Opsoclonus-Myoclonus Syndrome Following Influenza A Infection

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Abstract

A 60-year-old woman developed opsoclonus-myoclonus syndrome (OMS) a week after being diagnosed with influenza A infection by a rapid antigen test. She had no loss of consciousness. Opsoclonus, myoclonus, and truncal ataxia were noted. Two weeks after treatment with intravenous immunoglobulin and corticosteroids, her opsoclonus, myoclonus, and truncal ataxia disappeared. No malignant tumors were detected during the 3-year follow-up period. There has been no previous report of postinfectious OMS following confirmed influenza A infection. OMS without a loss of consciousness has been reported to be statistically less common in cases of non-paraneoplastic OMS. This finding was consistent with the present patient’s clinical manifestations.

Key words: influenza A infection, opsoclonus-myoclonus syndrome, ataxia, postinfectious

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Introduction

Several neurological complications associated with influenza infection, such as encephalopathy, Reye’s syndrome and myelitis, have been described (1). We encountered an adult case of opsoclonus-myoclonus syndrome (OMS) following influenza A virus infection. This is the first case of postinfectious OMS following confirmed influenza A infection to be reported in the literature.

Case Report

The patient was a 60-year-old woman who visited our hospital with gait disturbance. Five days before visiting our hospital, she displayed flu-like symptoms that were diagnosed as influenza A infection based on a positive result of a rapid antigen test from a pharyngeal mucus specimen. Oseltamivir (150 mg/day for 5 days) was administered, and her fever gradually declined. However, a day before visiting our clinic, she noticed changes in her speech and gait. She was admitted to our hospital for detailed examinations. She had a history of hypertension and hyperlipidemia, and was being treated with antihypertensive drugs. She had a 180-pack-year history of cigarette smoking, which had spanned a 20 year period, but which she had discontinued 20 years before this hospitalization. At the time of hospital admission, her blood pressure was 153/90 mmHg and her pulse was 105 beats/min. Her temperature was 36.5°C. Her other physical examination data revealed no abnormalities. She was alert and oriented. Chaotic bursts of conjugate eye movements were present in all meridians, increasing with eye movements and attempts to fix her gaze. Myoclonic jerks were present in the right side of the face and the right upper limb. No palatal myoclonus was seen. Limb weakness was not present, but the limb and truncal ataxia were severe. For this reason, she could not stand or sit without assistance. Hyper-reflexes in the limbs with pathological reflexes were present. No sensory loss, including bathyaneesthesia, meningeal irritation, or bladder and rectal disturbances were noted.

Her blood tests revealed the following: hemoglobin, 14.5 g/100 mL; leukocyte count, 7,100/mm³ (neutrophils, 73%; lymphocytes, 20%); aspartate aminotransferase, 38 IU/L;
alanine aminotransferase, 53 IU/L; lactate dehydrogenase, 275 IU/L; alkaline phosphatase, 142 IU/L; γ-glutamyl transpeptidase, 52 IU/L; creatinine, 1.07 mg/100 mL; sodium, 145 mEq/L; potassium, 3.5 mEq/L; total cholesterol, 224 mg/100 mL; hemoglobin A1c, 5.7%; creatinine phosphokinase, 84 IU/L; lactic acid, 12.2 mg/100 mL; pyruvic acid, 1.31 mg/100 mL. The thyroid function tests and anti-nuclear antibody test were within the normal limits. An examination of her serum for antibodies against the human immunodeficiency virus, hepatitis C virus, hepatitis B virus and lues were negative. She was anti-Ri antibody negative. Her cerebrospinal fluid contained the following: leukocytes, 11/mm³ with 25 mononuclear cells and 8 polymorphonuclear leukocytes; protein, 95 mg/100 mL; glucose, 71 mg/100 mL (plasma glucose, 159 mg/100 mL); and IL-6, 4.3 pg/mL. The oligoclonal IgG band was negative.

The serial rapid antigen test for influenza virus at her admission was negative. The serum antibody titer against influenza A virus was X8. Influenza A virus RNA was not detected in the cerebrospinal fluid by the reverse transcription polymerase chain reaction (RT-PCR) method. Cultures of blood and cerebrospinal fluid were negative. The cerebrospinal fluid cytology was class II. The anti-ganglioside antibody level in her serum was assessed using an enzyme-linked immunosorbent assay. Tests for IgG and IgM antibodies against GM1, GM2, GM3, GD1α, GD1b, GD3, GT1b, GQ1b, GA1, and Gal-C were all negative. Magnetic resonance imaging, including T1-, T2-, and diffusion-weighted images demonstrated no abnormalities. A whole body evaluation for malignant tumors and foci of infection was negative.

The patient was treated with intravenous immunoglobulin (25 g/day for 5 days), corticosteroids (methylprednisolone 1,000 mg/day for 3 days and then dexamethasone 8 mg/day for the following 5 days, which was tapered), and acyclovir (500 mg every 8 hours for 14 days). On the fifth hospital day, her limb and truncal ataxia improved and the opsoclonus had disappeared. On the 26th hospital day, she was discharged with no sequelae. At the 3-year follow-up, no malignant tumors had been detected.

### Discussion

Influenza-associated acute encephalopathy, including more severe acute necrotizing encephalopathy and Reye’s syndrome, occurs relatively frequently and is well known (1). Recently, the cases of a 15-year-old girl with neuromyelitis optica following influenza A infection (2), an adult patient with acute motor axonal neuropathy following a pandemic H1N1 influenza A infection (3), an adult patient with acute ophthalmoparesis (4), and two children with impaired ocular movement (5) following influenza A infection have been reported. In these articles (2-5), no concomitant opsoclonus, myoclonus, or truncal ataxia was noted.

Opsoclonus-myoclonus syndrome is characterized by a subacute onset of opsoclonus, myoclonus, and cerebellar dysfunction with dysarthria and truncal ataxia (6). Opsoclonus consists of involuntary, arrhythmic, multidirectional saccades that are irregular in amplitude and frequency without an intersaccadic interval (7, 8). Opsoclonus is usually associated with arrhythmic-action myoclonus that predominantly involves the trunk, limbs, and head (9).

The most common etiologies are idiopathic, paraneoplastic, and infectious disorders. In cases of paraneoplastic OMS, small cell lung cancer, breast cancer, and ovarian cancer were most commonly encountered in adults (10), whereas more than half of these cases were associated with neuroblastoma in children (11, 12). In OMS with a confirmed infectious agent, psittacosis (10, 13), Mycoplasma infection (14), Salmonella infection (10, 15, 16), group A streptococcal infection (17), neuroborreliosis (18, 19), Rickettsia infection (10), St. Louis encephalitis (10, 20), coxsackievirus (10), enterovirus 71 (21), cytomegalovirus (22), Epstein-Barr virus (23), human immunodeficiency virus (24), and hepatitis C virus (25) have been described as the causative agents. Although the case of a 30-year-old woman with OMS 15 days after anti-rubella vaccination has been reported (26), seasonal influenza vaccination-related OMS has not yet been reported. We considered the cause of our patient’s OMS to be the influenza A infection based on the positive result for the rapid antigen test, the efficacy of oseltamivir for her flu-like symptoms, and the lack of any abnormalities in the whole body evaluation for foci of infection. In a pediatric OMS case, thallium intoxication has been reported (10). The present patient also had no history of exposure to thallium. There has been no previous report of an adult patient showing OMS associated with influenza A infection.

The anatomic neural substrate that causes OMS is unclear. Three major groups of premotor neurons, “burst”, “tonic” and “pause” cells, which are all located in the pontine reticular formation, control the eye movements. Burst cells initiate the ocular saccade, and the continuous firing from tonic cells holds the eyes in the new position. The pause cells inhibit the burst cells. The selective loss or impairment of pause cells is considered to produce opsoclonus (23, 27). The patient’s subjective symptom of OMS was opsoclonus. The associated ataxia and myoclonus in OMS suggested additional neuronal involvement, perhaps in the cerebellar-brain stem circuitry (23, 27).

Bataller et al. reported that patients with paraneoplastic OMS were older, had a lower response to immunotherapy, (e.g. intravenous immunoglobulins and/or corticosteroids), and had a significantly higher frequency of encephalopathy compared with patients without paraneoplastic OMS (6). Our patient’s clinical manifestations of OMS were not associated with unconsciousness, and immunotherapy was effective, which was consistent with non-paraneoplastic OMS. OMS is a very rare syndrome. In the United Kingdom, the incidence of OMS has been described to be 0.18 cases per million total population per year (12). The collection of more patients with non-paraneoplastic OMS is needed to as-
s the relationship between non-paraneoplastic OMS and infectious agents.

In conclusion, we encountered the first known patient presenting with OMS following influenza A virus infection. In adult patients, OMS without loss of consciousness indicates non-paraneoplastic OMS, and early immunotherapy could lead to an early recovery, especially in older patients with OMS.

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

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References

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