Anorexia Heralding the Onset of Neuromyelitis Optica

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Abstract

Neuromyelitis optica (NMO) is an inflammatory disease of the central nervous system (CNS) that preferentially affects the optic nerves and spinal cord. An autoantibody (NMO-IgG) targeting the aquaporin-4 water channel distinguishes NMO from other inflammatory disorders of the CNS. Recent studies have demonstrated that the area postrema and other circumventricular organs (CVOs) can be targeted in NMO. We herein report the case of a 12-year-old girl who experienced anorexia six months before the onset of NMO. Anorexia caused by hypothalamic or CVO dysfunction may herald the onset of NMO.

Key words: aquaporin-4, circumventricular organs, anorexia

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Introduction

Neuromyelitis optica (NMO) is an idiopathic inflammatory disease of the central nervous system (CNS) that preferentially affects the optic nerve and spinal cord. An immunoglobulin G (IgG) autoantibody (NMO-IgG) targeting the water channel protein aquaporin-4 (AQP4) is the biomarker that distinguishes the NMO spectrum disorders (NMOSD) from multiple sclerosis (MS) and other CNS demyelinating disorders (1, 2). Compelling evidence suggests that this IgG plays a pathogenic role in NMOSD. AQP4 is concentrated in astrocytic foot processes at interfaces between the CNS parenchyma and fluid compartments, including both cerebrospinal fluid (CSF) and blood (1, 2), and in areas involved in the regulation of fluid balance and energy homeostasis, including the hypothalamus and sensory circumventricular organs (the subfornical organ, the organum vasculosum of the lamina terminalis and the area postrema). Neuroimaging has revealed NMO-typical lesions in these AQP4-rich areas (3). To date, two cases of young female patients with NMO who developed anorexia have been reported. In one case, the anorexia was associated with intractable nausea and vomiting and an inflammatory lesion involving the area postrema (4). In the other patient, the anorexia was accompanied by psychotic symptoms and was associated with an inflammatory lesion of the hypothalamus (5).

We herein describe the case of a young girl who experienced isolated anorexia six months before the onset of NMO and discuss the involvement of the circumventricular organs (CVOs) in AQP4 autoimmunity.

Case Report

A 12-year-old girl developed a fever that lasted for three days. When the fever subsided, the patient began to lose her appetite. Her baseline height was 161 cm and her baseline weight was 56 kg. During psychological counseling, she denied dieting or inducing vomiting. She also experienced irregular menstrual periods. She never developed nausea, vomiting, hiccups or symptoms of autonomic dysfunction. She lost 12 kg in six months. Thereafter, she experienced acute bilateral visual loss in the setting of a demyelinating disease diagnosed as acute disseminated encephalomyelitis at a local hospital. After six months, she developed dizziness and upper limb paresthesias and was referred to our clinic. Brain MRI revealed multiple hyperintense lesions on T2-weighted images, all showing ring-enhancement after gadolinium administration (Figure A-C). Spinal cord MRI showed a longitudinally extensive lesion involving C1-C2-C3-C4 (Figure D). A cerebrospinal fluid analysis revealed no pleocytosis along with normal glucose and protein levels and the presence of oligoclonal bands. The visual evoked potentials showed a bilateral increase in P100 latency (P100 right eye: 133 msec; P100 left eye: 166 msec). The somatosensory evoked potentials were altered in the upper limbs...
The traditional view that NMO lesions are restricted to the optic nerve and spinal cord has been challenged by recent studies (3) that have revealed that the brain can be targeted in NMO. Brain lesions are now a well-recognized feature of NMO (3), and the presence of “cloud-like” enhancement has been described as being specific for the disease (6). In particular, pathological (7), radiological (3) and clinical (8, 9) studies have shown that brain sensory CVOs (the area postrema, organum vasculosum lamina terminalis and subfornical organ) are preferentially involved in NMO.

Sensory CVOs are specialized structures of the CNS with fenestrated capillaries that represent a “window” through which the autonomic nervous system gains direct information about the status of variables in the systemic circulation (10). The morphologic and functional features of CVOs, in particular, the absence of an intact blood-brain barrier, allow access of circulating IgG and cytokines to these regions. Sensory CVOs play a key role in regulating the fluid and energy homeostasis of the body, thereby influencing feeding and drinking behavior through connections with the hypothalamus and limbic system (7). We hypothesize that the anorexia observed in our patient was caused by a dysfunction of the sensory CVOs. Unfortunately, we were unable to obtain the images of the first brain MRI of our patient, and subsequent MRIs did not reveal any inflammatory lesions in these regions. Eating disorders have already been reported in the setting of neuromyelitis optica. Both anorexia (4, 5) and an increased appetite (11) associated with inflammatory lesions involving the area postrema or the hypothalamus have been described in NMO patients. Pathologic studies have revealed that inflammatory lesions of the area postrema are present in up to 40% of NMO patients (9). However, the subfornical organ and the organum vasculosum of the lamina terminalis have not yet been studied in patients with NMO.

These two CVOs are both strongly interconnected with the median preoptic nucleus of the hypothalamus, and together these three structures form the “anteroventral third ventricle region” that, in conjunction with the area postrema, is critical for the maintenance of body energy homeostasis and the regulation of feeding behavior (12). The brain lesions observed in our patient fulfilled the MS criteria for dissemination in space (13). Young patients with MS may have long spinal cord lesions, similar to patients with NMO (14). Therefore, this case shows that, in young patients, making the differential diagnosis between NMO and MS may be harder than in adults and that testing for AQP4 antibodies is critical to reach the correct diagnosis and provide appropriate therapy. Dysregulated feeding behavior, syndrome of inappropriate antidiuresis (SIAD) and intractable nausea and vomiting due to CVOs or hypothalamic dysfunction are part of the spectrum of symptoms of NMO, and the presence of these clinical findings may be of help in making an accurate differential diagnosis with MS.

The authors state that they have no Conflict of Interest (COI).

References