Posterior reversible encephalopathy syndrome in a patient with anticentromere positive Sjögren's syndrome/ mixed connective tissue disease overlap: a case report and review of the literature

Sirs,

Posterior reversible encephalopathy syndrome (PRES) is defined by a range of reversible neurological symptoms and signs of acute/subacute onset including alterations of consciousness, confusion and epileptic seizures along with distinctive neuroimaging findings reflecting vasogenic oedema (1). It has diverse aetiology, but frequently develops in the context of arterial hypertension, renal disease, sepsis, (pre)eclampsia, autoimmune disorders and immunosuppressive medications (2). Symptoms related to blood pressure fluctuations, visual disturbances because of occipital lobe involvement, headache and focal neurological deficits depending on the location of the lesions, can also occur (2). The treatment of PRES is symptomatic and the management of the underlying disease is crucial along with control of blood pressure and administration of anti-seizure medications. The overall prognosis is favourable, since clinical and imaging findings are reversible in most patients (2). In this report, we describe a case of PRES in a 58-year-old female patient with a known history of anticentromere antibody positive Sjögren's syndrome (SS) and mixed connective tissue disease (MCTD) [ACA (+) SS/MCTD] overlap (3-4), treated with azathioprine 50mg bid and low doses of oral steroids. The diagnosis was based on a constellation of clinical symptoms/signs and immunological findings including objectively confirmed sicca complaints, Raynaud's phenomenon, pulmonary hypertension, myositis, recurrent serositis, small joint polyarthritis along with positive antinuclear (>1:320, speckled pattern) and anticardiolipin antibody titres (only IgM type), as well as the presence of reactivities against Ro52, U1RNP and CENPB. She was admitted to the hospital because of auditory and visual illusions and a 2-month history of progressive gait, mood and memory alterations along with urinary incontinence. Physical examination revealed normal blood pressure and left pyramidal signs. Magnetic resonance imaging (MRI) showed multiple, large hyperintense lesions in T2- weighted and fluid-attenuated inversion recovery (FLAIR) sequences (for distribution, see Figure 1A). Electroencephalography (EEG) showed frequent recordings of slow waves in the frontal areas and paroxysmal rhythmic delta activity, without suggestive recordings for Creutzfeld-Jacob disease. A new MRI brain (Fig.1 B-F), performed 2 weeks later, revealed imaging deterioration. Given the absence of arterial stenosis on MR angiography and of vessel wall enhancement on T1 black blood images, the diagnosis of a vasculitis was considered less likely. Reduced relative cerebral blood volume on perfusion imaging and choline concentrations on MR- spectroscopy were suggestive of a non-neoplastic diagnosis. Cerebrospinal fluid (CSF) analysis revealed elevated albumin and albuminocytologic dissociation. Blood, urine and CSF cultures did not show any significant growth and anti-ribosomal P-protein and anti-β2GPI antibodies were negative. Infective, demyelinating, paraneoplastic causes, as well as autoimmune encephalitis, were also ruled out following extensive work up. Based on the above findings, PRES diagnosis was undertaken in the context of ACA (+) SS/MCTD overlap. She was treated with intravenous high steroid doses (total 8gr of methylprednisolone), followed by oral steroids with slow tapering. From the 4th day of the treatment, she gradually began to show clinical improvement. Within 17 days following therapy onset, the patient recovered completely. A new brain MRI (Fig.1 G-J) revealed significant reversal of lesions and intravenous rituximab treatment was initiated. At one year of follow-up, the patient was stable without symptoms with unremarkable MRI findings. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

To the best of our knowledge, this case is the first report of PRES in a patient with ACA (+) SS/MCTD overlap. In Table I, a sum-

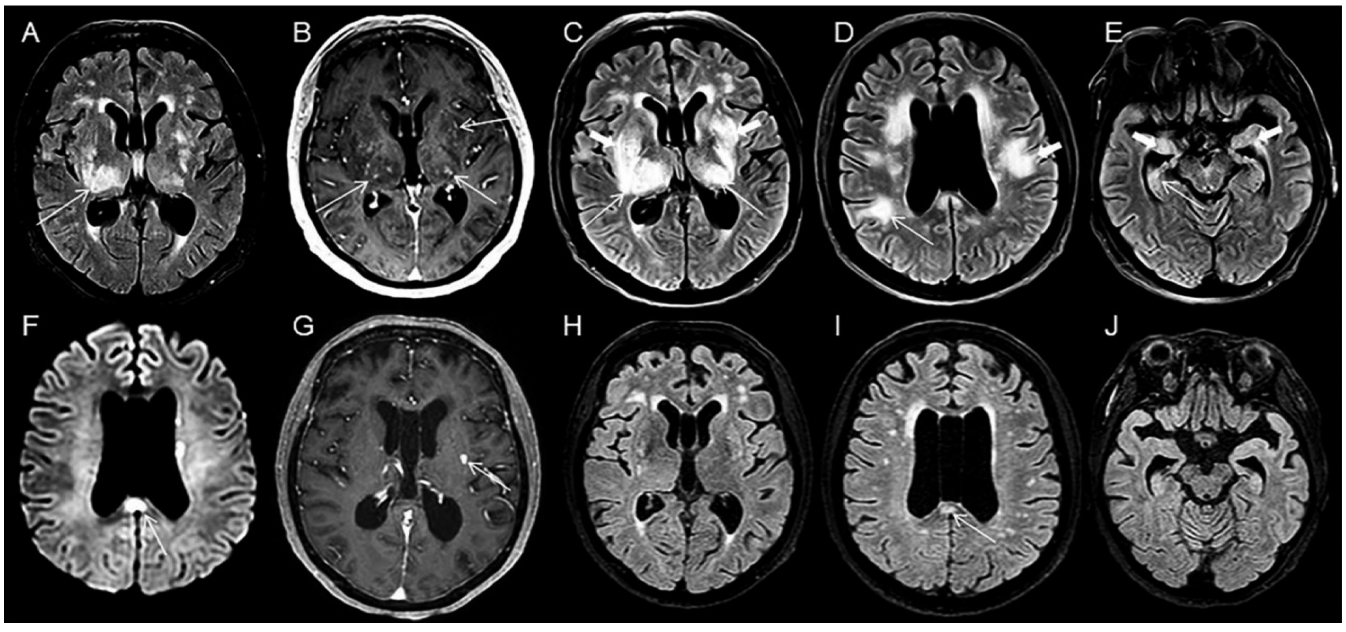

Fig. 1. Axial FLAIR image (**A**) of the initial MRI shows hyperintensities in bilateral thalami, external capsules and putamen, most evident in the right thalamus (arrow A). T1 weighted axial image post contrast administration two weeks later (**B**) shows areas of linear and punctate enhancement (arrows B) in basal ganglia and thalami. Axial FLAIR images of the same examination (**C, D, E**) reveal increase of lesion size in bilateral thalami (arrows C), basal ganglia, internal and external capsules (thick arrows C), subcortical parietal (arrow D) and frontoparietal (thick arrow D) white matter, bilateral temporal poles (thick arrows E) and right hippocampus (arrow E). Restriction on DWI (**F**) in the same examination was seen in the splenium of the corpus callosum (arrow F) and in the left corona radiate. Axial T1 post contrast image 17 days after treatment onset (**G**) shows only few spots of enhancement (arrow G). Lesions resolution is seen on axial FLAIR images of the same exam (**H, I, J**), with remaining T2-hyperintensities mainly in the frontal periventricular white matter and in the splenium of the corpus callosum (arrow I).

Table I. Summary of overlap CTDs cases in the literature complicated by PRES.

Source	Age	Sex	Rheumatologic diagnosis	Clinical findings	Brain MRI hyperintense lesions (T2-FLAIR)
Kobatake *et al*. (5)	56	F	SSc/PM	HE, V, VD, HY, S	Occipital, Basal ganglia, Thalamus, Cerebellum, Brainstem
Gatla *et al*. (6)	37	F	SLE/RA	HE, HY, AC	Posterior fossa, Supratentorial, Infratentorial
Matsui *et al*. (7)	51	F	SSc/DM	HE, HY, VD, AC, S	Frontal, Parietal, Occipital, Pons
Yong *et al*. (8)	39	F	SSc/SLE	HY, S, VD	Frontal, Parietal, Occipital, Cerebellum
Our patient	58	F	SS/MCTD	AC, VD	Frontal, Parietal, Temporal, Thalamus, Basal Ganglia, Hippocampus, Pons, Cerebellum

AC: altered cognition; DM: dermatomyositis; F: female; HE: headache; HY: hypertension; MCTD: mixed connective tissue disease; PM: polymyositis; RA: rheumatoid arthritis; S: seizure; SLE: systemic lupus erythematosus; SS: Sjögren's syndrome; SSc: systematic sclerosis; V: vomiting; VD: visual disturbances.

mary of previously published overlap connective tissue disease syndromes cases complicated by PRES are presented (5-8). While the underlying pathophysiological mechanism remains partly unclear endothelial cell damage, vasculopathy and autonomic dysfunction have been postulated (1, 9). Awareness for this rare association is crucial for timely diagnosis and treatment to minimise the risk of permanent neurologic deficits.

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