Viral meningitis and encephalitis

Philip Rice

Viral meningitis

Definition and epidemiology – the term 'aseptic meningitis' was introduced because it seemed to represent a specific aetiological entity – namely, patients with symptoms and signs of meningitis in whom bacterial cultures are negative. It is now known that almost all such cases are caused by viral infections. A wide range of viruses can cause meningitis (Figure 1); most cases are caused by enteroviruses (70–90%), genital herpes simplex virus (HSV) or mumps.

The exact incidence of viral meningitis is unknown in the UK; in the USA, the estimate is 75,000 cases/year. Any age group can be affected, but childhood disease is more common than that in adults. Transmission usually occurs by droplet infection, close personal contact or faeco-oral contact. The exception is zoonotic infection with lymphocytic choriomeningitis virus, an arenavirus related to Lassa fever that is excreted in the urine of small rodents; transmission of this organism occurs by inhalation when changing bedding contaminated with urine.

Clinical features – the typical syndrome of viral meningitis comprises acute onset of fever, headache and accompanying signs of meningeal irritation (photophobia, neck stiffness, Kernig's sign and jolt accentuation of headache). Nonspecific symptoms include arthralgia and myalgia, sore throat, weakness and lethargy. Other symptoms and signs are specific to the causative agent.

Enteroviruses

The enteroviruses comprise 70 serotypes, including poliovirus, Coxsackie virus A and B, and echovirus. Most enterovirus infections are asymptomatic – up to 10% of the population have detectable enterovirus-specific IgM at any one time. Most infections occur in late summer and autumn, and outbreaks may occur in nurseries and day-care centres. Rarely, outbreaks in neonatal units have been described; these have a high mortality.

A rash may be seen; this may be erythematous and maculopapular, vesicular on the palms and the soles of the feet and inside the mouth (as in hand, foot and mouth disease), or an exanthem in the oral cavity (seen in herpangina). Enterovirus serotype 71

Philip Rice *is Consultant Virologist at St George's Hospital, London, UK. He qualified from St Thomas' Hospital, London, and trained in medical microbiology and virology in Sheffield and at St Thomas' Hospital. His research interests include human papillomavirus, hepatitis C, rapid diagnosis of CNS infections and hantaviruses. Conflict of interests: none declared.*

Viral causes of meningitis

- Mumps
- Enteroviruses
  - Poliovirus types 1, 2 and 3
  - Coxsackie virus type A (23 serotypes)
  - Coxsackie virus type B (6 serotypes)
- Echovirus (31 serotypes)
- Others
  - Enterovirus 71 (hand, foot and mouth disease)
  - Enterovirus 70 (epidemic conjunctivitis)
- Genital herpes simplex virus types 1 and 2
- Other herpes viruses
  - Cytomegalovirus
  - Epstein–Barr virus
  - Varicella-zoster virus
- HIV
- Lymphocytic choriomeningitis virus
- Adenovirus types 3 and 7
- Arboviruses

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can also induce acute flaccid paralysis identical to that caused by poliovirus.[1]

HSV and varicella-zoster virus (VZV)

It has been known for many years that primary genital HSV infection can be associated with meningitis. More recently, a syndrome of benign recurrent aseptic meningitis has been shown to be caused by reactivation of genitally acquired HSV infection, most commonly HSV-2. This syndrome occurs predominantly in women (female: male ratio 6:1), and episodes can occur as much as 20 years apart. The average number of episodes recorded by patients is four. In one study, the recurrence rate in those presenting with a first episode of HSV meningitis was found to be 19%. Headache may be associated with genital recurrences. However, the risk of recurrent meningitis after genital infection, and the host and viral factors underlying its development, remain poorly understood.

Reactivation of VZV usually presents as shingles, but can also present as meningitis without a cutaneous component.[2] Such patients may suffer excruciating headaches.

Mumps virus

When parotitis is present, mumps is the probable diagnosis. Classically, mumps meningitis occurs about 7–10 days after the onset of parotitis. However, the epidemiology of viral meningitis has changed dramatically since the introduction of the MMR vaccine in 1988. Before this, mumps virus was the most common cause of meningitis (annual incidence 5–11/100,000 population, 1200 hospital admissions each year); the current incidence is about 0.3/100,000 population.

HIV

Headache occurs in about 50% of patients during primary HIV infection, and meningism is not uncommon. Higher HIV RNA levels in the CSF correlate with neurological symptoms.

Viral encephalitis

Definition and epidemiology – encephalitis is an uncommon outcome of many common viral infections (Figures 2 and 3). Infection of the brain parenchyma can have devastating consequences; mortality is high, and there is long-term morbidity in many survivors. A diverse range of agents is responsible, and infection may occur at any time from the neonatal period to old age; both primary infection and reactivation of latent viruses are possible. Acute encephalitis is a notifiable disease in the UK; 20–40 cases are reported annually, probably reflecting laboratory-confirmed cases only. In the USA, the estimated incidence is 20,000/year; most cases are mild because they are primarily caused by infection with arthropod-borne viruses.

Pathogenesis of infection – viruses may reach the CNS by the haematogenous or neuronal route.

- The haematogenous route is used by arthropod-borne viruses, after injection into capillary blood by a tick or mosquito bite. Local replication in the surrounding skin is followed by primary viraemia, which seeds the major organs. A second bout of multiplication produces secondary viraemia, which, if of sufficient magnitude, can cross the blood–brain barrier via infected WBCs or locally in vascular endothelia.
- The neuronal route of entry is exemplified by rabies (Figure 4) and HSV, which are transported directly into the brain by retrograde axoplasmic flow. This is a viral immune evasion mechanism – once inside the axon, the virus is invulnerable to immune control.

Clinical features – the onset of viral encephalitis is commonly acute, with fever and headache. Because the injury is directly to the brain, there are disturbances in higher mental function (e.g. confusion, delirium, behaviour changes, dysphasia/aphasia, temporal lobe seizures, focal neurological signs proceeding to coma). These distinguish viral encephalitis from meningitis, in which there is no nervous tissue involvement.

Herpes simplex encephalitis

In developed countries, the most common and most important cause of viral encephalitis is HSV, though such cases are rare (incidence 1/250,000–500,000/year); one-third occur in the under-20s and one-half in the over-50s. About two-thirds of cases are caused by virus reactivation, the risk factors for which are unknown; the remaining one-third are caused by primary infection in the neonatal period (when HSV infection occurs during labour) or in childhood.

It is believed that virus accesses the CNS via the olfactory ganglia, but there is evidence for direct reactivation of latent virus within the brain. Entry via viraemia is seen only in disseminated infection. The presence of a cold sore is almost always coincidental. HSV has a particular affinity for the temporal lobes and, because it is cytolytic, considerable destruction of nervous tissue occurs. The site of replication is then reflected in the symptoms – temporal lobe seizures, speech disorders, personality changes and altered behaviour.

Infection in the immunocompromised

A slightly different group of (mostly latent) viruses is responsible for encephalitis in immunocompromised individuals. Cytomegalovirus (CMV) and VZV may lead to encephalitis and granulomatous arteritis with spinal cord myelopathy caused by