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LETTERS TO THE EDITOR

Longitudinal extensive transverse myelitis and Zika virus: A diagnostic challenge in a hospital in Colombia☆

Mielitis longitudinalmente extensa y virus del Zika, reto diagnóstico: a propósito de un caso en hospital de Colombia 2016

Dear Editor:

Zika virus is an arbovirus of the genus *Flavivirus*, which also includes the Japanese encephalitis, yellow fever, West Nile, and dengue viruses. Zika virus is spread by an arthropod, *Aedes aegypti*, and was first described in a population of rhesus monkeys in Uganda in 1947. Zika virus infection was described in humans in 1968, in Nigeria, when Zika-neutralising antibodies were isolated in a group of people presenting fever, skin rash, arthralgia, and conjunctivitis. The virus has since reached other parts of Africa and Asia. Since 2007, it has rapidly spread across several islands in the Pacific Ocean and various South American countries, including Brazil, French Guiana, and more recently Colombia. Zika virus infection causes a wide range of neurological complications, including longitudinally extensive transverse myelitis.[1,2]

We present the case of a patient with Zika virus infection manifesting as longitudinally extensive transverse myelitis.

The patient was a 23-year-old man presenting with pelvic pain followed by urinary retention; 24 h after onset of the initial symptoms, he developed progressive loss of strength in the lower limbs, resulting in paraplegia, and left-sided paraesthesia and hypoaesthesia below the upper abdomen (T6-T7 dermatomes). The physical examination revealed normal cranial nerve function, no meningeal signs, flaccid paralysis (0/5 strength), hyperactive patellar and Achilles reflexes (3-4), and hypoaesthesia below the T7 sensory level. The patient had experienced non-purulent conjunctival injection, fever, and arthralgia 15 days previously. A cranial and thoracolumbar CT scan, complete blood count, electrolyte study, renal function study, C-reactive protein (CRP) and procalcitonin tests, and blood and urine cultures all yielded normal results. A CSF cytochemical study revealed pleocytosis and low protein levels (200 leukocytes/mm^3, 90% monocytes, 10% polymorphonuclear; glucose 41 mg/dL; proteins 31.4 mg/dL; HDL 26 mg/dL). Nigrosin, Gram, and KOH staining and serology, HIV test, serum culture, and a blood lead test yielded negative results, and complement C3 and C4 levels were normal. The patient also tested negative for cardiolipin IgG and IgM antibodies, beta-2 glycoprotein 1 antibodies, IgM for dengue and chikungunya, antinuclear antibodies, anti-DNA antibodies, and C- and P-ANCA. ANA titre was 1:80. Protein electrophoresis revealed mild hypoalbuminaemia in alpha-1 and alpha-2 zones, and polyclonal hyperalbuminaemia in the gamma region. A spinal cord MRI scan revealed signal alterations from C1 to the conus medullaris, with hyperintense foci in the anterior part of the spinal cord on T2-weighted and FLAIR sequences (Fig. 1A-D). Symptoms were compatible with longitudinally extensive transverse myelitis associated with lymphocytic pleocytosis in the context of Zika virus infection 15 days previously; infection was confirmed by the presence of CRP in the serum. The patient started treatment with corticosteroids (methylprednisolone 1 g/day for 5 days), with no clinical improvement. He was subsequently treated with 5 sessions of plasmapheresis; at discharge, he was able to walk with a cane and strength had increased to 4/5.

Zika virus is an RNA virus containing 10 974 nucleotides coding for 3419 amino acids. The virus is arthropod-borne and replicates rapidly in dendritic cells near the inoculation site. It can be isolated in the blood from day 1 to day 11 after inoculation. Some studies suggest changes in the virus' biological cycle affect signalling pathways and various organelles; animal studies have shown alterations in the endoplasmic reticulum, which is associated with multiple disorders of the central nervous system.[3,4] Some case reports have shown positive CSF CRP test results for Zika virus, indicating a certain degree of neurotropism; this was also seen in our patient, whose cytochemical results revealed viral infection. Neurotropic flaviviruses may cause encephalitis, transverse myelitis, or longitudinally extensive transverse myelitis.[1,5,6] The lumbosacral nerve roots have also been found to be involved.[7,8]

Diagnostic tests for Zika virus infection include serum CRP determination and other tests for detecting specific antibodies against Zika virus in the serum. There is evidence of cross-reactivity in patients with a history of flavivirus infection, which makes IgM testing less reliable. CRP tests can be performed from day 5 to day 11 after infection; a second sample can be taken 2-3 weeks after the first.[3]

In our patient, clinical symptoms compatible with longitudinally extensive transverse myelitis, the clearly visible spinal cord MRI alterations (Fig. 1A-D), the classic

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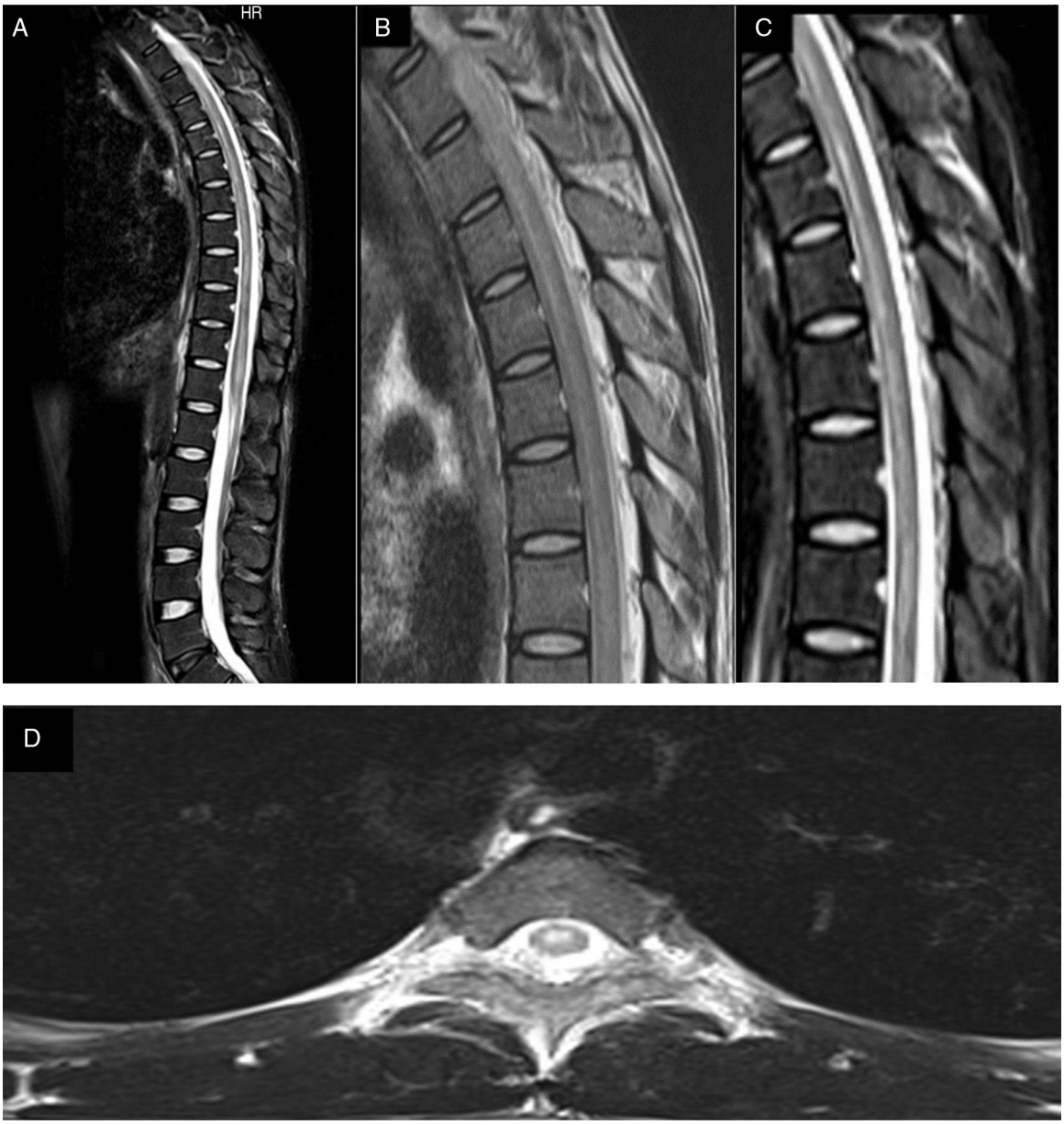

Figure 1 MR image of the thoracic spinal cord. (A-C) Sagittal T2-weighted and FLAIR sequences showing a longitudinally extensive hyperintensity in the anterior part of the spinal cord. (D) Axial plane of the thoracic region at the T2 level, showing a hyperintense lesion.

symptoms of Zika virus infection, and positive serum CRP results for the virus enabled correct management, leading to an optimal outcome.

Zika virus infection should be suspected in patients with acute myelitis who come from or live in endemic areas; further studies should aim to determine the spectrum and magnitude of the associated neurological complications.

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Early and recurrent macular oedema in a patient treated with fingolimod☆

Edema macular precoz y recurrente en paciente en tratamiento con fingolimod

Dear Editor:

Multiple sclerosis (MS) is a chronic autoimmune disease predominantly affecting young women.[1] Fingolimod is a sphingosine-1-phosphate receptor modulator used to treat very aggressive or relapsing-remitting forms of MS that are refractory to other types of treatment.[2]

We present the case of a 56-year-old woman with a 20-year history of MS and no other systemic or ocular diseases. Due to poor control of relapses and the rapid progression of the disease, treatment was started with oral fingolimod (0.5 mg/day). The patient was referred for evaluation at the neuro-ophthalmology department one week later due to blurred vision. The examination determined visual acuity (VA) of 0.6 in the right eye and 0.7 in the left. No alterations were observed in the anterior segment of the eye. Fundus examination revealed mild cystoid macular oedema bilaterally. Optical coherence tomography determined central macular thickness at 480 μm in

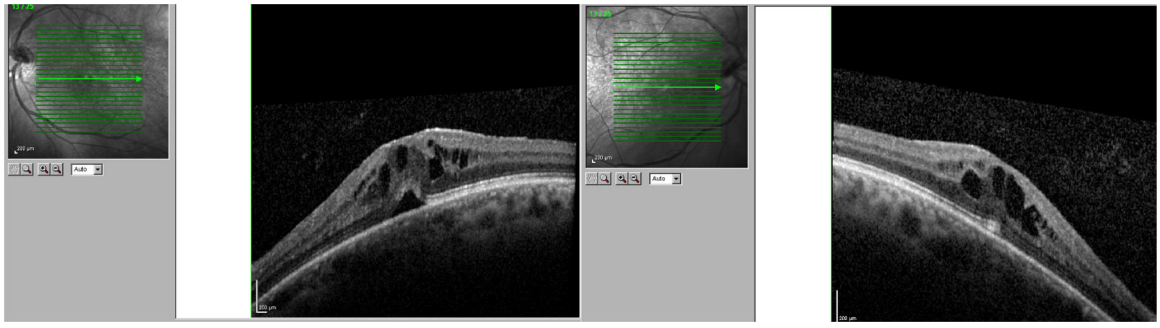

Figure 1 Cystoid macular oedema in the right and the left eyes, one week after onset of treatment with fingolimod.

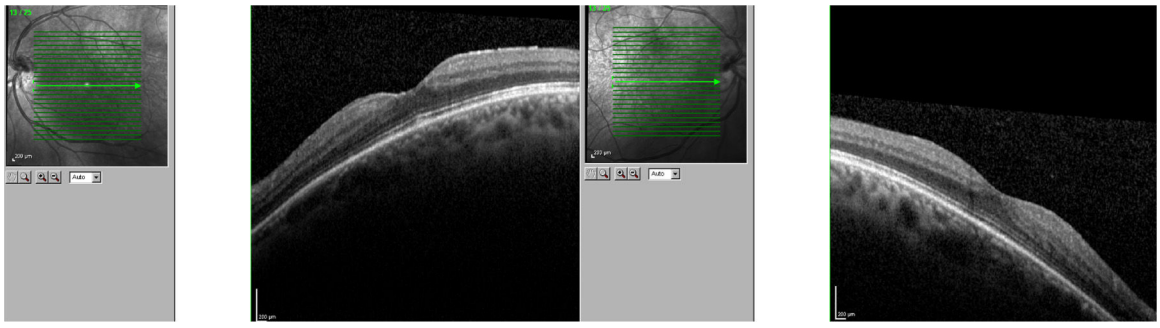

Figure 2 Complete resolution of macular oedema, 20 days after fingolimod was withdrawn.

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