Case report

Intravenous immunoglobulins in an adult case of post-EBV cerebellitis

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SUMMARY

Post-Epstein-Barr virus (EBV) cerebellitis is very rare complication of infectious mononucleosis and only a few adult cases are reported in literature. We present a 23-year-old patient who was admitted to the neurology service with worsening ataxia, nystagmus and dysarthria, 1 week after infectious mononucleosis. Imaging and cerebrospinal fluid studies were normal, serum studies revealed acute transaminitis and positive EBV viral capsid IgM and IgG. The patient underwent a 5-day course of intravenous immunoglobulins with rapid resolution of all his symptoms and was safely discharged home. The pathophysiology of post-EBV cerebellitis involves autoreactive antibodies, rather than a direct viral insult. Antineuronal antibodies might be the result of a mimicry between EBV proteins and neuronal antigens or they can be secreted by the EBV-transformed lymphocytes themselves. Many reports stress the benign, self-limiting nature of this syndrome; however, immunotherapy might de facto decrease the severity and duration of illness.

BACKGROUND

Post-Epstein-Barr virus (EBV) cerebellitis has been reported in children <6 years of age, but it is very rare in young immunocompetent adults. We present the case of post-EBV cerebellitis in a young adult treated with intravenous immunoglobulins.

CASE PRESENTATION

A 23-year-old right-handed Caucasian man presented to the emergency department in September with worsening ataxia. A week prior to that he had developed fever up to 103°F (39.4°C), diaphoresis, headache and bilateral retro-orbital pain. The symptoms were partially relieved by scheduled nonsteroidal anti-inflammatory drugs (NSAIDs). A few days later, he developed gait ataxia and slurred speech which prompted him to visit the emergency department. He denied any history of drugs, alcohol use or recent travels. He had a coworker sick with cold, but no other sick contacts.

INVESTIGATIONS

His initial physical examination revealed scanned speech, impaired Holmes rebound sign on the left outstretched arm and unsteady gait without clear signs of gait ataxia. Liver, spleen and lymph nodes were not palpable and no rashes were noted. Labs revealed positive EBV viral capsid IgM and IgG (at >160 and 114. respectively), but his Epstein-Barr nuclear antigen IgG was negative (<18.00), consistent with a recent infection. IgM antibodies directed against the viral capsid antigen of EBV are useful in confirming the diagnosis of recent EBV infection along with clinical presentation and liver function tests. EBV IgM viral capsid antigen (VCA) titers decrease in most patients after 3–6 months but may persist in low titer for up to 1 year. EBV IgG VCA antibodies rise later than the IgM VCA antibodies but remain elevated with variable titers for life. Liver function tests showed alanine aminotransferase of 169, aspartate aminotransferase of 65, alkaline phosphatase of 189. Alcohol levels were normal; Lyme antibodies were negative. He underwent a brain MRI, which was, as expected in a case of postinfectious cerebellitis, completely normal (figures 1 and 2).

They are characterised by signs of acute or subacute cerebellar dysfunction and by normal cerebrospinal fluid (CSF) studies, with elevated serum EBV antibodies.[1 2] The role of MRI in patients with postinfectious cerebellitis is limited, as the MRI demonstrates no abnormalities in the majority of patients.[3 4] Brain single-photon emission computed tomography (SPECT), on the other hand, may be useful in some cases as it might reveal regional perfusion abnormalities. In particular, regional hyperperfusion, which is related to tissue acidosis and necrosis, has been reported, .[5–7] Our patient was not evaluated via SPECT, as this test is not routinely administered in these cases at our institution.

Despite his symptoms, he opted to be discharged home with a close neurology follow-up. A few days later, however, he was admitted to the neurology service again with worsening symptoms. A repeat physical examination revealed significant dysarthria, bilateral nystagmus, dysdiadochokinesia—worse on the left—and clear gait ataxia. A lumbar puncture was performed and the results were grossly normal, except for a slightly increased protein count at 55. EBV PCR within the CSF was, as expected, negative.

TREATMENT

The patient underwent a 5-day course of intravenous immunoglobulins.

OUTCOME AND FOLLOW-UP

After the initiation of treatment with intravenous immunoglobulins, the patient showed a rapid improvement in all his symptoms and was safely

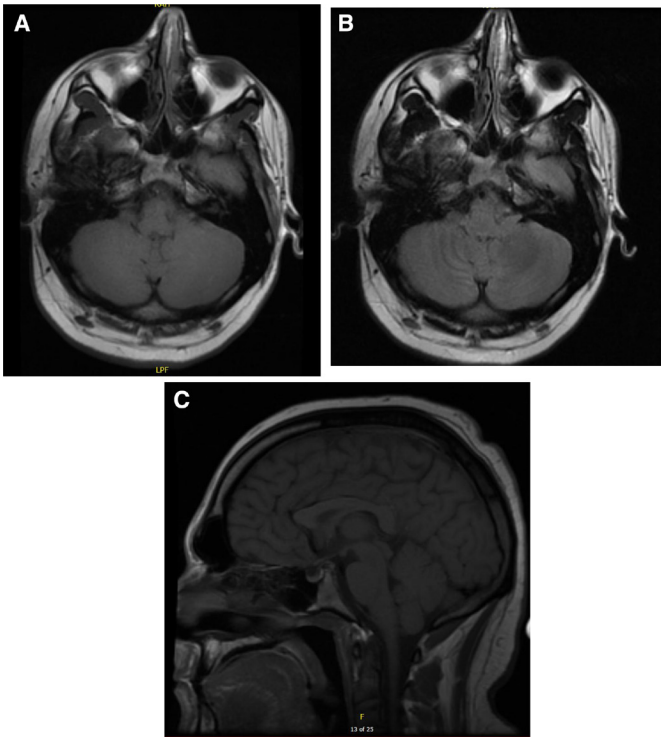

Figure 1 Brain MRI. (A) Axial precontrast T1, (B) axial T2/FLAIR, (C) sagittal precontrast T1.

discharged home without the need for additional assistance or physical therapy.

DISCUSSION

Cerebellitis is defined as inflammatory encephalitis limited to the cerebellum.[8 9] It is characterised by symptoms of ataxia, nystagmus and dysarthria. Both the acute (infectious) and the subacute (postinfectious) forms of cerebellitis have been reported in children <6 years of age,[10 11] but they are rare occurrences in young adults.[12] In particular, postinfectious cerebellitis has been observed following many infectious diseases,[13] but only a few cases of cerebellitis after EBV mononucleosis appear in literature.[14–16] EBV mononucleosis is a viral illness that presents in young adults as a triad of fatigue, pharyngitis and lymphadenopathy. It is generally considered a self-limiting condition; however, neurological manifestations occur in 1% of the cases and include meningitis, encephalitis, transverse myelitis, Guillain-Barre syndrome and ataxia.[17–19] In particular, EBV-associated cerebellar ataxias are preceded by infectious mononucleosis by 1–3 weeks. They are characterised by signs of acute or subacute cerebellar dysfunction and by normal CSF studies, with elevated serum EBV antibodies.[1 2] The pathophysiology of this syndrome involves antiviral and autoreactive antibodies, rather than a direct viral insult,[20] and the autoantibody titers can be increased even before the appearance of cerebellar symptoms. Among others, antineuronal and antitriosephosphate isomerase antibodies have been studied.[21 22] The mechanisms underlying the production of such antibodies is still partly unknown but might involve antineuronal antibodies secreted by EBV-transformed B-cells or a mimicry between EBV proteins and neuronal antigens. These observations suggest that therapies directed at the immune response might be effective in treating post-EBV cerebellitis. Corticosteroids, plasmapheresis and intravenous immunoglobulins have been used in acute and subacute

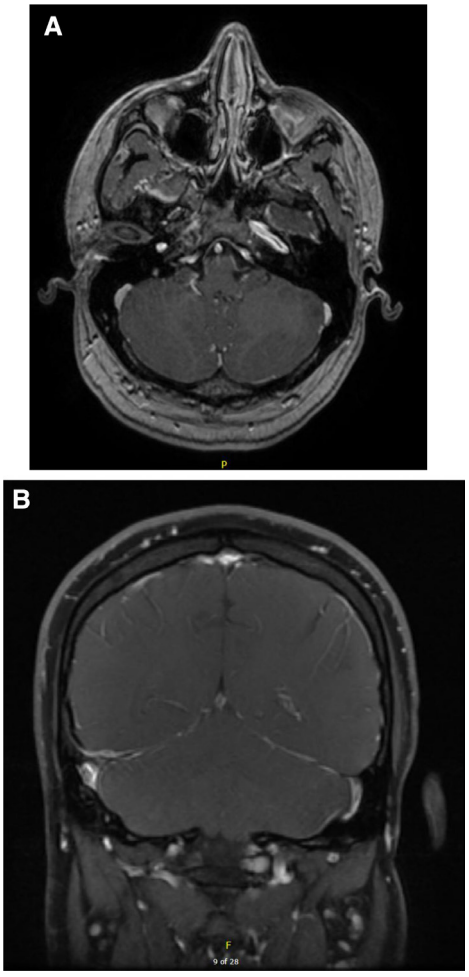

Figure 2 Brain MRI. (A) Axial postcontrast T1, (B) coronal postcontrast T1.

(postinfectious) cerebellar ataxias, especially in the paediatric population;[3 9 23 24] however, no consensus guidelines have been published for the treatment of these entities. Many reports stress the benign, self-limiting nature of postinfectious cerebellar ataxias;[10 13 14] however, residual cognitive and motor deficits can affect patient for months and cases of persistent cerebellar ataxias in adults have been described as well.[25] Early intervention with immunotherapy might de facto decrease the severity and duration of illness and improve the patients' quality of life.[26 27] The case presented here, of post-EBV cerebellitis in a young male, reinforces the importance of early recognition and treatment of such patients to prevent adverse outcomes. Ours is one of the few examples of the efficacy of intravenous immunoglobulins for

Learning points

- Post-Epstein-Barr virus (EBV) cerebellitis is a rare occurrence in adults.
- Post-EBV cerebellitis is characterised by ataxia, nystagmus and dysarthria.
- Post-EBV cerebellitis is associated with the presence of autoreactive antibodies, in particular, antineuronal antibodies.
- Post-EBV cerebellitis is usually a self-limiting condition; however, treatment with intravenous immunoglobulin decreases the severity and duration of the syndrome.

treating this condition.[28] The patient presented to the hospital with progressively worsening signs of cerebellitis and demonstrated a dramatic improvement in his symptoms after the first dose of intravenous immunoglobulins. He completed a 5-day treatment course with complete resolution of the initial symptoms and was safely discharged home without additional need for physical or occupational therapy.

Contributors ED'A presented the case report. Both authors, ED'A and FK contributed to the final version of the manuscript. CI supervised the project.

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