Radiology Case Reports 18 (2023) 1334–1336

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case Report

Progressive multifocal leukoencephalopathy selectively affecting Broca's and Wernicke's areas in an immunocompetent patient: A case report ☆

Renaid B. Kim, BS[a], *David N. Irani, MD*[b], *John Kim, MD*[a,*]

[a] *Division of Neuroradiology, Department of Radiology, University of Michigan, 1500 E Medical Center Dr, Ann Arbor, MI 48109, USA*

[b] *Department of Neurology, University of Michigan, Ann Arbor, MI 48109, USA*

ARTICLE INFO

Article history:
Received 12 December 2022
Revised 3 January 2023
Accepted 4 January 2023

Keywords:
Progressive multifocal leukoencephalopathy
JC polyomavirus
Encephalopathy

ABSTRACT

Progressive multifocal leukoencephalopathy (PML) is a rare, often fatal, demyelinating disease of the central nervous system. The disease almost exclusively presents in immunosuppressed patients, such as those with acquired immunodeficiency syndrome, a hematopoietic malignancy, or a transplanted organ; it is extremely rare in patients without immunosuppression. We present a case of a 74-year-old female with radiographic and histopathological findings consistent with PML that possibly arose in the setting of Sjögren's-related vasculitis but no immunosuppression.

© 2023 The Authors. Published by Elsevier Inc. on behalf of University of Washington. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/)

Introduction

Progressive multifocal leukoencephalopathy (PML) is a rare and often fatal demyelinating disease of the central nervous system caused by reactivation of the John Cunningham polyomavirus (JCV). Only few studies have reported on the epidemiology of PML in the general population, and long-term incidence trends are largely unknown [1]. PML almost exclusively presents in the setting of immunosuppression, such as hematopoietic malignancy, acquired immunodeficiency syndrome , or organ transplantation. Very few cases have been reported in the absence of immunodeficiency [2–4]. Here, we describe a case of PML in a 74-year-old patient who presented with global aphasia.

Case report

A 74-year-old female with a past medical history of hypertension, hyperlipidemia, stroke, and possible Sjögren's-related vasculitis presented to the emergency room (ER) with 6 weeks of gradually worsening receptive and expressive aphasia. Initial workup demonstrated a normal complete blood count and urinalysis. A cranial CT did not reveal any acute intracranial abnormalities, although a brain MRI and MRA 10 days prior to

☆ Competing Interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

* Corresponding author.
E-mail address: johannk@med.umich.edu (J. Kim).

https://doi.org/10.1016/j.radcr.2023.01.011

1930-0433/© 2023 The Authors. Published by Elsevier Inc. on behalf of University of Washington. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/)

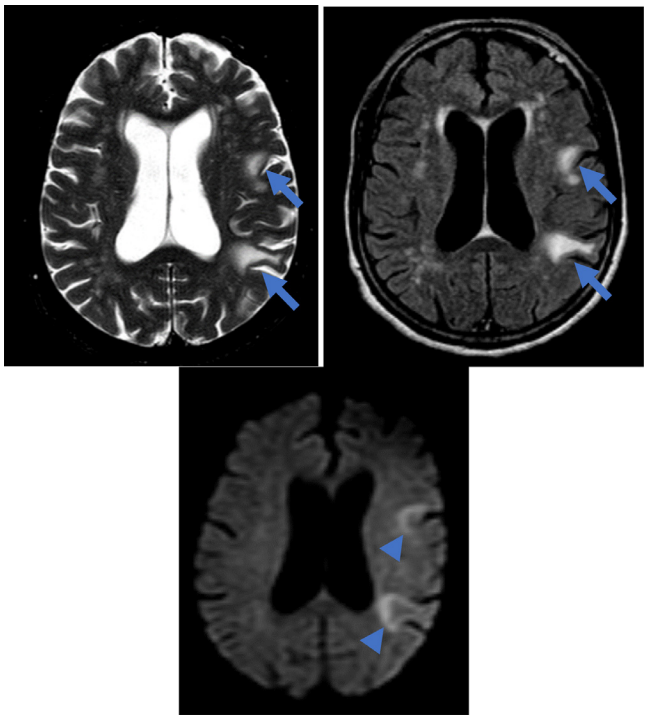

Fig. 1 – The T2 (A), T2 FLAIR (B), and DWI (C) images of the patient's brain MRI, characterized by numerous punctate, patchy T2 and FLAIR signal areas in bilateral cerebral white matter and a more focal confluent hyperintensities in the left inferior frontal gyrus and temporoparietal white matter that extend to the subcortical U-fibers (arrows) with mild peripheral leading edge of restricted diffusion (arrowheads).

her ER visit showed new patchy hyperintense FLAIR signal in the left inferior frontal gyrus and left temporoparietal white matter with sparing of the gray matter concerning at the time for a vasculitis flare or subacute ischemia (Fig. 1).

The patient was subsequently admitted. A lumbar puncture showed a normal cell count and differential, but the cerebrospinal fluid JCV polymerase chain reaction was positive at 201 copies/mL, despite none of the laboratory tests showing signs of immunosuppression. The cerebrospinal fluid autoimmune encephalopathy antibody panel was negative. A second lumbar puncture performed 2 weeks later was again positive for JCV at 73 copies/mL, but was negative for cytomegalovirus, varicella-zoster virus, herpes-simplex virus, herpes zoster virus, and human immunodeficiency virus. A repeat brain MRI 1 month later showed minimal progression from the original study. A CT angiogram was negative for any evidence of vasculitis. The ENA10 was positive for anti-SSa/anti-Ro but was otherwise negative. Antinuclear antibodies test by indirect immunofluorescence was negative. Rheumatoid factor, cyclic citrul peptide antibody, and antineutrophilic cytoplasmic antibody were all negative. Her C-reactive protein, erythrocyte sedimentation rate, thyroid stimulating hormone, C3, and C4 were all within normal limits. A serum protein electrophoresis showed mildly decreased total protein and albumin levels but was otherwise within normal limits. The patient subsequently underwent a brain biopsy, and the histopathological

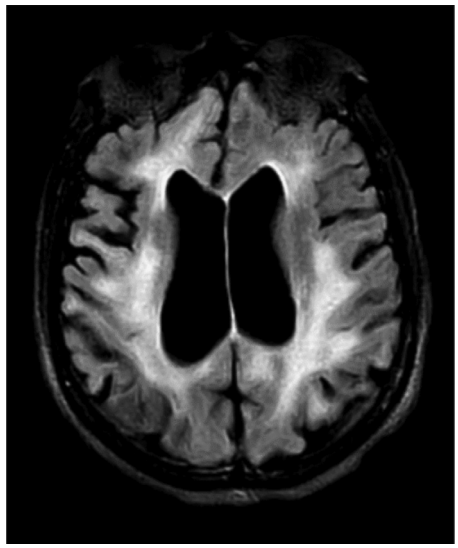

Fig. 2 – T2 FLAIR image of the brain after 1 year following initial presentation shows extensive white matter signal abnormalities with global volume loss compatible with JC virus disease progression.

findings demonstrated SV40-positive nuclei, indicative of active JC virus infection. Serum human immunodeficiency virus RNA polymerase chain reaction and human T-lymphotropic virus antibody testing were both negative. None of the subsequent laboratory tests showed any indicator of ongoing immunosuppression.

One-year follow-up visit demonstrated continued significant clinical deterioration of global aphasia with inability to follow commands, repeat words, or produce spontaneous speech. A third brain MRI performed 1 year after her initial presentation showed extensive bilateral white matter changes with progressive volume loss (Fig. 2).

Discussion

PML, a rare demyelinating disorder of the central nervous system, is typically suspected in patients with subacute neurological deficits that emerge in the setting of immunosuppression; it is exceedingly rare in immunocompetent patients, with only few cases reported to date [2–4]. This patient's positive anti-SSa/anti-Ro status and prior history of possible autoimmune vasculitis may have contributed to this patient's PML, as there have been reports of the disease in patients with a primary autoimmune disease, including Sjögren's [1]. However, most of these patients had received prior immunosuppressive therapy for their underlying diseases as their main PML risk factor [1,5]. Although this patient had history of possible Sjögren's-related vasculitis, along with positive anti-SSa/anti-Ro antibody during the hospital stay, she was not taking any immunosuppressants.

PML has been reported to occur in the setting of minimal or occult immunosuppression, such as with hepatic

cirrhosis or renal failure [6]. Our patient did not have any comorbid conditions that would be concerning for occult immunosuppression.

Interestingly, the initial MRIs of our patient showed only selective involvement of Broca's (left inferior frontal gyrus) and Wernicke's (left temporoparietal) areas, which presumably explained her worsening expressive and receptive aphasia.

In conclusion, PML is an extremely rare diagnosis and yet may be considered in an immunocompetent individual, if the patient displays symptoms, signs, and radiographic findings consistent with PML otherwise.

Patient consent

Informed consent was obtained from the patient.

REFERENCES

[1] Kartau M, Sipilä JO, Auvinen E, Palomäki M, Verkkoniemi-Ahola A. Progressive multifocal leukoencephalopathy: current insights. Degener Neurol Neuromusc Dis 2019;9:109.

[2] Rockwell D, Ruben FL, Winkelstein A, Mendelow H. Absence of immune deficiencies in a case of progressive multifocal leukoencephalopathy. Am J Med 1976;61(3):433–6.

[3] Fermaglich J, Hardman JM, Earle KM. Spontaneous progressive multifocal leukoencephalopathy. Neurology 1970;20(5):479–84. doi:10.1212/wnl.20.5.479.

[4] Tan IL, Koralnik IJ, Rumbaugh JA, Burger PC, King-Rennie A, McArthur JC. Progressive multifocal leukoencephalopathy in a patient without immunodeficiency. Neurology 2011;77(3):297–9. doi:10.1212/WNL.0b013e318225ab3f.

[5] Molloy ES, Calabrese LH. Progressive multifocal leukoencephalopathy: a national estimate of frequency in systemic lupus erythematosus and other rheumatic diseases. Arthritis Rheum 2009;60(12):3761–5. doi:10.1002/art.24966.

[6] Gheuens S, Pierone G, Peeters P, Koralnik IJ. Progressive multifocal leukoencephalopathy in individuals with minimal or occult immunosuppression. J Neurol Neurosurg Psychiatry 2010;81(3):247–54. doi:10.1136/jnnp.2009.187666.