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Case Report

Enterovirus D68 Myelitis: The First Reported Case in Hong Kong

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Abstract A 3-year-old Chinese boy presented with acute onset of left facial nerve palsy with significantly impaired neck and upper limb power. Magnetic resonance imaging of brain and spine showed T2W hyperintense signals over both cerebral peduncles and posterior pons, and a long segment at cervical spinal cord. Enterovirus D68 was positive in stool. The boy was treated as a case of viral myelitis and given a course of corticosteroid and intravenous immunoglobulin. Despite rehabilitation, he still sustained significant residual right upper limb weakness two years after the acute illness. This is the first reported local paediatric case of enterovirus D68 infection related acute flaccid myelitis.

Key words *Acute flaccid myelitis; Enterovirus D68; Myelitis*

Case Presentation

Our case is a 3-year-old boy with good past health. He was admitted to our unit on 26th September 2017, presented with generalised weakness and neck pain for three days. He also had fever and coryzal symptoms five days preceding symptoms onset.

On admission, the boy was irritable but had full Glasgow coma scale. Blood pressure, heart rate, respiratory rate and temperature were normal. Pupils were equal and reactive to light, with normal extraocular movement. However, he had left facial nerve palsy which was compatible with lower motor neuron lesion. He was not able to sit up straight without support. His neck and truncal tone were markedly decreased with generalised hypotonia, affecting upper limbs more than lower limbs. Muscle power was grade 1/5 over right shoulder, grade 2/5 over left shoulder, grade 3/5 over bilateral elbows and grade 4/5 over bilateral wrists. Lower limb power was grade 4/5 over both proximal and distal parts. Reflexes were present and symmetrical over four limbs. The anal tone was intact. There were no rash or insect bite marks. The patient did not cooperate with sensory level and cerebellar exams. Other systems examination was unremarkable.

Full septic workups were performed. Complete blood count, liver function, electrolytes, serum glucose, c-reactive protein and immunoglobulin pattern were normal. Nasopharyngeal aspirate (NPA) for respiratory viruses and mycoplasma pneumoniae polymerase chain reaction (PCR) were negative. Epstein bar virus and measles virus IgM, borrelia burgdorferi, brucella, syphilis and anti-HIV antibodies were negative. Stool for polio virus and blood culture were also negative. Cerebrospinal fluid (CSF) microscopy found elevated white blood cell 37/cmm with 97% lymphocyte and red blood cell 3/cmm. CSF gram stain, Indian ink stain, acid-fast bacilli smear, bacterial culture and viral PCR were negative. CSF protein and IgG were not elevated. There was no detectable CSF oligoclonal band. Besides, autoimmune markers were all negative and vitamin B12 and folate levels were not low. Anti-aquaporin 4 antibody was also negative.

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Urgent magnetic resonance imaging (MRI) of brain and spine with contrast showed T2W and FLAIR hyperintense lesions at bilateral cerebral peduncles and both sides of posterior pons. In addition, there was a long segment of T2W hyperintense signal at the cervical spinal cord, spanning from cervicomedullary junction to the level of C6. On axial image, the signal involves both sides of the cord with more than 50% cord area, affecting both grey and white matter (Figures 1 & 2). On the other hand, electroencephalogram showed no epileptiform discharges or slowing. Nerve conduction study showed normal compound muscle action potential and conduction velocity over median, ulnar, tibial and peroneal nerves.

Patient was empirically covered with intravenous (IV) ampicillin, cefotaxime, acyclovir and oseltamivir for possible meningoencephalitis. They were taken off subsequently when CSF bacterial culture, viral PCR and NPA result came back negative. With the MRI findings, the boy was treated as a case of transverse myelitis. He was given IV methylprednisolone 30 mg/kg/day for five days, followed by oral prednisolone 2 mg/kg/day for two weeks then gradually tapered off. The patient sustained an episode of aspiration pneumonia during stay, required continuous positive airway pressure (CPAP) support and transpyloric tube feeding for two weeks. Overnight oximetry and transcutaneous CO2 monitoring showed normal results. Oral feed was resumed after assessed by speech therapist with normal video fluoroscopic swallowing study result.

Two weeks after admission, stool culture came back enterovirus D68 positive. Patient's diagnosis thus refined to be case of viral myelitis. He was further treated with two grams intravenous immunoglobulin (IVIG) for two days. With the pros and cons discussed, caretakers declined plasmapheresis as a further treatment option. Neurorehabilitation with physiotherapy and occupational therapy were given, and the boy made slow clinical improvement. He had improved neck power and was able to walk unaided indoor. He was fit for discharge on 2nd November 2017 and was referred to the day centre at Caritas Medical Centre for continuation of rehabilitation.

Anti-aquaporin 4 antibody was repeated three months later with anti-myelin-oligodendrocyte glycoprotein (MOG) IgG. Results were negative. Progress MRI showed resolved abnormal T2W hyperintense signals at cervical spinal cord, bilateral cerebral peduncle and posterior pons. The boy continued to make slow improvement, though still had significantly impaired right upper limb power upon writing up of this case report.

Discussion

Acute flaccid paralysis (AFP) or acute flaccid myelitis (AFM) is a medical emergency in children, with poliomyelitis once being the most classical cause. With the invention of polio vaccine, poliomyelitis becomes extremely uncommon in developed countries nowadays. Other differential diagnoses include causes of myelopathy

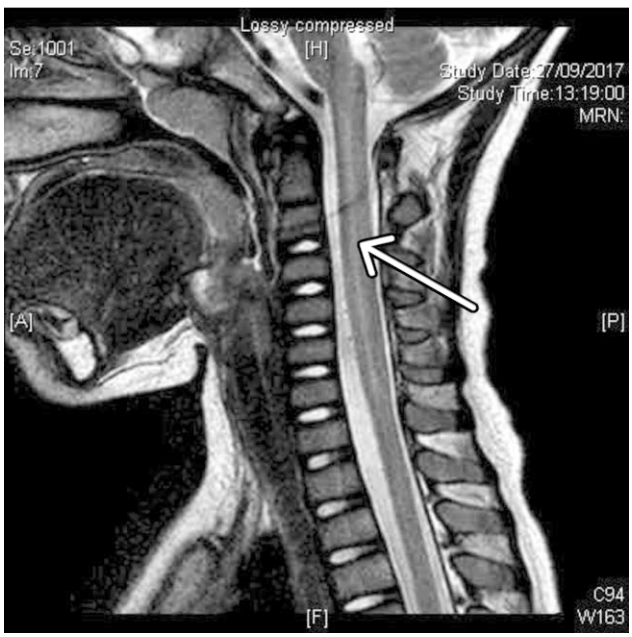

Figure 1 MRI spine showing long segment of T2W hyperintense signal at the cervical spinal cord (arrow).

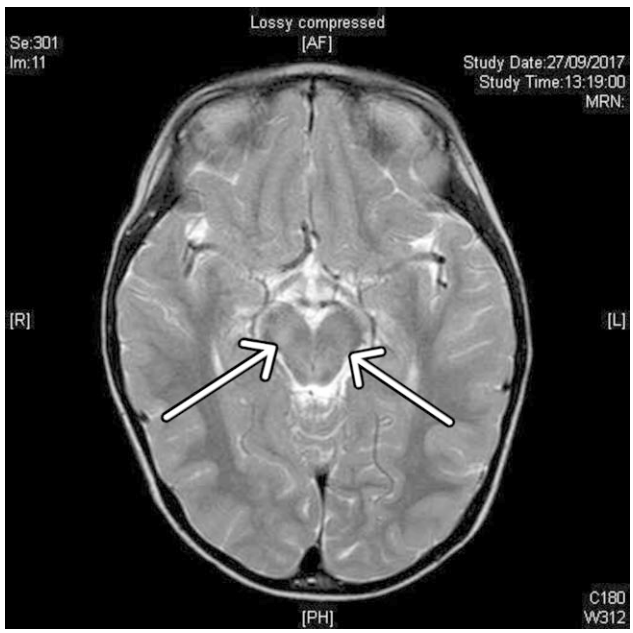

Figure 2 MRI brain showing T2W hyperintense signals over bilateral posterior pons (arrows).

such as traumatic spinal injury, spinal mass compression, transverse myelitis, and neuropathy such as Guillain-Barré syndrome. A detailed history, physical examination, MRI brain and spine and CSF studies are essential to delineate the underlying cause and to provide treatment timely.

Our patient presented with acute onset of truncal and proximal muscle weakness along with asymmetric bilateral upper limb involvement. These findings are uncommon in usual AFP cases, which would preferentially affect the lower limbs. On top, he suffered from neck pain and lower motor neuron seventh cranial nerve palsy. These features indeed matched the typical presentations of enterovirus D68 related AFM.[1-3] Patients with enterovirus D68 myelitis may also experience limb pain, hemiparesis, autonomic disturbances and respiratory muscle weakness. Like our case, many of them required non-invasive ventilatory support, or even invasive mechanical ventilation under intensive care units.

Urgent MRI brain and spine are mandatory for patients presented with flaccid paralysis. Our patient's MRI brain showed that his pons was affected, sparing the supra-tentorial structures. MRI spine found a pure C-spine involvement, with lesions spanning more than three vertebral levels with T2 hyperintense signals at the centre of the cord. These findings are typically found in enterovirus D68 myelitis.[4] Moreover, CSF analysis is also invaluable in establishing the diagnosis. Normal CSF protein, IgG and absence of oligoclonal band speak against possible acute demyelinating encephalopathy and multiple sclerosis; negative anti-aquaporin 4 and anti-MOG antibody make diagnosis of neuromyelitis optica and MOG-associated demyelinating diseases unlikely. On the other hand, detection of enterovirus D68 mostly relies on nasopharyngeal swabs, throat or rectal swabs and stool cultures, as more than 90% cases of AFM reported negative viral PCR or culture in CSF. Despite the absence of direct virus isolation in CSF, the causal relationship between enterovirus D68 and AFM was supported in prior study using Bradford Hill criteria.[3,5] It was postulated that the virus reaches the anterior horn by retrograde axonal transport and causes cellular damage.[3]

There is so far no standardised treatment for enterovirus D68 myelitis or AFM.[3,6] IV pulse steroid and IVIG are the most common treatment in acute setting, reflected by the possible inflammatory or immune-mediated causes of the disease. However, exact dosage, duration and the actual effects of these treatment are largely unknown.[7] Use of plasmapheresis during acute stage is also not well described. With the invasive nature of the procedure with doubtful benefits, a thorough discussion with the family is needed on this treatment option. Furthermore, role of maintenance steroid or immunosuppressants on improving outcomes are uncertain. Prognosis is variable, but patients usually sustain permanent neurological deficit despite early treatment and vigorous rehabilitation.[3,7]

Conclusion

This is the first reported Paediatric case of enterovirus D68 AFM in Hong Kong. While we are vigilant in preventing polio and actively watching out for demyelinating diseases, the deleterious effects of non-polio viruses, notably enterovirus, are often overlooked. In Hong Kong, enterovirus tests are handled by the virology laboratory of the Department of Health. A specific request is required if we want to perform sequencing for D68 serotype. Undeniably, routine sequencing for D68 serotype in all enterovirus samples is unnecessary as most of the enterovirus related illnesses are mild and self-limiting. Nevertheless, early recognition of the rare complications of enterovirus is important, and we should make special requests for serotyping if we encounter acute flaccid paralysis cases presented with atypical features.

Declaration of Interest

None

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