Acute Ophthalmoparesis Accompanied with Influenza A Infection

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Abstract

We report the first adult case of Influenza A virus infection with acute unilateral oculomotor nerve palsy. Unlike previous reports, our patient showed isolated unilateral oculomotor nerve palsy as soon as she developed general symptoms with Influenza A infection, and demonstrated no significant increases of anti-ganglioside antibodies including anti-GQ1b IgG antibody. She recovered immediately after treatment of oseltamivir phosphate. As for the mechanism by which Influenza A infection caused ophthalmoparesis, small vessel vasculitis due to direct invasion of the virus was speculated. Although influenza encephalitis/encephalopathy including acute necrotizing encephalopathy are most frequently reported in children, it is noteworthy that influenza virus can also cause focal neurological signs such as ophthalmoparesis in adult cases.

Key words: Influenza A virus, acute ophthalmoparesis, unilateral oculomotor nerve palsy, anti-ganglioside antibody, oseltamivir phosphate


Introduction

Influenza infection causes several neurological complications such as polyneuritis, meningitis, encephalomyelitis, encephalopathy, and Guillain-Barré syndrome (GBS) (1). Herein, we report an unusual adult case of Influenza A virus infection with acute unilateral oculomotor nerve palsy that occurred simultaneously with systemic symptoms.

Case Report

A 39-year-old woman noticed a high fever (38.5°C), cough, and polymyalgia affecting her back and limb at the morning of early February 2004. Three months earlier she received the immunization for influenza virus. She was prescribed cefaclor (750 mg/day), acetaminophen (450 mg/day), salicylamide (810 mg/day), and amantadine (100 mg/day) by her primary physician because she was suspected having as influenza infection. At night, her temperature became elevated to 39.2°C and she noted diplopia as well as headache (day 1). On day 2, her temperature fell to around 37°C, but she still suffered from diplopia. She went to our hospital on day 3. Neurological examination revealed blepharoptosis and limitation of adduction and vertical gaze on the right side. The pupils were normal and responded promptly to light. The other cranial nerves were intact. There was no limb weakness, ataxia, or sensory disturbance. Deep tendon reflexes were all normal and plantar responses were flexor. Laboratory examinations demonstrated an increase of segment neutrophils (4,558/μL, 86.0% of total WBC count) and a slight elevation of C-reactive protein (0.98 mg/dL). Cerebro-spinal fluid (CSF) examination, which was performed on day 6, revealed 1 mononuclear cell/mm³, protein of 41 mg/dL, and glucose of 51 mg/dL with a plasma glucose of 100 mg/dL. The rapid test for influenza was positive for Influenza A virus. The serum antibody titer against influenza A virus (H1N1) on admission was significantly elevated to X40, compared with those of 4 weeks later which were less than X10. The CSF antibody titer against influenza A virus (H1N1) on admission was also elevated to X40. Magnetic resonance imaging (MRI) including T1-, T2-,
and diffusion-weighted images with/without gadolinium enhancement and MR angiography, demonstrated no abnormality in the orbits and brain at day 3. Anti-ganglioside antibody was assayed by an enzyme-linked immunosorbent assay using the serum obtained on day 3. Tests for IgG and IgM antibodies against GM1, GM1b, GD1a, GD1b, GalNAc-GD1a, GT1a, and GQ1b were insignificant. Anti-acetylcholine receptor antibody was also negative. Cultures of blood and CSF were negative. She was treated with oseltamivir phosphate (150 mg) in addition to acetaminophen, salicylamide, and amantadine for 5 days, because she was diagnosed as having Influenza A infection accompanied with acute ophthalmoparesis. Her ocular symptoms gradually improved and after 10 days she completely recovered.

Discussion

We report a patient with Influenza A virus infection with acute unilateral oculomotor nerve palsy. Unilateral oculomotor nerve palsy could be attributed to several disorders including cerebral aneurysm, vascular disorders, tumors, or diabetes mellitus. These differential diagnoses were ruled out by the physical examination and laboratory data.

In addition, unilateral oculomotor palsy also could be occurred after antecedent infection. Ichikawa et al (2) described a patient who had acute unilateral oculomotor nerve palsy with a high titer of anti-GQ1b IgG antibody 2 weeks after an upper respiratory infection although his pathogens was not specified. Moreover, Yuki et al (3) summarized clinical features of 21 patients who had acute ophthalmoparesis (AO) without ataxia associated with anti-GQ1b IgG antibody. In this report, they mentioned that 57% of their patients had a preceding upper respiratory infection such as sore throat, but Streptococcus pyogenes was only one agent isolated from those patients. They also stated that AO without ataxia associated with anti-GQ1b IgG antibody could be considered a mild form of Miller-Fisher syndrome (MFS), or a regional variant of GBS. Unlike these reports, our patient showed acute unilateral oculomotor nerve palsy as soon as she developed general symptoms associated with Influenza A infection, and demonstrated no significant increases of anti-ganglioside antibodies including anti-GQ1b IgG antibody. Migita et al (4) reported two children who had impaired ocular movement as unusual complications of Influenza A infection. Interestingly, one of those patients showed bilateral ophthalmoparesis rather simultaneous with the developing systemic symptoms. Although the other patient developed diplopia caused by impaired abduction of the eyes 2 weeks after infection, her tests for anti-ganglioside antibodies were all negative. We were therefore, unable to exclude the possibility that our patient manifested the unilateral oculomotor nerve palsy due to an immunological mechanism.

Recently, numerous clinicians have described that influenza vaccination might induce systemic vasculitis. Hull et al (5) reported a case of post-vaccination small vessel vasculitis with involvement of skin and peripheral nerves, mimicking Guillain-Barré syndrome. Uji et al (6) described a patient with microscopic polyangiitis after influenza vaccination, which represented a severe adverse effect. They assumed two mechanisms of damage to the vessel wall, which were a direct effect of the vaccine itself and through an immunological activation like T or B cell activation. In contrast to the influenza vaccination, fewer reports have been published regarding the association with influenza infection and vasculitis. Vincenzo (7) described a case of encephalopathy with cerebral arteritis following influenza infection. Jo et al (8) presented a patient with frosted retinal branch angitis following presumed influenza virus type A infection. Although MR angiography on our patient revealed no angiography, digital subtraction angiography, serum markers for vasculitis, and so on. Our patient recovered immediately after treatment with oseltamivir phosphate. These observations might suggest that the mechanisms by which Influenza A infection causes ophthalmoparesis are the result of direct viral invasion of central nervous system rather than humoral factors induced by viral infection, whereas the pathogenesis of MFS and AO with anti-GQ1b IgG antibody is believed to involve a post-infectious immune-mediated mechanism.

To our knowledge, this is the first report that an adult patient showing isolated unilateral oculomotor nerve palsy as a complication of Influenza A infection. Although influenza encephalitis/encephalopathy including more severe acute necrotizing encephalopathy is most frequently reported in children, it is important to note that influenza virus also could cause focal neurological signs such as ophthalmoparesis in adult cases.

References
