LETTER TO THE EDITOR

A case of anti-N-methyl-D-aspartate receptor encephalitis with systemic sclerosis

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Sir,

Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis is characterized by the presence of antibodies against NR1–NR2 heteromers of the NMDAR (anti-NMDAR antibodies) with ovarian teratoma [1]. However, recently, it has become clear that anti-NMDAR encephalitis is not always paraneoplastic [2]. We present a female patient affected with anti-NMDAR encephalitis and systemic sclerosis (SSc), the disease activity of which synchronized with each other.

A 70-year-old female patient had Raynaud's phenomenon, weight loss, easy fatigability, muscle weakness, and skin sclerosis. Six months later, she presented with cognitive impairment and gait disturbance. Physical examination showed skin sclerosis and ulcers on the hands, face, and feet. Neurological examination revealed dementia (15/30 in the Mini-Mental State Examination), resting tremor, ataxia, rigidity, and muscle weakness in the extremities. Pathological reflexes were bilaterally positive. Brain magnetic resonance imaging (MRI) showed high intensities in bilateral basal ganglia and thalamus on fluid-attenuated inversion recovery (FLAIR) images (Fig. 1). Brain magnetic resonance angiography showed normal. Initial cerebrospinal fluid (CSF) examination showed normal cell count, elevated total protein (112 mg/dl) and IL-6 (5.8 pg/ml). Oligoclonal IgG Bands were negative. Chest computed tomography (CT) showed mild interstitial pneumonitis (Fig. 1). Serological analysis showed increased serum antinuclear antibody titer (1:80 with diffuse speckled pattern). Elevation of tumor markers (CEA, NSE, Pro-GRP, and AFP) or paraneoplastic antineuronal antibodies were not revealed. Anti-NMDAR anti-

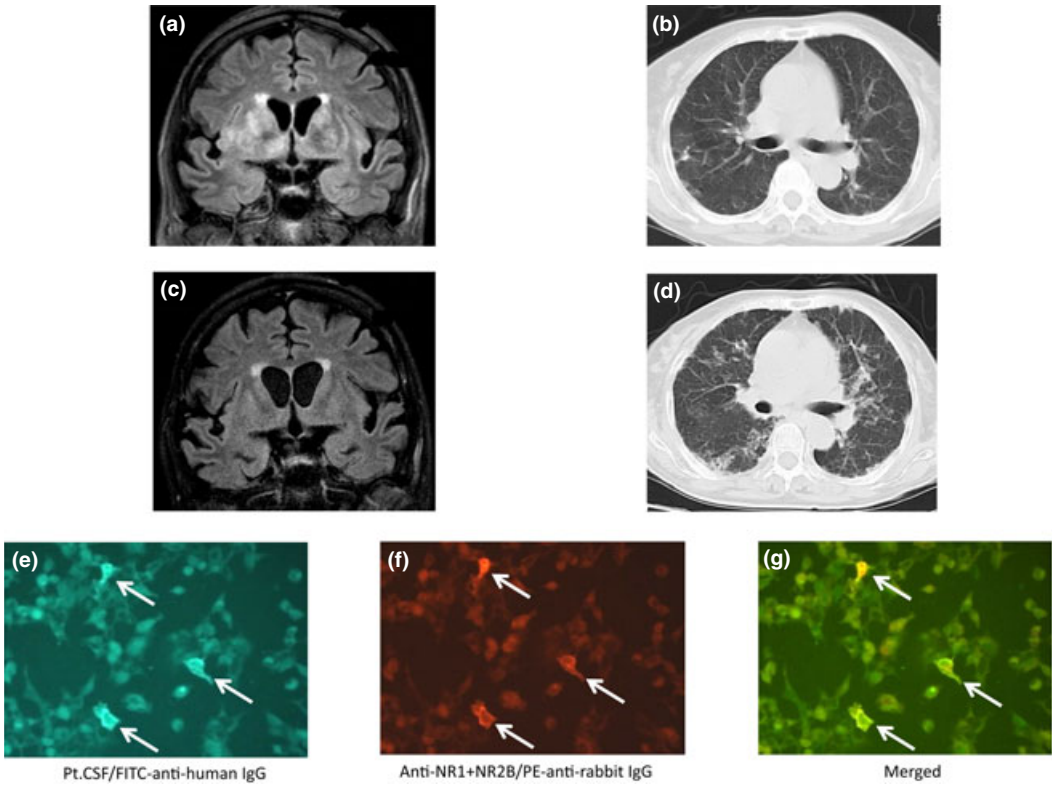

Figure 1 Brain MRI, chest CT and antibody assay. (a) Brain MRI on admission showed high signal lesion in the basal ganglia and thalamus on FLAIR images. (b) Chest CT showed mild interstitial pneumonitis. (c) Brain MRI after 3-courses of high dose intravenous methylprednisolone showed improvement of high signal lesions on FLAIR images. (d) Two weeks later, chest CT showed severe interstitial pneumonitis. Immunohistochemical demonstration of antibodies against NMDAR. (e) CSF of the patient showing positive immunoreactivity against heteromers of NR1 and NR2B subunits of NMDAR. (f) Anti-NR1 + NR2B antibodies produced in rabbits were visualized with PE-anti-rabbit IgG. (g) Merge image. Arrows indicate positively stained HEK cells (original magnification ×200).

bodies were present in CSF (Fig. 1). The patient's clinical diagnosis was anti-NMDAR encephalitis with SSc. Three courses of high-dose intravenous methylprednisolone (a course: 1000 mg/day for 3 days) led to complete recovery and disappearance of MRI abnormalities (Fig. 1).

Two weeks later, she showed cognitive impairment again (10/30 in the Mini-Mental State Examination) and severe dyspnea. Brain MRI results showed normal. The results of CSF examination showed normal cell count and normal protein concentration. Chest CT showed aggravated interstitial pneumonitis (Fig. 1). Anti-NMDAR antibodies were present in serum and CSF. A course of high-dose intravenous methylprednisolone, followed by oral prednisolone (20 mg/day) and cyclophosphamide (50 mg/day), led to complete recovery from cognitive impairment, but interstitial pneumonitis remained. Despite an extensive oncologic workup such as pelvic MRI and whole-body FDG positron emission tomography, there was no evidence of tumor, thus confirming the diagnosis of anti-NMDAR encephalitis with SSc.

There is no report that antibodies against NR1–NR2 heteromers of the NMDAR were present in patients with SSc. Recent reports support the idea that central nervous system (CNS) involvement in SSc is not uncommon [3,4]. Not only stroke events such as transient ischemic attacks, ischemic stroke, and hemorrhage but neuropsychiatric manifestations such as loss of memory, disorientation, depression, hallucinations, and reduced mental acuity have also been described. Whether symptomatic or not, MRI revealed CNS involvement in the form of white matter hyperintensities mostly because of ischemic vasculopathy which was significantly more common in patients with SSc than in control groups [3]. In this case, abnormalities in basal ganglia and thalamus were detected by brain MRI, which corresponded well with the clinical observations. Both neurological abnormalities and brain MRI abnormalities were improved by immunotherapy. We consider that the pathogenetic mechanism of anti-NMDAR encephalitis was related to SSc, because the disease activity synchronized with each other. It is necessary to accumulate antibody-positive cases to delineate the clinical manifestations of anti-NMDAR encephalitis. This case may add to our understanding of central nervous system involvement in SSc.

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Disclosure of conflict of interest

There is no actual or potential financial and other conflict of interest related to the submitted manuscript.

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