CASE REPORT

Influenza B-related meningoencephalitis in adults

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SUMMARY

We present a case involving an 85-year-old man with acute confusion and new onset seizure following a 1-week history of respiratory prodrome. This case report describes a case of influenza B-related meningoencephalitis supported by evidence of an influenza B infection and temporal relation of the neurological event and respiratory illness in the absence of other identifiable cause. Diagnosis is guided by cerebrospinal fluid profile and nasopharyngeal PCR. Treatment is largely supportive and the effect of vaccination on prevention of this neurological complication remains unclear.

BACKGROUND

Influenza B-related meningoencephalitis is a less recognised entity with only few published articles in the literature thus far. While influenza A-associated encephalopathy especially is more widely described especially in paediatric population, influenza B-related meningoencephalitis is an important entity to recognise given the increasing influenza activity over recent years in Australia.

CASE PRESENTATION

An 85-year-old man was brought to hospital with acute confusion. This occurred following return from a cruise holiday trip to New Zealand 3 days prior during which he complained of having 1-week history of respiratory prodromal symptoms and fever. Background medical history was significant for moderate aortic stenosis and mild chronic obstructive airway disease without previous neurological condition.

On presentation, he was alert but was disorientated with a body temperature of 38.5 degrees Celsius. There was no neck stiffness or rash and examination was otherwise largely unremarkable. While initial work-up was being carried out, he developed two episodes of generalised tonic-clonic seizures. He required intubation with mechanical ventilation due to concern for airway compromise in the setting of reduced consciousness and was admitted to an intensive care unit.

INVESTIGATIONS

Initial investigations revealed mild leucopenia ($3.84 \times 10^9/L$), lymphocytopenia ($0.85 \times 10^9/L$) and C reactive protein of 40 mg/L. Other tests including renal function, liver function tests and urine microbiology were normal. Viral PCR on nasopharyngeal swab tested positive for influenza B virus. Lumbar puncture on day 1 of admission revealed an elevated

cerebrospinal fluid (CSF) protein of 2.15 g/L with mononuclear cell pleocytosis ($35 \times 10^6/L$). Further CSF examination including bacterial, fungal and acid-fast bacilli was also negative. Viral PCR of CSF was negative for influenza virus.

MRI head with gadolinium series were performed, which showed generalised moderate atrophy including the medial temporal lobes.

TREATMENT

Aciclovir, which were given on presentation, were discontinued in light of the CSF viral PCR result. He was commenced on levetiracetam and sodium valproate with no further seizure activity since. In retrospect, given temporal relation of the neurological event and respiratory illness and failure in identifying other reversible causes, influenza B viral infection was thought to be the most likely explanation of lymphocytic meningoencephalitis.

OUTCOME AND FOLLOW-UP

His admission was complicated by slow neurological recovery due to severe encephalopathy, requiring extensive physiotherapy and occupational therapy involvement. He was transferred to the geriatrics department to undergo further restorative care.

DISCUSSION

The 2017 influenza season in Australia has recorded higher influenza-like illness (ILI) activity than recent years. This is supported by higher average general practitioner ILI consultation rate during the seasonal period (14.8 per 1000 consultations) compared with 5-year average for the period (10.3 per 1000 consultations).¹ Influenza B was circulating at high levels and contributed 37% to the notifications of laboratory-confirmed influenza.¹

Influenza B virus belongs to a family of RNA virus known as *Orthomyxoviridae*, which also include influenza A virus and influenza C virus. Influenza is an acute respiratory infection caused by influenza A or B virus, which occurs in outbreaks of varying extent every year. It usually begins abruptly with fever, myalgia, headache along with respiratory tract illness. Complications of influenza include pneumonia, myositis, myocarditis and neurological events including encephalitis as well as Guillain-Barre syndrome.

Influenza-associated encephalopathy is more common in children, usually in the setting of an influenza A infection.² There are limited articles in the literature studying influenza B-related meningoencephalitis in adults. To the best of our knowledge, few published articles have specifically

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Table 1 Main features of published influenza B-related meningoencephalitis

Authors	Sex/age (years)	Presentation	CSF	Imaging	Treatment	Outcome
Hawkins <i>et al</i> ³	F/37	2/7 Fever Confusion Neck stiffness Status epilepticus	Lymphocytes 75×10 ⁶ /L Protein 0.32 g/L No virus	Normal CT head	Dexamethasone Anticonvulsant	Complete resolution after 1 year
Jensen and Felding ⁴	F/30 Pregnant	1/7 Prodromal Chills Seizure Disorientation	Normal No virus	CT head—diffuse oedema of brain	Methylprednisolone	Complete resolution after 10 days
Ak <i>et al</i> ⁵	F/61	3/7 Fever Rhinitis Altered mental state	No cells Protein 1.14 g/L	Normal CT head Normal MRI head	Oseltamivir 5/7	Complete resolution after 7 days
	M/45	4/7 Fever Rhinorrhoea Cough Seizure	No cells Protein 0.28 g/L	Normal CT head Normal MRI head	Oseltamivir 5/7	Complete resolution after 10 days
Popescu <i>et al</i> ⁶	F/55	5/7 Fever Confusion Coma	Pleocytosis 10×10 ⁶ /L Protein 2.30 g/L No virus	Normal CT head MRI head symmetric diffusion restriction in bilateral anterior frontal cortex	Dexamethasone Oseltamivir	Complete resolution after 18 days
	F/27	3/7 Prodromal Fever Headache Seizure Coma	Pleocytosis 13×10 ⁶ /L Protein 7.16 g/L	Normal CT head MRI head Multiple areas of hyperintensities	Methylprednisolone Oseltamivir	Died in 3 days
Bayer ⁷	M/41	3/7 Fever Rhinitis Confusion Seizure	Leucocyte 21×10 ⁶ /L Protein 0.54 g/L	Normal CT head Normal MRI head	Anticonvulsant	Complete resolution within 1 month

examined and discussed this less recognised entity.^{3–9} Table 1 illustrates the characteristics of influenza B-related encephalitis in patients for whom information is available. It is more common among women, with one patient reporting having previous history of Influenza A encephalitis.⁶ No clear predisposing factors were identified on review. Most patients involved in previous case reports were young to middle-aged individuals with no history of cognitive or intellectual impairment, while cerebral atrophy demonstrated on neuroimaging in our patient may have contributed to his prolonged neurological recovery as compared with previous cases.

Neurological symptom preceded by respiratory prodrome is a common theme among most reported cases. Patients usually suffer from prodromal features including fever and rhinorrhoea before developing deterioration in their neurological function. Generalised seizure activity has been reported in five patients while most patients developed altered mental state ranging from confusion to coma. A total of two patients required intubation due to comatose state. In our case, there was a clear 1-week history of respiratory prodromal illness prior to development of acute neurological symptoms characterised by confusion and generalised seizure activity.

Diagnosis may be difficult given that influenza viral RNA has rarely been detected in the CSF by PCR.² Influenza B virus were detected through nasopharyngeal swab viral PCR or serum haemagglutination inhibition test. CSF samples in previous case reports were negative for influenza B virus, as in our patient. Meijer *et al* reported that influenza virus RNA in CSF was detected in 16% of cases, which may be explained by viral CSF concentrations of influenza virus being too low for detection by regular diagnostic tests.¹⁰ Otherwise, CSF may reveal lymphocytosis or raised protein, which was similar

to our patient. Neuroimaging finding on MRI are largely non-specific in diagnosing influenza B-related meningoencephalitis but certainly has a role in ruling out other structural causes of neurological function decline.

Most patients from previous reports received course of oseltamivir. Antiviral therapy achieved complete resolution in symptoms over a shorter duration of time as compared with patients who did not receive this. Interestingly, two patients in the study by Popescu *et al* did not receive vaccination prior to neurological complications,⁶ while influenza vaccination was administered in our patient. Unfortunately, the vaccination status in patients with influenza-associated meningoencephalitis was not studied in other literature. Thus, it remains an area for future research to determine the effect of vaccination on neurological complication secondary to influenza infection.

Learning points

- ▶ Influenza B-related meningoencephalitis is an important entity to recognise given the increasing influenza activity.
- ▶ Neurological sequelae are usually preceded by respiratory prodromal illness.
- ▶ Diagnosis is guided by cerebrospinal fluid profile and nasopharyngeal PCR.
- ▶ Treatment with antiviral should be considered if other clear cause is not identified and there is no contraindication.
- ▶ Effect of vaccination on prevention neurological complication remains unclear.

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