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CASE REPORT

Myeloradiculopathy associated with chikungunya virus infection

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Abstract Chikungunya virus (CHIKV) is a mosquito-borne alphavirus that is endemic to parts of Africa, South and Southeast Asia, and more recently the Caribbean. Patients typically present with fever, rash, and arthralgias, though neurologic symptoms, primarily encephalitis, have been described. We report the case of a 47-year-old woman who was clinically diagnosed with CHIKV while traveling in the Dominican Republic and presented 10 days later with left lower extremity weakness, a corresponding enhancing thoracic spinal cord lesion, and positive CHIKV serologies. She initially responded to corticosteroids, followed by relapsing symptoms and gradual clinical improvement. The time lapse between acute CHIKV infection and the onset of myelopathic sequelae suggests an immune-mediated phenomenon rather than direct activity of the virus itself. Chikungunya virus should be considered in the differential diagnosis of myelopathy in endemic areas. The progression of symptoms despite corticosteroid administration suggests more aggressive immunomodulatory therapies may be warranted at disease onset.

Keywords Chikungunya · Viral myelopathy · Infectious myelopathy · Myelopathy

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Case presentation

A 47-year-old woman experienced fevers, rash, and diarrhea while traveling in the Dominican Republic and was diagnosed with chikungunya virus infection clinically by a local physician in August 2014. Ten days later, she developed left leg weakness and decreased sensation below the umbilicus. She subsequently developed left hip flexion, knee extension, and knee flexion weakness, with minimal movement against gravity. Sensation was decreased in all modalities up to the T12 level. Reflexes were preserved.

MRI of the spine demonstrated intramedullary enhancement dorsally from T12 to L1 spinal levels (Fig. 1). MRI of the brain demonstrated a solitary 4-mm non-enhancing T2 hyperintense lesion in the right posterior parietal lobe that was non-specific. Cerebrospinal fluid studies showed 22 white blood cells (90 % lymphocytes), two red blood cells, and elevated protein to 68 mg/dL. Serum CHIKV IgG and IgM were detected at 1:1280. Other infectious studies including serum HIV and HTLV-1 and 2, CSF EBV, WNV, VZV, CMV, enterovirus, HSV-1 and 2, schistosomiasis, Lyme, VDRL, and mycoplasma were negative. Serum NMO was negative. Oligoclonal bands and IgG index were not performed as these tests provide non-specific evidence of inflammation.

After 5 days of intravenous methylprednisolone, she was able to walk short distances but had residual lower extremity weakness and impaired sensation. She returned 6 weeks later with new right-sided lower extremity pain. MRI demonstrated persistence of the thoracic lesion with probable new abnormal cauda equina enhancement (Fig. 2). Cerebrospinal fluid showed nine white blood cells (97 % lymphocytes), no red blood cells, and persistently elevated protein to 91 mg/dL. She was treated with 2 days of intravenous methylprednisolone with minimal improvement.

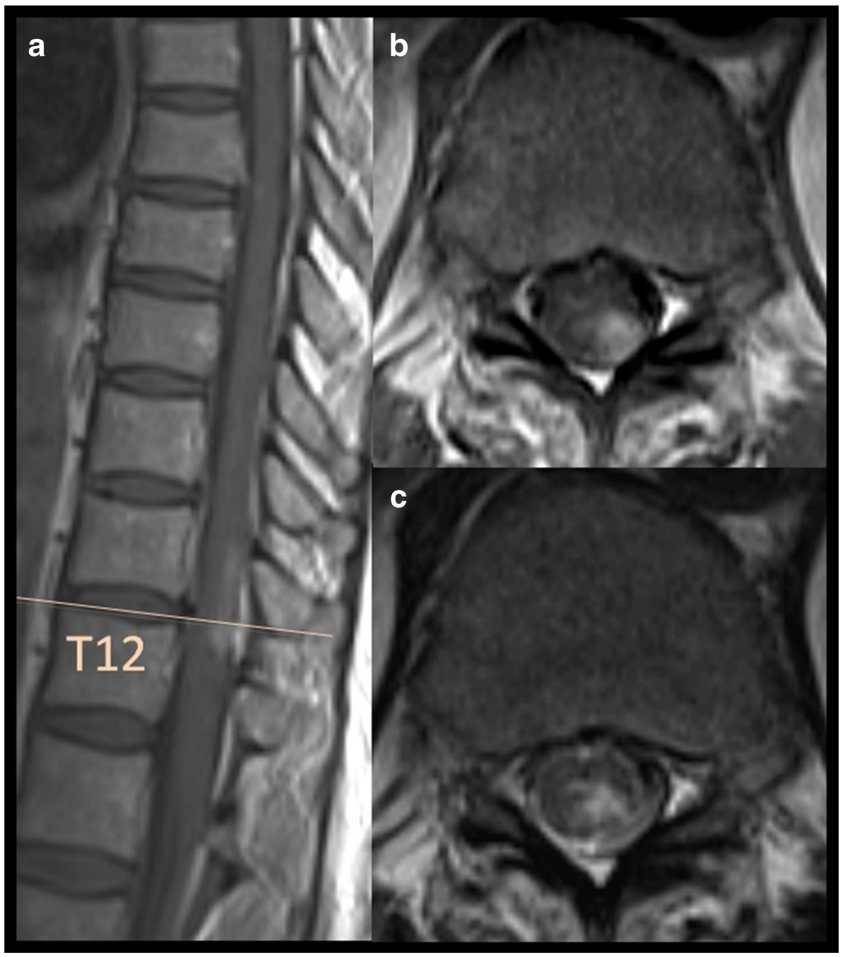

Fig. 1 Initial sagittal T1 post contrast (**a**) and axial T1 post contrast (**b**) and T2 (**c**) MRI demonstrate enhancing leuko- and poliomyelitis most prominent at the level of T12 involving the left greater than right lower spinal cord and conus medullaris

Over the next 2 months, her weakness improved considerably, but she complained of persistent burning pain in the right lower extremity. Repeat serum CHIKV serologies were detected at lower levels than on initial presentation (IgG 1:640, IgM 1:40). She regained full strength by 6 months from the initial presentation and was able to return to work but continued to have residual neuropathic pain.

Discussion

Chikungunya virus is a mosquito-borne alphavirus that is endemic to parts of Africa, South Asia, and Southeast Asia, first recognized in the 1950s and isolated in Calcutta, India in 1963 (Shah et al. 1964). The first outbreaks in the Western Hemisphere were identified as recently as 2013, in the Caribbean island of St. Martin. Since then, 379,788 cases of CHIKV have been recorded in the Caribbean islands, Latin America, and the United States (WHO Media Centre 2015). The classic presentation consists of fevers, chills, rash, and severe arthralgias, although neurologic symptoms were recognized as early as the 1960s (Carey et al. 1969). Encephalitis and acute disseminated encephalomyelitis, the most commonly reported neurologic complications, have been described in South Asia (Ganesan et al. 2008, Gauri et al. 2012, Taraphdar et al. 2015, Musthafa et al. 2008, Maity et al. 2014), Reunion Island off the coast of Madagascar (Borgherini et al. 2007), and Italy (Casolari et al. 2008).

Myelopathy, myeloneuropathy, and myeloradiculopathy without brain involvement are less commonly reported, again typically in South Asia (Krishnan et al. 2012, Chandak et al. 2009), with one report from Thailand (Chusri et al. 2011). To our knowledge, no other cases of isolated spinal cord involvement have been reported in the Americas.

Prognosis and optimal treatment of these neurologic complications are not well understood. Several patients have been treated with corticosteroids, with variable degrees of clinical improvement. In a series of 300 patients in India with clinical CHIKV infection, 49 (16.3 %) had neurologic complications (Chandak et al. 2009). Among these patients, 14 (28.6 %) had either myelopathy or myeloneuropathy. Seven developed sequelae more than 5 days after disease onset, including three who developed symptoms more than 10 days later and one who experienced symptoms more than 20 days later. Thirty-four of the 49 patients with neurologic complications were treated with steroids; there was no difference in clinical

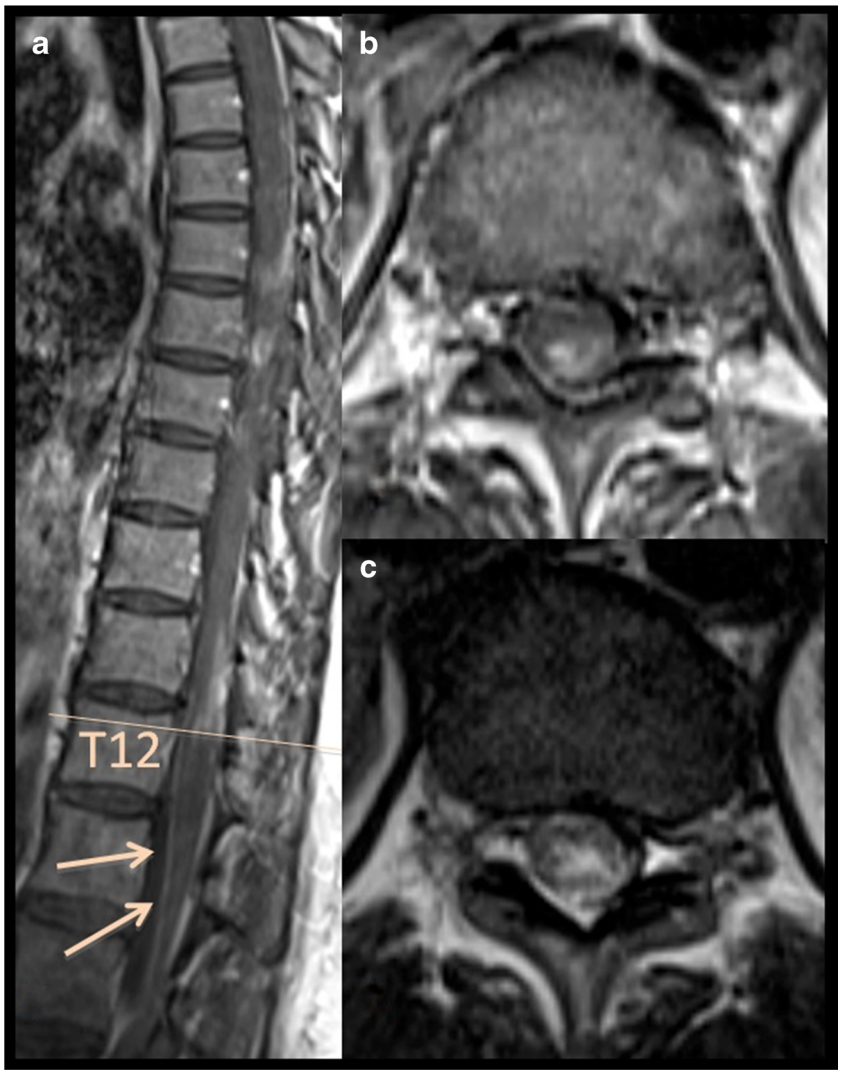

Fig. 2 Repeat sagittal T1 post contrast (**a**) and axial T1 post contrast (**b**) and T2 (**c**) MRI demonstrate persistence of prior findings and new possible cauda equina enhancement

improvement between patients who received steroids and those who did not.

Acute chikungunya virus infection in humans is associated with elevated levels of inflammatory cytokines such as interleukin-1b, interleukin-6, and tumor necrosis factor-α (Ng et al. 2009). Studies in mice have shown that chikungunya virus infection leads to production of antibodies that limit viral replication (Lum et al. 2013). We suspect that the activity of these antibodies resulted in an immune-mediated post-infectious myelopathy, as has been described previously with other viruses, including dengue, another arbovirus (de Sousa et al. 2014).

Immunosuppressant medications might therefore be useful in reducing inflammation and limiting antibody activity. A retrospective study comparing corticosteroids, plasma exchange, and cyclophosphamide for immune-mediated transverse myelitis showed that plasma exchange was more effective than steroids for patients with moderate disease, and plasma exchange with cyclophosphamide was more effective than steroids for patients with severe disease (Greenberg et al. 2007). Therefore, our patient may have benefited from plasma exchange, either with or without cyclophosphamide.

Conclusions

Although neurologic complications of CHIKV have been described previously, isolated myeloradiculopathy in the absence of encephalitis is unusual. Chikungunya virus should be considered in the differential diagnosis of myelopathy in endemic areas. The time lapse between acute CHIKV infection and the onset of myelopathic sequelae, with an asymptomatic interval prior to the onset of myeloradiculopathy, suggests an immune-mediated phenomenon secondary to

CHIKV infection, rather than direct activity of the virus itself. Ongoing viral infection cannot be definitively excluded, however, because viral replication becomes undetectable within a week of the initial infection (Panning et al. 2008).

The optimal treatment remains unclear. Our patient's symptoms progressed despite corticosteroids, suggesting that this therapy was insufficient to control inflammation, and that more aggressive immunomodulatory strategies, such as plasma exchange or cyclophosphamide, early in the treatment course may help prevent disease progression.

Conflict of interest The authors declare that they have no competing interests.

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