Lessons from practice

A case of Japanese encephalitis in a Victorian infant

Clinical record

A previously well 4-month-old boy was admitted to a tertiary Victorian paediatric hospital in February 2022 following a febrile convulsion. He had a 2-day prodrome characterised by fevers to 39°C and reduced energy and feeding. The self-limiting febrile convulsion occurred on day 3 of illness and was characterised by left eye deviation, tonic extension of upper limbs, shallow breathing, and pallor. He did not appear unwell on initial examination and no convincing source of fevers was identified. He was born at term and was developing appropriately for age.

Initial laboratory investigations were significant for mild thrombocytosis and blood film, with occasional reactive lymphocytes. The white cell count, red cell count, serum inflammatory markers, electrolytes, ketones, glucose, and liver function were unremarkable. Ceftriaxone, flucloxacillin and acyclovir were commenced before lumbar puncture as empirical treatment for sepsis with additional antiviral cover. Lumbar puncture on day 1 of admission demonstrated a lymphocyte-predominant pleocytosis with elevated protein and decreased glucose (Box 1). Initial microbiological investigations did not identify a causative pathogen; these included cerebrospinal fluid (CSF) Gram stain and bacterial culture, BioFire FilmArray Meningitis/Encephalitis Panel (Biomérieux), and in-house herpes simplex virus polymerase chain reaction (PCR). Blood and urine culture and a respiratory panel, tested on a deep nasal/oral sample on a commercial respiratory panel (16-well Respiratory Pathogens Panel [Ref 20620], AusDiagnostics), were also negative.

The patient continued to have further seizures of similar semiology, requiring levetiracetam, phenobarbital and phenytoin. Maintenance levetiracetam was commenced on day 3 of admission, with resolution of seizures.

On day 4 of admission, an electroencephalogram (EEG) demonstrated slower, lower amplitude and poorly organised activity, with focal slowing over the right posterior temporal region. Magnetic resonance imaging (MRI) of the brain demonstrated signal change with restricted diffusion of bilateral thalami and diffuse pachymeningeal enhancement.

Investigations for Japanese encephalitis virus (JEV) were initiated on day 14 of admission in response to a public health alert of JEV detection in Victoria. CSF from day 1 of admission was positive on a pan-flavivirus PCR assay and subsequently identified as JEV by Sanger sequencing. Convalescent Japanese B encephalitis virus serum serology was IgG positive (Box 2). Retrospective history identified mosquito exposure during travel to a town on the border of Victoria and New South Wales, 15 days before symptom onset. Other family members remained asymptomatic. Clinically, the patient returned close to baseline neurological function with some residual but improving mild left upper-limb weakness. He was planned for ongoing daily levetiracetam and close neurodevelopmental follow-up.

Discussion

To our knowledge, this is the first described case of Japanese encephalitis in a Victorian infant, reflecting a growing epidemic involving spread to new regions of Australia. In late February 2022, JEV was detected in pigs in Victoria, Queensland and New South Wales.[1] As of 4 May 2022, there have been 38 human cases of Japanese encephalitis in Australia, including four deaths.[2] To date, most of these cases have occurred in adults. This is consistent with established data that symptomatic infections in children predominate in endemic areas, but occur in both children and adults in newly affected regions.[3]

JEV infection is most commonly asymptomatic. This case describes a typical symptomatic presentation (1% of infections) characterised by a 5–15 day incubation period, a 2–4 day non-specific prodrome followed by progression to aseptic meningoencephalitis.[3,4] Seizures are well reported in association with encephalitis and are more common in children compared with adults.[3] Our patient also demonstrated characteristic investigation findings, including a lymphocyte-predominant CSF pleocytosis, diffuse EEG slowing, and bilateral thalamic lesions on MRI scan.[3] No specific treatments exist and management should focus on supportive care, close neurodevelopmental follow-up, and early intervention. Paediatric patients may exhibit normal development at discharge, with deficits only becoming apparent as neurodevelopment progresses. Disease at the extremes of age confers a worse prognosis; however, this is based on small case series and there is a paucity of infant-specific outcome

1 Cerebrospinal fluid results

Component	Result (reference range)
Polymorphs, $\times 10^6$/L	10 (0)
Lymphocytes, $\times 10^6$/L	233 (≤ 5)
Total white cell count, $\times 10^6$/L	243 (0–5)
Red blood cell count, $\times 10^6$/L	3 (0)
Protein, g/L	0.46 (0.20–0.40)
Cerebrospinal fluid glucose, mmol/L	2.7 (2.8–4.0)
Macroscopic	Clear and colourless
Culture	No growth after 5 days

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2 Japanese encephalitis virus testing

Day of illness	Sample	Test	Result
3	CSF	Japanese B encephalitis virus serology	IgG negative (< 10), IgM not detected
3zz	CSF	Flavivirus RT-PCR	Detected; identified as Japanese encephalitis virus by Sanger sequencing
12	Serum	Japanese B encephalitis virus serology	IgG negative (< 10), IgM not detected
12	Serum	Flavivirus RT-PCR	Not detected
16	Urine	Flavivirus RT-PCR	Not detected
20	Serum	Japanese B encephalitis virus serology	IgG positive (titre ≥ 10), IgM not detected

CFS = cerebrospinal fluid, RT-PCR = reverse transcription polymerase chain reaction. ◆

data in the literature. In general, neurological sequelae occur in approximately 50% of patients with Japanese encephalitis, with motor deficits, cognitive deficit, and seizures reported.[3]

Despite its high morbidity and mortality, little progress has been made in the past decade to investigate new treatments for Japanese encephalitis. There have been only four clinical trials involving random assignment of < 400 patients with proven Japanese encephalitis.[5] Instead, a current focus on prevention is essential. Two JEV vaccines are available in Australia: Imojev (Sanofi-Aventis Australia), a live attenuated vaccine available for people aged ≥ 9 months, and JEspect (Seqirus), an inactivated vaccine available from age ≥ 2 months in a two-dose schedule.[6] In response to the current outbreak, Australian vaccination recommendations have expanded to include individuals involved in the care or handling of pigs and mosquitos or people ≥ 2 months of age residing in high risk Australian settings.[7]

During the past two decades there has been mounting evidence that the climate emergency is a driving factor in the spread of waterborne and zoonotic diseases.[8] As the sentinel pigs had been known to test positive for JEV for a period of time before the current human cases, this highlights the need to strengthen the One Health approach at the human–animal–environment interface.

Lessons from practice

- There is an evolving epidemic of Japanese encephalitis in Australia; this diagnosis should now be considered in all patients with meningoencephalitis in whom an alternative causative pathogen has not been identified, particularly where epidemiological risk factors are present.
- Infection with Japanese encephalitis virus is most commonly asymptomatic, but when clinical disease is present it can cause significant morbidity and mortality.
- Typical investigation findings include lymphocyte-predominant pleocytosis, diffuse electroencephalogram slowing, and bilateral thalamic lesions on magnetic resonance imaging.

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