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Unusual initial manifestation of HIV Infection

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Case presentation

- A 57-year-old woman presented with cognitive changes, behavioral disturbances, and right hemiparesis that had progressively started 3 months ago.
- The patient had no known medical history, was not taking any medications, and her F.H was unremarkable.

On initial presentation:
The patient appeared confused.

Vital signs :

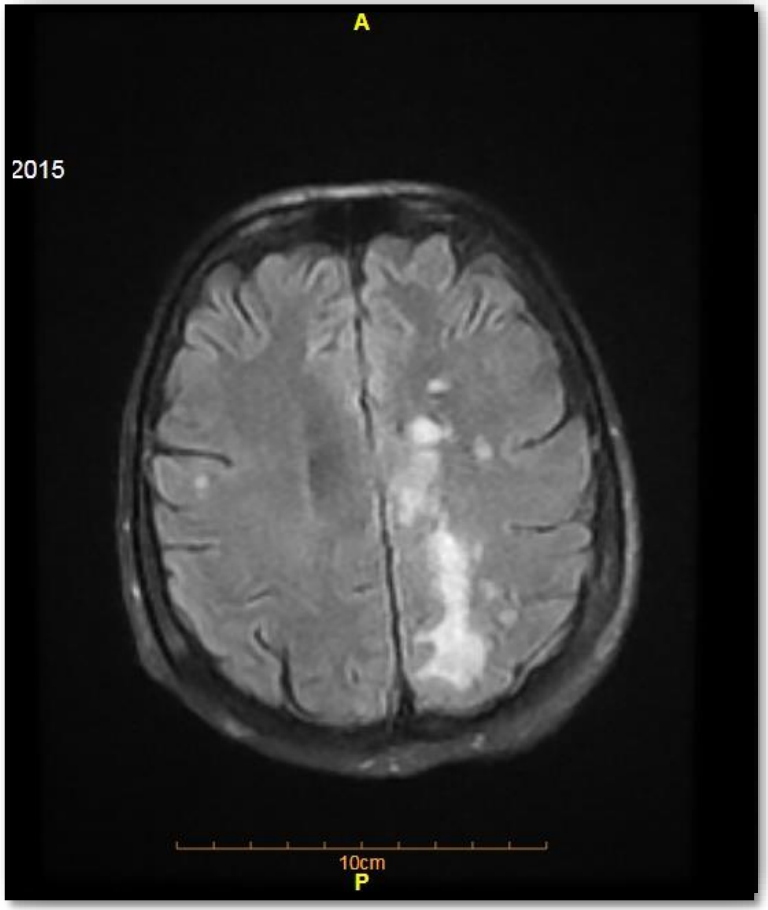
- ✓ BP: 110/85 mmHg,
- ✓ HR: 87 beats/
- ✓ RR: 17 breaths/min,
- ✓ T: 37.2°C
- ✓ and oxygen saturation: 97% on room air.

- **On neurological examination**:
- She exhibited **right hemiparesis**, **global aphasia**, marked **cognitive dysfunction**, and **obtundation,** indicating extensive cerebral involvement.
- Her other Physical examinations were not remarkable.

- **Initial laboratory results** :
- microcytic anemia, mild hyponatremia

MRI of the brain revealed:

- Multiple **well-defined hyperintense lesions** in T2-WI and FLAIR images in the **bilateral subcortical white matter** with **multiple peripheral foci of satellite lesions,** a **"milky way"**appearance.
- No mass-effect, restriction, or hemorrhagic foci were seen.



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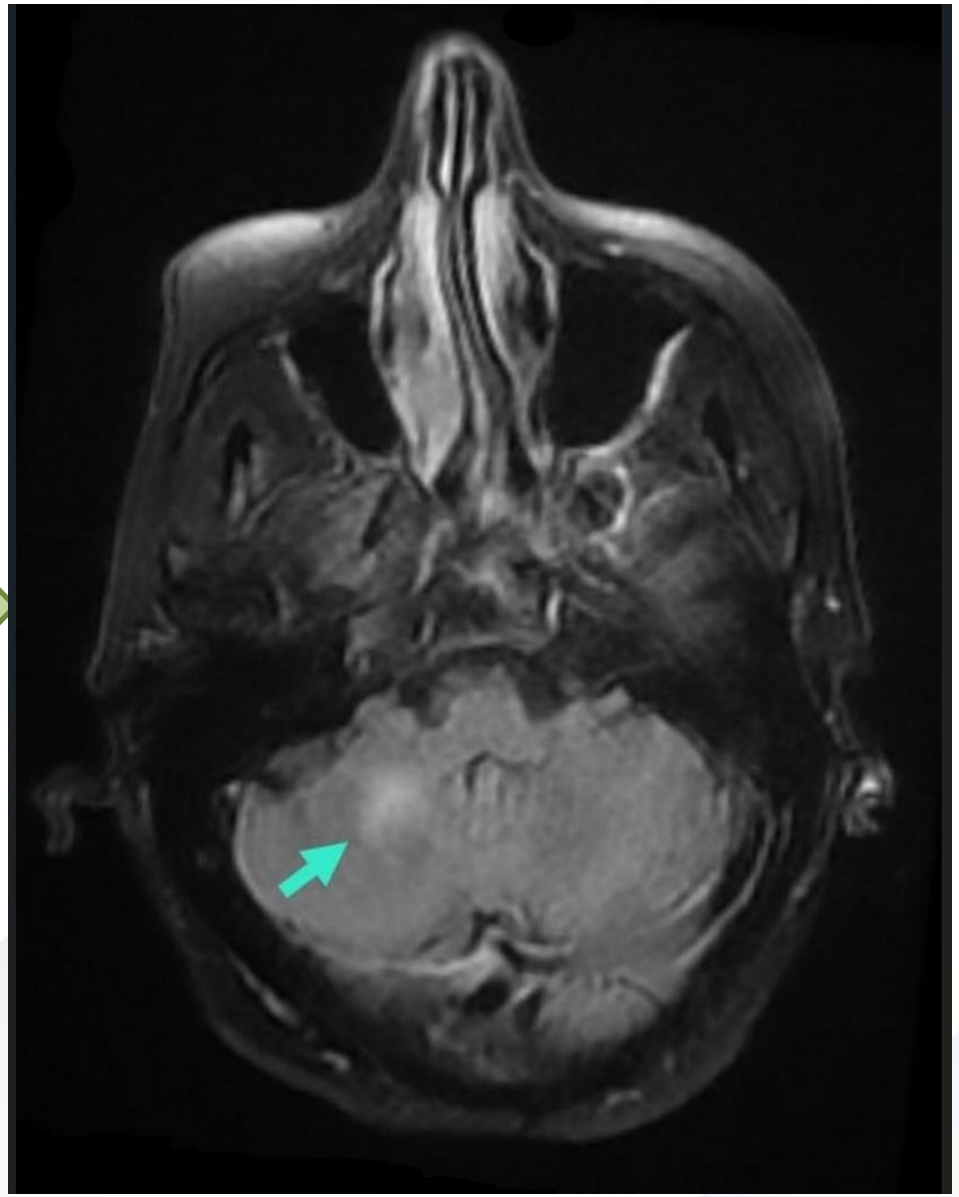
Although usually seen in Progressive Multifocal Leukoencephalopathy (PML), it can be seen in other disorders like **CNS vasculitis**, **neurosarcoidosis**, **posterior reversible encephalopathy syndrome (PRES), HIV/AIDS encephalopathy,** and **acute disseminated encephalomyelitis (ADEM)**

- Signal changes in the right cerebellar peduncle, with a **crescent sign in the cerebellum findings highly suggestive of PML.**



Shrimp sign in PML

Core Inclusion Criteria of the Shrimp Sign

White matter lesion
- Well-defined lesion in the cerebellar white matter
- The lesion is hyperintense on T2-weighted and FLAIR imaging
- The lesion is hypointense on T1-weighted imaging
- The lesion abuts and sharply demarcates the dentate nucleus and outlines the dentate nucleus in horizontal, parasagittal, and/or coronal views
- The lesion must encompass at least 50% of the dentate nucleus (partial shrimp); if there are multiple lesions adjacent to the dentate, they do not need to be contiguous

Other features compatible with PML
- There may be a mottled appearance of the white matter lesion on T2-weighted imaging
- The white matter hilum of the dentate nucleus may be involved
- The lesion may occur together with, or independent of, cerebral hemisphere and brainstem PML lesions

MRI Shrimp Sign in Cerebellar Progressive Multifocal Leukoencephalopathy: Description and Validation of a Novel Observation

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ABSTRACT

BACKGROUND AND PURPOSE: There are no validated imaging criteria for the diagnosis of progressive multifocal leukoencephalopathy in the cerebellum. Here we introduce the MR imaging shrimp sign, a cerebellar white matter lesion identifiable in patients with cerebellar progressive multifocal leukoencephalopathy, and we evaluate its sensitivity and specificity.

MATERIALS AND METHODS: We first identified patients with progressive multifocal leukoencephalopathy seen at Massachusetts General Hospital between 1998 and 2019 whose radiology reports included the term "cerebellum." Drawing on a priori knowledge, 2 investigators developed preliminary diagnostic criteria for the shrimp sign. These criteria were revised and validated in 2 successive stages by 4 additional blinded investigators. After defining the MR imaging shrimp sign, we assessed its sensitivity, specificity, positive predictive value, and negative predictive value.

RESULTS: We identified 20 patients with cerebellar progressive multifocal leukoencephalopathy: 16 with definite progressive multifocal leukoencephalopathy (mean, 46.4 [SD, 9.2] years of age; 5 women), and 4 with possible progressive multifocal leukoencephalopathy (mean, 45.8 [SD, 8.5] years of age; 1 woman). We studied 40 disease controls (mean, 43.6 [SD, 21.0] years of age; 16 women) with conditions known to affect the cerebellar white matter. We defined the MR imaging shrimp sign as a T2- and FLAIR-hyperintense, T1-hypointense, discrete cerebellar white matter lesion abutting-but-sparing the dentate nucleus. MR imaging shrimp sign sensitivity was 0.85; specificity, 1; positive predictive value, 1; and negative predictive value, 0.93. The shrimp sign was also seen in fragile X–associated tremor ataxia syndrome, but radiographic and clinical features distinguished it from progressive multifocal leukoencephalopathy.

CONCLUSIONS: In the right clinical context, the MR imaging shrimp sign has excellent sensitivity and specificity for cerebellar progressive multifocal leukoencephalopathy, providing a new radiologic marker of the disease.

A lumbar puncture was conducted.

- Cerebrospinal fluid (CSF) examination revealed:
  - 3 cells/mm^3 , all of them lymphocyte,
  - Raised protein (112 mg/dl with normal range 15-60 mg/dL)
  - and normal sugar levels.
  - The remaining CSF examinations were normal.
  - and absence of bacterial organisms on Gram staining and
  - No acid-fast bacilli was seen.

- PCR of the CSF was positive for **JC virus (JCV) DNA**, with a **viral load of less than 10 copies/µL**, thus confirming the **diagnosis of PML due to JCV**.

Progressive Multifocal Leukoencephalopathy

- PML is a rare and often fatal neurological disorder occurring in immunocompromised patients.

- Although **AIDS remains the most common etiology** of PML through out the world, the increased use of biological immunosuppressive/ modulatory agents has contributed to a progressively larger proport ion of cases.
- Some of those immunotherapies are **natalizumab, efalizumab, fingolimod, dimethyl fumarate,** and **rituximab**.

- Other risk factors are **post-transplant**: bone marrow or solid organ transplants, and leukemia.

- Given that the patient had no underlying disease and was not taking any specific medication, she was **tested for HIV**, which yielded a positive result.
- Due to the positive HIV result, combination ART was immediately initiated with a once-daily regimen of dolutegravir/ tenofovir / emtricitabine.

- Following the diagnosis of PML, he was prescribed **five days of Intravenous Immunoglobulin (IVIG) therapy.**

- Despite comprehensive medical interventions, the patient's neurological condition deteriorated, with no significant improvement in either cognitive or motor functions.
- After three weeks of hospitalization and continued supportive care, the patient unfortunately expired.

Progressive Multifocal Leukoencephalopathy

- PML remains a devastating opportunistic demyelinating disorder of the central nervous system caused by the **reactivation of latent JC virus.**
- JCV transmission is thought to occur by person-to-person contact or contaminated food and water.
- The virus remains latent in the gastrointestinal tract and the tubular epithelial cells of the kidney.
- It is thought that the virus spreads from oropharynx hematogenously to secondary sites such as bone marrow, lymphoid tissues, or kidneys.

- In **healthy individuals**, JCV establishes an **asymptomatic persistent infection** in the kidney, leading to its **intermittent excretion in urine**.

- Publications indicate 39 to 70% of the general population are seropositive for antibodies to JCV.
- **The JC virus is harmless except in cases of weakened immune systems.**
- Upon **alteration of the cellular immune response**, JCV may acquire mutations and gain the ability to infect the CNS.

- **PML is most common in people with HIV1 infection**; prior to the advent of effective ART, as many as 5% of people with AIDS eventually developed PML.

- Why PML occurs more frequently in people with AIDS than in other immunosuppressive conditions is unclear; some research suggests the effects of HIV on brain tissue, or on JCV itself, make JCV more likely to become active in the brain and increase its damaging inflammatory effects.

symptoms

- Symptoms can develop over **several weeks to months**, and they depend on **location of damage in the brain** and the **degree of damage.**

- The most prominent symptoms are "clumsiness, progressive weakness, and visual, speech, and sometimes personality changes.

Diagnosis

- PML is diagnosed in a patient with a progressive course of the disease, finding **JC virus DNA in CSF** together with consistent **white-matter lesions on brain MRI**.

- Alternatively, a **brain biopsy** is diagnostic.when the typical histopathology of demyelination, bizarre astrocytes, and enlarged oligodendroglial nuclei are present, coupled with the presence of JC virus by IHC.

Imaging

Progressive multifocal leukoencephalopathy

Last revised by Kang Wei Esther Lim on 13 Sep 2025

- Characteristic evidence of PML on brain CT scan images are multifocal, noncontrast enhancing hypodense lesions without mass effect.

MRI is far more sensitive than CT:

- **T1:** involved regions are usually **hypointense**
- **T2**:involved regions are **hyperintense** specially in the subcortical white matter of frontal and parietooccipital lobes.

Milky Way sign: multiple punctate high T2 signal lesions surrounding the main area.

barbell sign: parieto-occipital signal abnormality crossing the splenium.

shrimp sign: cerebellar white matter sparing dentate nucleus.

- **T1 C+ (Gd):** typically there is no enhancement.

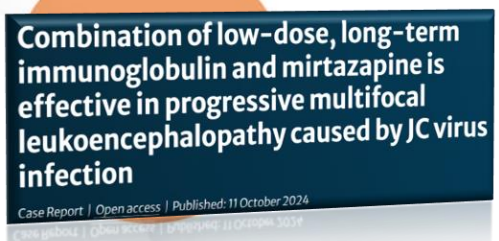
enhancement can be seen in PML-IRIS, AIDS with ART, and in patients on natalizumab.

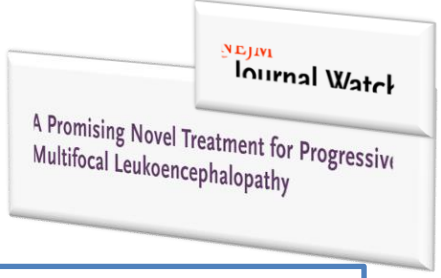
- **DWI/ADC**: peripheral patchy diffusion restriction particularly at the leading edge.

Treatment

- Management consists of **immune reconstitution** to slow or stop the disease progress.
  - **In patients with HIV: ART should be initiated.**
  - **In patients on immunosuppressive medications**: **these should be withdrawn if possible.**

- However, such improved immunity may lead to **an immune reaction known as immune reconstitution inflammatory syndrome (IRIS).**
- IRIS may cause a paradoxical neurological worsening in a patient whose immune system had started to recover.
- If PML-IRIS manifests, high-dose glucocorticoid therapy is recommended.





- Medications with potential antiviral properties against JCV in vitro such as **mirtazapine** or **mefloquine** did not show efficacy in PML patients, except in few case reports, (Combination of low-dose, long-term immunoglobulin and mirtazapine)
- **Cytarabine** a chemotherapy drug used to treat certain cancers, has been prescribed on an experimental basis for a small number of non-AIDS PML patients, and stabilized the neurological condition of a minority of these patients.
- Two case reports of using **interleukin-2** successfully have been published.
- Otherwise, **pembrolizumab** has also been shown to be an effective treatment for PML in small case series.
- **Brincidofovir** suppresses JCV but has been found to have toxicity at therapeutic dosage.
- **Infusion of donor T cells specific to the related BK polyomavirus** has shown possible effect in treating PML in one small study, but needs further study.

Prognosis

- **One-third to one-half** of people with PML die in the first few months following diagnosis, depending on the severity of their underlying disease.
- Survivors can be left with variable degrees of neurological disability.

Conclusion

- **PML** is a rare but devastating complication in **HIV positive** patients and can be the first presentation of AIDS.
- Early recognition through characteristic MRI findings and confirmatory CSF analysis is crucial.

Thanks for your attention!