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# Kissing Disease Presenting with Encephalomyeloradiculitis in a 65-year-old Immunocompetent Woman: A Case Report

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**Case Report**

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# Abstract

### Background

Epstein-Barr virus (EBV) is a ubiquitous virus typically causing infectious mononucleosis, with rare neurological complications usually occurring after primary infection or in immunosuppressed patients. We report a case of encephalomyeloradiculitis in an elderly immunocompetent patient, highlighting an atypical presentation of primary EBV infection.

### Methods

Case report at an academical medical center. Brain and spinal cord MRI, electroneuromyography, evoked potentials, serum and CSF analysis were performed.

### Case presentation

A 65-year-old woman, who had recently experienced a relationship breakup presented with subacute gait disturbance, bilateral lower-limb paresthesias, psychomotor slowing, cough and xerostomia.

Neurological examination revealed mild cognitive impairment, pyramidal syndrome in the upper limbs, lower-limb proximal paraparesis with absent knee reflexes and decreased sensation.

Systemic examination revealed cervical adenopathy and pharyngitis.

MRI showed focal pachymeningeal enhancement. Electrophysiologic investigations showed peripheral and medullar dysfunction. CSF analysis revealed lymphocytic pleocytosis.

EBV PCR was positive in both blood and CSF, while anti-EBV IgG/IgM values indicated seroconversion. Encephalomyeloradiculitis caused by primary EBV infection was diagnosed. Ganciclovir and intravenous immunoglobulins dramatically improved symptoms.

Immunological investigations showed elevated anti-SSA/SSB antibodies prompting investigations for Sjögren-related autoimmunity.

### Conclusions

Primary EBV infection can cause extensive neurological involvement at any age. EBV testing should be considered, in case of subacute neurological symptoms with an infectious context.


# Introduction

Epstein–Barr virus (EBV) is highly prevalent, infecting more than 90% of adults. [1]

Although often asymptomatic, primary infection manifests as infectious mononucleosis (IM) in approximately 10% of cases, typically presenting with fever, lymphadenopathy, pharyngitis and fatigue. [1]

Neurological complication are uncommon occurring in 1–5% of patients with IM[2] and may include encephalitis, meningitis, cerebellitis, myelitis, radiculitis and anterior horn syndrome. [2–5]

## Methods

This case was identified during the patient's admission in the neurology service at a tertiary university hospital. The case report was prepared with the Case Report (CARE) guidelines. [6] Clinical, laboratory, CSF, and neuroimaging data were extracted from the electronic medical record. Written informed consent was obtained for publication.

## Case presentation

A 65-year-old woman known for depression, Ménière's disease and at-risk alcohol consumption, had recently experienced a relationship breakup and subsequently resumed an active social life, including nightlife activities.

She presented to the Emergency Department with sudden gait disturbance, lower limb paresthesias, neuralgic pain and psychomotor slowing. She also complained of dry cough and xerostomia. Symptoms developed overnight and remained stable over the following days.

Neurological examination revealed mnesic and executive impairment, symmetric iliopsoas mild paresis, hyperreflexia in the upper limbs, absent knee reflexes with preserved ankle reflexes and decreased sensation in both legs with sensory and gait ataxia. Systemic examination revealed cervical lymphadenopathy and pharyngitis.

Brain MRI demonstrated focal pachymeningeal enhancement in the left frontal and parietal regions with bilateral cervical lymphadenopathy. Spinal MRI did not show evidence of myeloradiculitis.

Electroneuromyography demonstrated myokymic discharges in the right vastus medialis muscle, suggesting peripheral nerve or nerve-root irritability. Somatosensory evoked potentials revealed delayed peripheral conduction after right tibial nerve stimulation and delayed spinal cord conduction for the left tibial nerve. Motor evoked potentials were normal.

Blood tests demonstrated lymphocytic leukocytosis (WBC count 11.38 G/l [N<11]), absolute lymphocyte count (6.83 G/L [N<4]), and CRP was mildly increased (22mg/l [N<10])). Peripheral blood smear revealed atypical hyperbasophilic lymphocytes compatible with Pfeiffer cells. Liver function tests showed elevated alkaline phosphatase (188 U/l [N<102]) and gamma-glutamyl transferase (248 U/l [N<35]) with normal bilirubin (6 µmol/L [N7-25]).

CSF analysis showed mild pleocytosis (29 M/l) with 98% lymphomononuclear cells, 2% macrophages) and elevated protein (1.00 g/L with a positive CSF/serum albumin ratio). A CSF multiplex PCR panel (BIOFIRE FILMARRAY Meningitis-Encephalitis Panel) was negative.

However, specific EBV PCR demonstrated elevated viral loads in both blood (1.41 x 103 UI/ml) and CSF (9.40 x102 UI/ml) with negative EBV serologies. (**Table**)

The following serology was non-contributive: HIV, hepatitis B/C/E, CMV, HSV1/2, VZV, HTLV-1, West Nile virus, Tick-born encephalitis, toxoplasma, Syphillis, Tuberculosis and *Borrelia burgdorferi.*
Onconeural antibodies (blood and CSF) were negative.

Given the severity of the symptoms, a comprehensive evaluation for immunodeficiency was performed. Lymphocyte subset analysis was normal. A CT scan of the thorax, abdomen and pelvis showed reactive generalized lymphadenopathies.

Following EBV infection confirmation, empiric acyclovir treatment (10mg/kg/tid iv) was replaced by ganciclovir (10mg/kg/bid iv) for 7 days along with intravenous immunoglobulins (IVIG) (0.4mg/kg/day) for 5 days.

Five weeks after admission, we noted a marked recovery of strength, cognitive and sensory deficits and a persistent mild instability at Romberg's maneuver. Neuralgic pain rapidly disappeared.

Serological testing showed positive EBV viral capsid antigen (VCA) IgG and Epstein–Barr nuclear antigen antibodies by electrochemiluminescence immunoassay, with negative IgM and serum EBV PCR confirming resolved primary EBV infection. (**Table**)

Immunological investigations revealed antinuclear antibodies at a titre of 1:320, anti-SSA (Ro60) and anti-SSB (La) reactivity; normal serum complement levels with absent rheumatoid factor and cryoglobulins. A transient monoclonal IgG-κ component in the context of oligoclonal restriction on immunofixation was detected that had disappeared at six-month follow-up. At that time, a peripheral-blood type I interferon gene-expression signature was elevated with persistent anti-SSA/SSB antibodies prompting evaluation for Sjögren disease (SjD). Labial salivary gland biopsy demonstrated focal lymphocytic sialadenitis with a focus score of 0.81 foci/4mm² (classification threshold ≥1 focus/4mm²). The unstimulated whole salivary flow rate was reduced to 0.18 mL/min (classification threshold ≤ 0.1 mL/min). The Schirmer I test demonstrated lacrimal hyposecretion (3 mm/5 min on both eyes).

In the absence of exclusion criteria, those results yielded a score of 4, fulfilling the 2016 ACR/EULAR classification criteria [7] for an undiagnosed primary SjD.

## Discussion and conclusions

Primary EBV infection in elderly adults is rare. Our patient developed an even rarer neurological complication in immunocompetent individuals. Primary EBV infection was demonstrated by serologies and PCR in both blood and CSF.

EBV accounts for 0.5-3% of encephalitis cases in immunocompetent adults [8] and for 1–10% of Guillain-Barré syndrome. [9] Peripheral manifestations besides the Guillain-Barre spectrum are reported almost

exclusively as case reports suggesting these entities are individually rare. [2,3,5] Concurrent central and peripheral manifestations represent an unusual presentation, likely representing viral neurotropism across the neuraxis. Interestingly, MRI abnormalities may be subtle, and electrophysiologic studies are needed to demonstrate central and peripheral nervous system involvement. [2] The prognosis is generally favorable even without antiviral or immunomodulating therapy; however, severe neurological deficits could persist like weakness, sensory loss, cognitive and sphincter impairment. [2]

The mechanism of EBV-related neurological complications is unclear. Active viral replication within the CNS, post-infectious inflammatory mechanisms have been evoked and molecular mimicry. [2,5,10]

Increased age is associated with thymic involution and reduction in the number and diversity of naïve T-cells [11], which may compromise the immune system's ability to mount an effective response to new antigens and could plausibly impair control of viral replication in the CNS after primary infection. [12] However, symptoms of primary EBV infection, notably IM, are primarily associated with the magnitude of CD8 + T cell expansion rather than viral load alone, suggesting that post-infectious inflammatory mechanisms have a role. [1] Consistent with this idea, CSF showed leucocytosis with relatively low EBV load, pointing to mechanisms relating to low viral replication and vigorous inflammation. [10] Furthermore, peripheral nervous system manifestations have more often been attributed to immune-mediated mechanisms rather than direct viral invasion: indeed, EBV can infect and transform B cells that release antibodies that cross-react with antigenic epitopes on peripheral nerve myelin or contain antigenic epitopes cross-reacting with peripheral nerve myelin via molecular mimicry. [5] These mechanisms appear distinct from cases driven by EBV reactivation or chronic active disease favoured by immunosuppression [13] in the setting of solid organ or bone marrow transplantation, HIV infection, lymphoma and other immunosuppressive conditions.

There are no established treatment guidelines for EBV-associated neurological disease. Evidence from case reports and series suggests good response to antivirals (acyclovir/ganciclovir), steroids or IVIG but remains controversial. [2–4] We used ganciclovir and IVIG assuming a possible Guillain-Barré-like syndrome, contraindicating corticosteroids, with a favourable outcome.

The association between EBV and autoimmune diseases, notably as a potential trigger of SjD, is well described in literature.[14,15] Patients with SjD more frequently display IgM anti-VCA and IgG anti-EA antibodies [14,15,] and EBV has been detected within salivary gland ectopic lymphoid structures.[14,15] Proposed mechanisms include local viral persistence or reactivation, bystander activation of autoreactive B cells, type I interferon induction, shuttling between epithelial and B-cells and molecular mimicry between EBV proteins and disease-specific autoantigens. [14,15]

The patient's transient immunofixation abnormalities support self-limited B-cell activation during the infection. This reversibility favours reactive, infection-associated paraproteinemia over a persistent plasma-cell clone. Because EBV can directly infect and activate B cells, this pattern may reflect the

transient expansion of EBV-infected and/or bystander-activated B-cell clones. These results contrasted with a subsequent elevated type I interferon signature and persistent anti-SSA/SSB antibodies. This temporal dissociation suggests that EBV-driven B-cell activation may have occurred on a pre-existing autoimmune background or contributed to amplifying Sjögren-related autoimmunity. Without pre-infection samples, whether EBV initiated, accelerated, or merely revealed SjD cannot be determined.

In conclusion, clinical presentation of encephalomyeloradiculitis should prompt EBV testing even in older adults. An early diagnosis may improve outcomes with appropriate antiviral and immunomodulatory therapy.

## Abbreviations

**EBV**
Epstein-Barr virus
**MRI**
Magnetic Resonance Imaging
**CSF**
cerebrospinal fluid
**WBC**
White blood cells
**CRP**
C-reactive protein
**PCR**
Polymerase Chain Reaction
**CT**
Computed Tomography
**IVIG**
intravenous immunoglobulins
**SjD**
Sjögren disease
**CNS**
central nervous system
**IM**
Infectious Mononucleosis

## Declarations

**Ethics approval and consent to participate:** Not applicable.

**Consent for publication:** Written informed consent was obtained from the patient for the publication of this case report and any accompanying images. A copy of the written consent is available for review by

the editor-in-chief of this journal.

**Availability of data and materials:** All data generated or analyzed during this study are included in this article.

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Formal Analysis / Literature Review: JBP, IZ, JC, GU, PHL

Original Draft: JBP, IZ

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# Table

**Table** Biological data of the patient

| | Anti-EBV VCA IgM | Anti-EBV VCA IgG | Anti-EBV ECLIA IgG | EBV qPCR (plasma) | EBV qPCR (CSF) | CSF leucocytes |
|---|---|---|---|---|---|---|
| **At symptom onset** | 0.3 Ul/ml (N < 1.1) | 0.4 Ul/ml (N < 1.1) | 0.0 Ul/ml (N < 1.1) | 1.41 x $10^3$ (N < 2.0) | 9.4 x $10^2$ | 29 M/l (N < 5) |
| **At 5 weeks** | 0.3 Ul/ml (N < 1.1) | 784 Ul/ml (N < 1.1) | 103 Ul/ml (N < 1.1) | Negative | - | - |

Seroconversion of Epstein-Barr virus (EBV) showing the decrease in viral load in PCR testing and the development of Viral capsid antigen (VCA) and Epstein–Barr nuclear antigen antibodies (ECLIA) after primary EBV infection.