ACUTE DISSEMINATED ENCEPHALOMYELITIS FOLLOWING YELLOW FEVER VACCINATION

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Yellow fever (YF) is an acute viral disease caused by a flavivirus Yellow Fever Virus (YFV). There are 200,000 estimated cases and 30,000 deaths due to YF per year worldwide. Recently many cases of have been reported In South America. As a consequence, massive vaccination campaigns are being conducted. Even tough YF vaccine (YEL) has been seldom associated with complications, serious and potentially fatal adverse events have been reported among people receiving the vaccine.

We recently cared for a young college student who upon returning from a vacation to a sylvatic area in Perú had a severe meningo-encephalo-myelitis temporally associated with the administration of YEL.

CASE

A 23-year-old previously healthy man received immunization against yellow fever (17-D-204) 2 weeks prior to a travel to Perú. Three weeks later he developed fever, nausea, vomiting, severe bifrontal headaches and photophobia, followed by ascending weakness of the lower limbs, paresthesias of his feet, and urinary retention.

On examination, he was afebrile, had mild nuchal rigidity, and exhibited unsustained horizontal nystagmus on left gaze, discrete left arm dysmetria, bilateral symmetric lower extremity paresis, patellar and ankle hyperreflexia, and impaired sensation to light-touch and pinprick with an ill defined sensory level around T9.

Magnetic resonance imaging (MRI) of the brain (Fig 1A) and spinal cord (Fig 1B) showed areas of high signal intensity on T2 weighted and fluid attenuation inversion recovery (FLAIR) in the left middle cerebellar penduncle, right dorsal medulla oblongata and a multilevel lesion involving the thoracic spinal cord with subtle patchy heterogeneous enhancement after administration of gadolinium. Cerebrospinal fluid (CSF) analysis showed clear

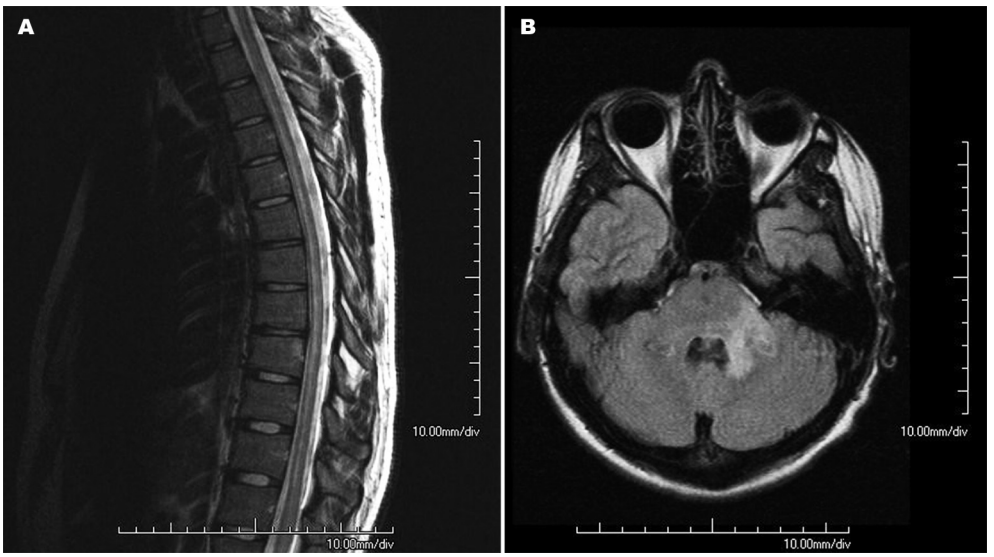

Fig 1. [A] Magnetic resonance imaging (MRI) showing areas of high signal intensity on fluid attenuation inversion recovery (FLAIR) in the left middle cerebellar penduncle, and right dorsal medulla oblongata. [B] Magnetic resonance imaging (MRI) demonstrating an extensive multilevel linear area of high signal intensity on T2 weighted along the cervico-thoracic spinal cord.

ENCEFALOPATIA AGUDA DISSEMINADA APÓS VACINAÇÃO DE FEBRE AMARELA

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and colorless fluid with a normal opening pressure. Cell count was elevated with 62 white blood cells (neutrophils 41%, lymphocytes 46%, monocytes 13%) 17 red blood cells, glucose 54 mg/100 mL (serum glucose 154 mg/100 mL) and a protein content of 105 mg/dL. CSF cultures were negative. Serum and CSF evaluations for herpes simplex virus type 1 and 2, epstein barr virus, varicella zoster virus, cytomegalovirus, human herpes virus type 6, enterovirus, human immunodeficiency virus, human T-lymphotropic virus 1 and 2, rabies virus, arbovirus, barthonella quintana, rickettsias, brucellas spp, leptospiras, salmonella, borrelias, mycobacterias, treponema pallidum, plasmodium, cryptococcus and mycoplasma were negative. CSF myelin basic protein (MBP) was elevated with a level of 618 ng/mL. CSF total IgG level, and IgG index were normal. CSF specific IgM antibodies to YEL were elevated with a level of 15.6, IgM and IgG specific antibodies to YEL levels in serum were 4.8 and 1.4 respectively (normal is less than 2.0). The patient received a five-day course of 1 gram daily of intravenous methylprednisolone, with marked clinical improvement. MRI of the brain and entire spine showed resolution of previous lesions 30 days after initiation of therapy.

DISCUSSION

YEL has been considered as one of the safest vaccine, with a very low incidence of adverse events. The risk of vaccine-associated neurotropic (YEL-AND) disease has been estimated as less than 8 per 1,000,000 persons[1,2]. Recent reports of post-vaccinal encephalitis suggest that onset of neurological symptoms may occur up to 30 days after vaccination. Clinically, YEL-AND might present as encephalitis, meningoencephalitis, myelitis, acute disseminated encephalomyelitis (ADEM), retrobulbar optic neuritis, seizures, cranial neuropathies, headaches, vertigo, paresthesias, Guillain-Barre syndrome (GBS), Fisher variant of GBS, and recently reported acute hemorrhagic fever among others. Autoimmune involvement of the central and peripheral nervous system have been proposed as a plausible pathophysiological mechanism of the disease[3-5].

In our patient the diagnosis of meningo-encephalomyelitis related to YEL was done based on epidemiological analysis, close temporal proximity with the vaccination, monophasic course of the disease, findings on physical examination and the results of ancillary test evaluations. YF-specific IgM titers were higher in CSF than in serum suggesting intrathecal antibody production. In addition, the dramatic clinical and neuroimaging improvement after intravenous corticosteroid therapy, lack of epidemiological evidence of native YF transmission, and the absence of any other cause for the disease suggested a clinical diagnosis of YEL associated ADEM.

Worldwide, YF remains an important cause of illness and death with an increasing rate of transmission in urban areas. Unvaccinated people can develop fatal forms of the disease. Consequently, despite the occurrence of severe cases of neurological complications, YF vaccination is still highly recommended for people exposed to YFV.

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