Acute transverse myelopathy in Epstein-Barr virus infection

Case reports

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Summary

Two patients with acute transverse myelopathy in association with Epstein-Barr virus infection are described. Evidence of Epstein-Barr virus infection should be sought in any young patient with an acute neurological illness, even in the absence of the usual features of infectious mononucleosis. The cases described confirm previous reports that the prognosis in patients with neurological complications of this infection is generally good.

Neurological complications of infectious mononucleosis are uncommon but can be life-threatening. With the development of tests for specific antibodies to Epstein-Barr (E-B) virus it is becoming evident that a patient with an acute neurological illness can be found to have raised levels of anti-E-B antibodies but no other manifestations of classic infectious mononucleosis; sometimes even heterophile antibody tests are negative.

Transverse myelopathy is one of the rarer neurological complications of E-B virus infection. I wish to report on 2 patients with transverse myelopathy who were shown to have this infection. One of these had classic infectious mononucleosis, while the other had a neurological illness with minimal systemic features.

Case reports

Case 1

A 20-year-old White student developed a pyrexial illness on 31 July 1981, associated with headache and myalgia but no sore throat. The following day bilateral leg weakness and painless urinary retention developed and a urinary catheter was inserted. Bulbar palsy and intercostal weakness developed 1 day later, necessitating intubation and positive-pressure ventilation.

On examination at that stage the patient had a macular semi-confluent rash over the trunk, rubbery bilateral axillary and posterior cervical lymphadenopathy, palatal petechiae and fused conjunctivae. The throat was normal, and the liver and spleen were slightly enlarged. Higher mental function was normal. The neck was stiff. Cranial nerve examination showed a left 6th-nerve palsy, bilateral lower facial weakness and a complete bulbar palsy with absent gag reflex. A clear sensory level was present at the 4th thoracic dermatome, below which all modalities of sensation were absent. Anal tone was absent. Power of the limbs was reduced to grade 3 out of 5 in the arms and to grade 1 out of 5 in the legs. All the limbs were hypotonic and by the following day all reflexes were absent. Plantar reflexes were flexor.

Investigations showed a white cell count of 9.9 x 10⁹/l with 30% neutrophils, 32% lymphocytes, 8% monocytes and 30% atypical lymphocytes. The Paul-Bunnell test was positive to a titre of 320 with unabsorbed serum; the titre fell to 160 after absorption with guinea-pig kidney and to zero after absorption with ox cells. When the test was repeated with unabsorbed serum 10 days later the titre was 640. Hepatic enzyme levels were raised, suggesting mild hepatitis. Cerebrospinal fluid examination on admission showed a clear colourless fluid containing protein 0.6 g/l, no globulin, 8 lymphocytes and 1 neutrophil. The glucose value was normal and no growth was obtained. Examination 1 week later showed a xanthochromic fluid, a protein level higher than 2 g/l, 4+ globulins, 16 atypical lymphocytes and 7 neutrophils.

A diagnosis of infectious mononucleosis complicated by a transverse myelopathy and associated cranial and spinal polyneuropathy was made. The evidence for transverse myelopathy was the clear sensory level associated with early painless sphincter involvement and leg weakness. Electrophysiological studies performed 2 weeks after the onset of the illness showed slowing of nerve conduction with no evidence of denervation, suggesting that the polyneuropathy was of the demyelinating variety.

Over the next 7 days the patient’s condition deteriorated until he was completely paralysed except for 3rd cranial nerve function bilaterally and some movement of the orbicularis oris. The sensory level rose to the 3rd thoracic dermatome with patchy sensory loss over the arms and face. Mental function remained normal.

On the 9th day of the illness treatment with prednisone 60 mg/d was commenced. On the 9th day recovery began with the return of power to the face and neck. The subsequent course was one of continuing neurological improvement complicated by staphylococcal pneumonia and urinary tract infections. Ventilation was discontinued 35 days after its commencement. The cranial nerves, sensation and sphincter function all returned to normal and limb power improved gradually. When last seen 6 months after the onset of his illness the patient could walk without assistance but still had difficulty climbing stairs.

Case 2

A 15-year-old White scholar developed lumbar backache followed by the relatively sudden onset of leg weakness on 6 March 1982. Within 12 hours he was unable to sit, stand or pass urine. There was no antecedent respiratory infection.

On examination he was pyrexial with no adenopathy, jaundice, petechiae or tonsillitis. There was no neck stiffness and mental function was normal. The fundi, the cranial nerves and the nerve
supply to the arms were normal. There was marked weakness of
trunk muscles, and power was reduced to grade 3 out of 5 in the
hips and knees and to grade 4 out of 5 in the ankles. Ankle
reflexes and the left knee reflex were absent, the right knee reflex
was reduced, plantar reflexes were flexor, and the abdominal and
crurematic reflexes were absent. There was a clear sensory level
at the 8th thoracic dermatome, below which light touch and pain
sensation were absent but proprioception was intact. The
bladder was painlessly distended with overflow incontinence,
but anal tone was normal.

Investigations showed a white cell count of 12.3 x 10^9/l with
82% neutrophils, 15% lymphocytes, 2% monocytes and 1%
cosinophils. Liver function was normal. The Paul-Bunnell test
was negative but antibodies to the D component of E-B virus
early antigen were present to a titre greater than 20. All other
screens for infective agents (including cytomegalovirus and
hepatitis B virus) and for collagen-vascular disease were negative.
A myelogram was normal. CSF examination showed a pressure
of 190 mm H2O; the fluid contained 1 lymphocyte, protein 0.1
g/l and no globulin. The glucose level was normal.

The patient was assessed as having a transverse myelopathy
sparring the posterior columns and related to E-B virus infection.
The evidence for myelopathy was the sensory level and early
sphincter involvement, but an associated polyradiculopathy
could not be excluded because of early absent reflexes with
relatively preserved distal power.

No specific treatment was given. The patient's temperature
rose to 39°C for 24 hours and he developed slightly enlarged
subependymal lymph nodes which resolved after a few days.
Bladder function returned to normal 2 days after onset. By the
7th day power in the legs was normal and the knee and ankle
reflexes had become brisk. Electrophysiological studies per-
duced 10 days after onset showed no evidence of denervation.
On discharge only truncal weakness and a persistent sensory
level remained. The patient was lost to further follow-up.

Discussion

Between 1% and 2% of patients with infectious mononucleosis
develop neurological complications. 1 Minor disturbances such as
headaches and mild meningeitis may be commoner, as may
abnormal electro-encephalograms. 2

Neurological manifestations can be classified as aseptic menin-
gitis, (meningo-) encephalitis, polyneuropathy (including Guil-
lain-Barré syndrome), mononeuropathy (monoradiculopathy)
and transverse myelopathy. The encephalitis can result in
disturbances of consciousness from confusion to coma, seizures
and focal disturbances including hemiplegia, chorea, and brain-
stem and cerebellar disorders. 3 Mononeuropathy of all 12 cranial
nerves as well as the spinal nerves has been described. 4

Transverse myelopathy is one of the rarest neurological
complications of E-B virus infections, with fewer than 10 cases
reported by 1969 5 and only isolated cases since then. 6,7 Both our
patients had early painless sphincter involvement with a clear
sensory level characteristic of transverse myelopathy. 8 The first
patient then developed severe polyneuropathy involving cranial
as well as spinal nerves.

Although the neurological complications usually follow the
classic illness, in certain patients neurological symptoms and
signs may be the initial, major or only clinical manifestation of
the disease. The most common such manifestation is encephalo-
pathy or meningo-encephalopathy. 9,10 but Guillain-Barré syn-
drome,11 cranial nerve palsies, isolated tonic-clonic seizures and
paraparesis have been described. 9 As specific tests of anti-E-B
virus antibody have been developed, so it has been realized that
E-B virus infection is implicated in many acute neurological
illnesses in young patients and that in these cases heterophile
antibody tests are often negative and there are sometimes no
manifestations of classic infectious mononucleosis.12

The first patient described here had fever, rash, adenopathy
and a positive Paul-Bunnell test, but the dominant feature was
his neurological disease. The second patient had a negative Paul-
Bunnell test but a raised titre of antibodies to the D component
of early E-B virus antigen, a test specific for new or reactivated
E-B virus infection in the absence of lymphoma, leukaemia or
other malignant lesions. 13 The only systemic features were a
transient fever and a slight enlargement of the submandibular
lymph nodes, both of which followed the onset of neurological
disease. These cases support the assertion of Silverstein et al. 4
that E-B virus infection should be considered in any young
patient with an acute neurological illness.

The prognosis of neurological complications of E-B virus
infection is good. 9 If the patient can be supported through the
acute illness, excellent recovery is usual. Most series report
complete resolution of encephalitis even when decorticate
rigidity was present 1 and show a similar outcome for the
Guillain-Barré syndrome. In some cases residual weakness has
remained after transverse myelopathy, but this has been mild. 15
The first patient started to recover from almost complete
paralysis on the 9th day of his illness and thereafter improved
slowly over 9 months to almost full recovery. The second patient
showed dramatic improvement after only 2 days and power was
normal by 7 days.

Corticosteroids were used in the first case, but their value
is controversial. 1 The almost uniformly good prognosis suggests
that such empirical therapy need not be given.

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REFERENCES

2. Gautier-Smith PC. Neurological complications of glandular fever (infectious
3. Schmid RG, Dyck PJ, Bowin EJW, Glass DW, Tarwell H. Infectious
mononucleosis: neurologic and EEG findings. Medicine (Baltimore) 1966; 45:
31-63.
4. Cotton PB, Webb-Peploe MM. Acute transverse myelitis as a complication
5. Munder MD. Querschnittsmyelitis beiinfektiöser Mononucleose. Med Klin
1969; 64: 1752-1755.
II: 902.
7. Dowling DC, Cook SD. Role of infection in Guillain-Barré syndrome: laboratory
confirmation of herpes viruses in 41 cases. Ann Neurol 1981; 9:
suppl, 44-45.
myelitis: incidence and etiologic considerations. Neurology (NY) 1982; 32:
966-971.
9. Silverstein A, Steinberg G, Nathanson M. Nervous system involvement in
infectious mononucleosis: the heralding and/or major manifestation. Arch
10. Friedland R, Tahr MD. Meningoencephalopathy secondary to infectious
Arch Neurol 1977; 34: 691.
Lancet 1972; II: 1285-1287.