Acute motor axonal neuropathy and H1N1 influenza A infection

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To the Editor,

The swine-origin influenza A (H1N1) virus was responsible for the pandemic infection in 2009. As of December 2009, 12,878 laboratory-confirmed cases were reported from Turkey, and as of January 2010, a total of 627 persons had died of confirmed H1N1 infection[1]. Seizures, encephalitis, encephalopathy, and cognitive and behavioral problems were described in association with H1N1 influenza A infection[2-4]. Although central nervous system manifestations of the virus are well described, little information about peripheral nervous system complications is available[5-7]. Guillain-Barré syndrome (GBS) is characterized by a classical triad of progressive motor weakness, areflexia and elevated cerebrospinal fluid protein without pleocytosis. The main types include acute inflammatory demyelinating polyradiculoneuropathy, acute motor axonal neuropathy (AMAN), acute motor and sensory axonal neuropathy, Miller-Fischer syndrome, polyneuritis cranialis, and acute pure pandysautonomia[8]. The clinical presentation of AMAN is similar to that of acute inflammatory demyelinating polyradiculoneuropathy and acute motor and sensory axonal neuropathy, but is distinguished by the discrete involvement of motor axons with sparing of sensory axons[9]. There have been a few adult cases of GBS associated with H1N1 infection, and to our knowledge, only one pediatric case, who had severe neuropathic involvement with axonal and demyelinating type of GBS[5-7,10]. Here, we describe a patient with AMAN associated with H1N1 influenza A infection.

An 18-month-old girl was admitted to the pediatric intensive care unit for respiratory distress and generalized flaccid weakness. Her complaints had started 10 days before presentation with low-grade fever, cough and serous nasal discharge. On the following days, her cough worsened with increased respiratory rate and wheezing, and she was diagnosed as bronchiolitis. Three days before admission, she began to suffer from weakness and was unable to walk and hold objects. On examination, she was an alert girl with good eye contact, but she had flaccid tetraplegia with absent deep tendon reflexes. She also had respiratory distress with widespread crackles. On the second day of hospitalization, the weakness worsened, and mechanical ventilation was started for respiratory insufficiency. A nasopharyngeal swab was performed, and H1N1 virus was detected by polymerase chain reaction. Electroneuromyography revealed low compound muscle action potentials, normal sensory nerve action potentials and mildly reduced nerve conduction velocity without conduction block. Needle examination showed large neurogenic motor unit potentials resulting from denervation and subsequent re-innervation. These findings were compatible with AMAN. Oseltamivir treatment was started, and she received two courses of intravenous immunoglobulin. Despite supportive care and medical treatment, her clinical condition worsened and she died due to sudden cardiopulmonary arrest.

The pathogenesis of GBS is probably autoimmune with many infections and vaccines[11]. AMAN is a variant of GBS, and the most antecedent event for AMAN is *Campylobacter jejuni* infection; however, other viral and bacterial infections were also described[11]. It is unclear whether AMAN is distinct from the demyelinating type or part of a continuum of the disease. After intravenous immunoglobulin treatment, patients with acute motor and acute motor and sensory axonal types recover more slowly than in the demyelinating type. A favorable outcome was reported for all types at 12 months except in some cases with acute motor and acute motor and sensory axonal types[12]. Our case is the

first pediatric case of AMAN associated with H1N1 influenza A infection. To our knowledge, there has been only one adult case with AMAN and only one pediatric case with axonal and demyelinating type of GBS associated with H1N1 influenza A infection[7,10]. This pediatric case was also reported from one of the largest pediatric hospitals in Turkey, which served as a reference pediatric center in Ankara for infections with H1N1 virus. Between 10 October and 22 December 2009, a total of 240 children were identified with confirmed H1N1 infection. Seventeen of 240 children with proven H1N1 infection manifested neurologic signs, and among those, there was only one case with GBS[10]. These two cases recovered with supportive care, immunoglobulin treatment and recurrent plasma exchanges[7,10]. Intravenous immunoglobulin is generally preferred for treatment of childhood GBS because of administrative ease. Plasma exchange is also a safe and effective treatment, which can be performed four to six times on an alternate date schedule[11]. We also planned plasma exchange after the first immunoglobulin treatment, but it could not be done because of the patient's unstable clinical condition.

H1N1 influenza A virus is a rare cause of antecedent infection for GBS in the pediatric population. Whether or not it has a propensity to induce AMAN type of GBS is not known. Plasma exchange may be tried as a choice of treatment in cases unresponsive to immunoglobulin treatment. Further pediatric cases are required to determine the prognostic factors and choice of treatments.

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