Open Forum Infectious Diseases

BRIEF REPORT

JC Virus Granule Cell Neuronopathy and Lymphoma

Alexis Demas,[1] Omar Bennani,[1] Anne Vandendriessche,[2] Laurence Hellouin de Menibus,[2] Vincent Langlois,[2] and Jacques Gasnault[3]

[1]Department of Neurology and [2]Department of Infectious Diseases and Internal Medicine, Hospital Jacques Monod, Le Havre, France; [3]UF SSR des Maladies Neurovirales, Médecine Interne & Immunologie Clinique, Centre Hospitalier Universitaire de Bicetre, IMVA INSERM 1184, Le Kremlin-Bicêtre, France

Neurological opportunistic infections are going to increase. Clinicians should be aware of the neurological spectrum of JC virus manifestations, including granule cell neuronopathy. Detection of JC virus DNA by polymerase chain reaction in cerebrospinal fluid should be realized in the assessment of a progressive cerebellar ataxia in an immunocompromised patient.

Keywords. cerebellar ataxia; immunodepression; infection; JCV, lymphoma.

A 79-year-old woman was hospitalized for subacute cerebellar ataxia. Indolent B-cell lymphoma (splenic marginal zone lymphoma) was diagnosed 6 years earlier. Surveillance was recommended.

She described progressive gait instability associated with dysarthria, worsening over 2 months.

On admission, she was found to have severe cerebellar ataxia. She required a rollator to mobilize and had a cerebellar dysarthria, swallowing problems, and occulomotor involvement (square wave jerks).

Brain imaging demonstrated diffuse cerebellar atrophy, hyperintense areas in the cerebellar cortex, and bilateral middle cerebellar peduncles on diffusion, T2 and FLAIR-weighted imaging, and T1 hypointensities (Figure 1). There was no gadolinium enhancement.

Blood test revealed cytopenias with thrombocytopenia (116 G/L) and T lymphopenia (0.766/µL, normal count 1–2.2/µL) with selective TCD8 lymphopenia (0.168/µL, 0.330–0.920/µL). Lymphocytes and TCD4 counts were normal. The CD4/CD8 ratio was elevated (3.25; range, 1.20–2.20). Severe hypogammaglobulinemia was associated (3 g/L; normal range, 8–13 g/L). The HIV test was negative.

Cerebrospinal fluid (CSF) analysis showed a normal cell count (1 white cell) and normal protein (0.21 g/L) with no malignant cells on cytology. Detection of JC virus (JCV) DNA by polymerase chain reaction (PCR) was positive in the CSF (5000 copies per mL).

After discussion, chemotherapy was not given because of the risk of worsening lymphopenia and progression of JCV infection. She was treated with intravenous immunoglobulin. Correction of immunoglobulin G subclass occurred, without clinical improvement. Interleukin-7 therapy was also discussed but rejected given the risk of lymphoma progression.

She deteriorated rapidly, becoming bed bound, and she died due to recurrent aspiration pneumonia. A post mortem examination was not carried out.

The cause of death was JC virus granule cell neuronopathy (JCV-GCN) associated with cerebellar peduncle progressive multifocal leukoencephalopathy (PML). This is a newly described complication of JCV [1–3], reported in the context of immunosuppression and chronic lymphopenia. The most common association is with HIV infection [4], but it has also been reported in sarcoidosis and with immunosuppressive treatments such as natalizumab and rituximab [5, 6]. JCV-GCN corresponds to specific lytic infection of cerebellar granule cell neurons, classically resulting in a chronic progressive ataxia [7]. It is associated with a JCV variant, with mutations in the DNA at the c-terminus of the VP1 capsid gene [5, 6].

Given the development of immunosuppressive treatments, particularly in the era of monoclonal antibodies, clinicians should be aware of the neurological spectrum of JCV manifestations, including JCV-GCN. We report the first case of JCV-GCN in a patient with untreated lymphoma. We also provide new clinico-radiological features of JCV-GCN with subacute and lethal evolution. Clinicians should consider CSF analysis for JCV DNA by PCR in the assessment of progressive cerebellar ataxia in immunocompromised patients.

Received 2 January 2018; editorial decision 9 May 2018; accepted 16 May 2018; published online May 21, 2018.

Correspondence: A. Demas, MD, Department of Neurology, Hospital Jacques Monod, 26 Avenue Pierre Mendes France, Le Havre, 76290, France (alexis.demas@ch-lehavre.fr or alexis.demas@yahoo.fr).

Open Forum Infectious Diseases®

DOI: 10.1093/ofid/ofy112

Acknowledgments

Author contributions. Alexis Demas: drafting the manuscript, study concept or design, analysis or interpretation of data, acquisition of data. Omar Bennani: drafting the manuscript, acquisition of data. Anne Vandendriessche: drafting the manuscript, study concept or design. Laurence Hellouin de Menibus: drafting the manuscript. Vincent Langlois: drafting the manuscript. Jacques Gasnault: drafting the manuscript, study concept or design, analysis or interpretation of data.

Potential conflicts of interest. All authors: no reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

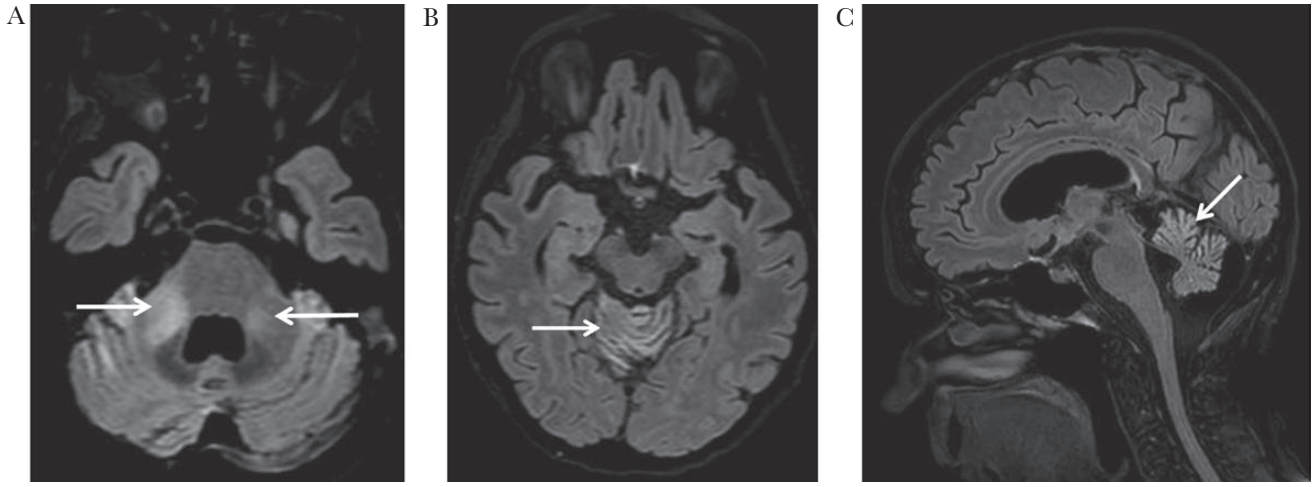

Figure 1. Axial magnetic resonance image (MRI) (A, B) showing, respectively, bilateral hyperintensity in the middle cerebellar peduncle (arrows) and cerebellar vermis cortex hyperintensities (FLAIR-weighted image). Sagittal MRI (C) showing cerebellar cortex hyperintensities (FLAIR-weighted image).

References

1. Koralnik IJ, Wüthrich C, Dang X, et al. JC virus granule cell neuronopathy: a novel clinical syndrome distinct from progressive multifocal leukoencephalopathy. Ann Neurol **2005**; 57:576–80.
2. Tan CS, Koralnik IJ. Progressive multifocal leukoencephalopathy and other disorders caused by JC virus: clinical features and pathogenesis. Lancet Neurol **2010**; 9:425–37.
3. Durali D, de Goër de Herve MG, Gasnault J, Taoufik Y. B cells and progressive multifocal leukoencephalopathy: search for the missing link. Front Immunol **2015**; 6:241.
4. Henry C, Jouan F, De Broucker T. JC virus granule cell neuronopathy: a cause of infectious cerebellar degeneration. J Neurol Sci **2015**; 354:86–90.
5. Agnihotri SP, Dang X, Carter JL, et al. JCV GCN in a natalizumab-treated MS patient is associated with mutations of the VP1 capsid gene. Neurology **2014**; 83:727–32.
6. Dang L, Dang X, Koralnik IJ, Todd PK. JC polyomavirus granule cell neuronopathy in a patient treated with rituximab. JAMA Neurol **2014**; 71:487–9.
7. Du Pasquier RA, Corey S, Margolin DH, et al. Productive infection of cerebellar granule cell neurons by JC virus in an HIV+ individual. Neurology **2003**; 61:775–82.