Case Report

Paraneoplastic striatal encephalitis and myelitis associated with anti-CV2/CRMP-5 antibodies in a patient with small cell lung cancer

Nese Dericioglu⁎, Rahsan Gocmen, Ersin Tan

⁎ Hacettepe University, Department of Neurology, Ankara, Turkey

1. Introduction

Paraneoplastic neurological syndromes (PNS) affecting the central nervous system are infrequent, presenting in < 1% of all those with cancer. The relevant auto-antibodies, that are detected in serum or cerebrospinal fluid, can target either neuronal cytoplasmic/nuclear proteins or neuronal cell surface proteins such as ion channels. The type of antibodies detected may determine the underlying malignancy and also response to immunotherapy.

Anti-CV2/CRMP-5 is a 62-kDa neuronal cytoplasmic protein of the collapsin response-mediator family that is usually correlated with thymoma or small cell lung cancer (SCLC). The PNS associated with anti-CV2/CRMP-5 is generally characterized by encephalomyelitis, paraneoplastic sensory neuronopathy, uveitis or chorea [1]. We have recently encountered a patient with prominent motor weakness and behavioral changes whose cranial MR investigation was compatible with striatal encephalitis and spinal MR imaging revealed longitudinally malignant myelitis. Paraneoplastic antibody screening was positive for anti-CV2/CRMP-5 antibodies. Meticulous workup disclosed small cell lung cancer (SCLC) as the underlying pathology.

2. Case report

A 54-year-old female patient was admitted due to weakness in the left arm and both legs. Her complaints began a year ago with left leg weakness and accompanying pain below the knee. Three weeks prior to admission she developed severe weakness in both legs and left arm. Her family also noticed abnormal movements in both arms. Meanwhile she also displayed altered behavior, and seemed to be more nervous than ever. She spoke too much, tended to repeat the same sentences, and could only sleep two hours at night. The patient had lost weight within the last 3 months. Besides, she complained of shortness of breath. Her past medical history revealed hypertension, total abdominal hysterectomy for uterine leiomyoma and cigarette smoking (one package per day for 30 years). Family history disclosed lung cancer in her mother. On neurologic examination she was conscious, however had difficulty in obeying commands. She had paraparesis and left upper extremity weakness, with corresponding hyperactive deep tendon reflexes. Cranial nerve functions and sensory exam were normal. Choreiform movements were not evident upon admission.

Her complete blood count, biochemistry and blood tumor markers (alpha-fetoprotein, CA-125, CA15-3, CA19-9, carcinoembryonic antigen) were within normal limits. ESR was 24 mm/h. CSF protein was 51.2 mg/dL, glucose was 86 mg/dL. There were no neoplastic cells on cytologic examination. IgG index was 3.8 and oligoclonal band studies were compatible with intrathecal synthesis. Electrophysiologic studies suggested anterior horn motor neuron or multiple radicular involvement in the cervical and lumbar regions (supplementary Tables 1 and 2). Cranial MR imaging was impressive for bilateral symmetrical hypointensity in basal ganglia, especially corpus striatum (Fig. 1A–C). MR perfusion showed mildly decreased blood volume (Fig. 1E), and MR spectroscopy indicated mildly decreased NAA peak (Fig. 1F). Spinal MR in cervical and thoracic segments revealed longitudinally extensive abnormal T2W signal (Fig. 1D). Due to the possibility of paraneoplastic striatal encephalitis and myelitis the patient underwent computed tomography of the chest, which was reported as two separate mass lesions.
Fig. 1. (A–G): MRI findings at the time of the neurologic event (A–F) and at follow-up one month later (G). Axial T2W image (A) shows symmetrical hyperintensity in the bilateral caudate nuclei and putamina. There is no contrast enhancement (B), diffusion restriction (C), hemorrhage, or expansion. Sagittal cervical spine T2W MRI image (D) shows longitudinally extensive T2 signal abnormality extending over 10 spinal segments. T2* MR perfusion –cerebral blood volume color map– (E) demonstrates mildly decreased blood volume. 1H MR spectroscopy (TE = 135 msec) (F) shows mildly decreased NAA peak; no abnormal lactate peak is observed. Follow-up axial T2W image (G) reveals substantial resolution in previously affected regions.

Fig. 2. Coronal PET image of the body demonstrates increased FDG uptake in two separate lesions located in the upper lobe of the left lung (roughly 4 cm and 3 cm in diameter; SUV: 12.9 and 14.4) and also left axillary lymph nodes (about 2 cm in diameter; SUV: 18.2).
Contrary to our patient, striatal hypermetabolism was reported in three patients with limbic encephalitis correlated with anti-voltage gated potassium channel antibodies [5]. In another case with anti-CRMP5 antibody associated paraneoplastic chorea, PET was consistent with bilateral caudate hypometabolism [1]. However cerebral PET imaging studies were normal in our patient. Different results may be due to different stages of the disease process in these patients or due to different characteristics of the autoimmune antibodies (i.e. attacking cell surface vs intracellular antigens).

Treatment modalities and response to therapy vary among patients. Chemotherapy was tried in a few patients [1,2], and so far seems to be the best choice of management. Neurologic deficits improved in some cases [1,2]. Corticosteroids, intravenous immunoglobulin or plasmapheresis were not usually helpful. Most patients died within several months of presentation. This finding is not surprising in patients with antibodies directed at intracellular antigen targets (i.e., onconeural antibodies). In these patients the neuronal dysfunction is mediated by cytotoxic T cells and usually results in irreversible neuronal damage. Autopsy studies in a few patients with PSE have shown diffuse perivascular lymphocytic infiltrates, microglial activation and neuronophagia in the striatum or throughout the neuraxis [1,3].

4. Conclusion

Our findings are in line with those of previous cases with PSE. Acute onset of chorea, muscle weakness, behavioral abnormalities in an elderly patient with hyperintense appearance of basal ganglia in cranial MR and spinal imaging should raise the possibility of PNS and prompt the investigation of onconeural antibodies (especially anti-Hu and anti-CV2/CRMP-5), especially in patients with high risk for malignancy. Rapid and aggressive tumor treatment may improve outcome in some patients.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi: https://doi.org/10.1016/j.clineuro.2018.05.010

References