients are predominantly female with a background of Hashimoto’s thyroiditis, usually normal thyroid function but markedly

Table 1  Main differential diagnoses considered and ruled out in the reported patient

(I) Autoimmune
- SLE with lupus cerebritis
- Ischemic CNS events due to APS
- Primary CNS vasculitis
- Paraneoplastic encephalopathy

(II) Drug-induced
- Neuroleptic malignant syndrome (olanzapine)
- Valproate encephalopathy
- Serotonin syndrome

(III) Infective
- Acute viral encephalitis
- Infective endocarditis with emboli
- Acute systemic infection affecting CNS
- CJD

(IV) Other
- Thyroid storm
- Hepatic encephalopathy
- Lethal catatonia
- Acute psychosis

¹The occurrence of thrombocytopenia and lymphopenia, even psychosis, in APS and the very low titer of ANA (common in APS but not in SLE) in the absence of any other autoantibodies or signs supporting lupus make lupus cerebritis unlikely. CJD: Creutzfeldt-Jakob disease.
increased thyroid autoantibodies. Their role remains questionable, though characteristic responsiveness to steroids or plasmapheresis makes an autoimmune pathogenesis likely.3 ‘Steroid-responsive encephalopathy associated with autoimmune thyroiditis’ is a grave but treatable illness that must be better recognized.

Conflict of interests: None declared.

References