

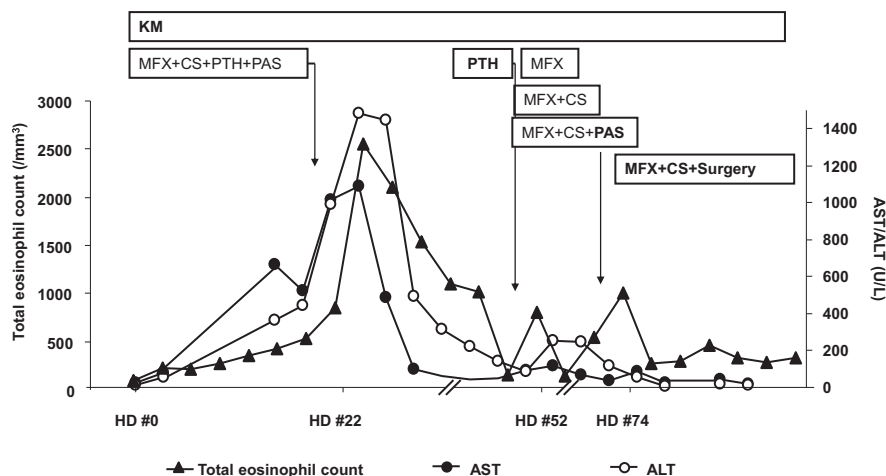


Figure 1. Clinical course, laboratory data, and re-challenge with second-line anti-tuberculosis drugs. AST, aspartate aminotransferase; ALT, alkaline aminotransferase; CS, cycloserine; HD, hospital day; KM, kanamycin; MFX, moxifloxacin; PAS, para-aminosalicylic acid; PTH, prothionamide; TEC, total eosinophil count.

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Persistent papilloma and polyoma virus infection in common variable immunodeficiency with progressive multifocal leukoencephalopathy

Common variable immunodeficiency (CVID) is a heterogeneous syndrome in which the main characteristic is hypogammaglobulinemia and impaired specific antibody responses with both B- and T-lymphocyte involvement.¹ Progressive multifocal leukoencephalopathy (PML) is an opportunistic demyelinating disease of the central nervous system caused by John Cunningham (JC) virus, a member of polyoma group DNA virus.² Any level of the central neuraxis may be affected, but the cerebral hemispheric white matter is the most common site, followed by cerebellar and bulbar localization.³ A study based on national inpatient diagnosis codes analyzed 9,675 PML cases from 1998 to 2005, including 82% with HIV, 8.4% with hematologic cancers, 2.83% with solid organ cancers, and 0.44% with hematologic diseases.⁴ JC virus receptor is present in several organs, including kidney, epithelial cells, B lymphocytes, platelets and in the central nervous system on glial cells and neurons. Although PML usually affects individuals with profound cellular immunosuppression, it has also been diagnosed in patients with no initial clinically apparent immunosuppression.⁵ PML is uncommon in CVID patients.⁶ Narula⁷ reported a 40-year-old man with CVID and PML and abnormal CD8 +T-cell subset,⁷ and Snyder⁸ reported a 21-year-old man with CVID and PML.

We describe a 29-year-old woman with CVID who underwent splenectomy because of thrombocytopenia and who was affected by JC virus–associated PML, and, despite progressive disease, CD4 and CD8 numbers remained normal, before and after PML.

Case Report

We describe a 29-year-old woman with a history of recurrent sinopulmonary infections since 3 y/o age. She developed splenomegaly and thrombocytopenia at 7 y of age. Bone marrow examination showed no significant abnormality. Splenectomy was performed at 9 years of age because of refractory thrombocytopenia. Immunologic studies showed only undetectable serum immunoglobulin A (IgA); hence, selective IgA deficiency was considered.

She developed 2 episodes of meningitis at 15 and 18 years of age, and, according to further work ups, CVID diagnosed. Immunologic findings are shown in Table 1. IVIG (Intratec, Manufactured from Iranian plasma farma GmbH, Germany, ordered by I.B.R.F) 400 mg/Kg was infused monthly since 18 y-o age which resulted in decreased frequency of sinopulmonary infections. She was referred to our allergy and immunology ward at 22 y of age because of multiple large palmar and plantar planar warts. Immunologic assays, including screening tests for humoral and cellular immunity, revealed normal results of the lymphocyte transformation test with phytohemagglutinin and candida and also normal values of delayed type hypersensitivity with candida and purified protein derivative but antibody response before and after vaccination failed to perform. Rheumatologic assays were within normal limits.

Results of imaging studies, including abdominal sonography and High Resolution Computed Tomography of the chest, were normal. Pulmonary function test revealed reversible obstructive airway disease. She experienced 1 episode of left knee septic arthritis. The patient remained well until 14 months ago, when she developed

Table 1
Immune System Screening Results

Test	First evaluation Age 9 years	Second evaluation Age 18 years	After PML Age 29 years
CD19	^a	8.7	9
CD4	^a	59.6	53.8
CD8	^a	28.4	24
CD16	^a	5.3	9.7
CD56	^a	6	7.8
IgA	0	Undetectable	Undetectable
IgG	980 mg/dL (6 y–adult 700–160 mg/dL)	246 mg/dL (6 y–adult 700–1,600 mg/dL)	640 mg/dL ^b
IgG1	^a	176 mg/dL (Adult 280–1,740 mg/dL)	496 mg/dL (adult 280–1,740 mg/dL)
IgG2	^a	78 mg/dL (adult 80–550 mg/dL)	155 mg/dL (adult 80–550 mg/dL)
IgG3	^a	16 mg/dL (adult 22–320 mg/dL)	19 mg/dL (adult 22–320 mg/dL)
IgG4	^a	3 mg/dL (adult 10–170 mg/dL)	8 mg/dL (adult 10–170 mg/dL)
IgM	55 mg/dL (6 y–adult 56–325 mg/dL)	21 mg/dL (adult 56–352 mg/dL)	98 mg/dL (adult 56–352 mg/dL)
IgE	^a	1.6 IU/mL	2.5 IU/mL
Iso	^a	1/8	1/16
hemagglutinin titer			
HIV1-2	^a	Negative	Negative
LTT (PHA)	^a	^a	>4.1 SI (NL range >3.5)
LTT(<i>Candida</i>)	^a	^a	>4.8SI (NL range >2.5)
DTH (PPD)	^a	^a	6 mm (NL range >5 mm)
DTH (<i>Candida</i>)	^a	^a	11.5 mm (NL range >10 mm)
ANA	^a	^a	Negative

Abbreviations: ANA, antinuclear antibody; IVIG, intravenous immunoglobulin; LTT, lymphocyte transformation test; PHA, phytohemagglutinin A; PML, progressive multifocal leukoencephalopathy; PPD, purified protein derivative; SI, stimulated index.

^aWe visited this patient at 22 years of age. Unfortunately, we do not have her previous results.

^bUnder IVIG.

mild dysarteria and fine motor abnormalities. Brain magnetic resonance imaging initially revealed mild cerebellar atrophy, but her condition deteriorated progressively and significant ataxia terminally led to a completely bedridden state. She developed slurred and distorted speech and also oculomotor apraxia. A second magnetic resonance imaging scan showed mild generalized cortical

atrophy and significant atrophy in the left cerebellar hemisphere and ill-defined focal enhancement in the left temporal lobe. Cerebrospinal fluid analysis was normal, with the exception of JC virus polymerase chain reaction. PML was confirmed according to radiographic and clinical findings and positive polymerase chain reaction results for JC virus. Further immunologic findings are shown in Table 1.

CVID is known to be a predominantly humoral immunodeficiency state. Viral infections can be problematic in CVID, although bacterial infections are a more prominent issue; CVID is not just a humoral response issue and involves a variety of immune surveillance and immunoregulatory abnormalities leading to enhanced malignancy risk and increased autoimmunity; these other aspects of CVID are likely causal if JC responses are impacted, leading to PML.

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Mannose-binding lectin deficiency in a patient with multiple opportunistic infections, strongyloidiasis, and spindle cell tumor

Mannose-binding lectin (MBL) plays an integral role in innate immunity through complement activation by the lectin pathway facilitating pathogen phagocytosis. Heterozygous or homozygous mutations of the *MBL2* gene may result in low levels of MBL.^{1,2} This predisposes one to a variety of infections with viruses,³ bacteria, protozoa, and fungi as well as malignancies (Table 1).⁴ Homozygous mutations of the *MBL2* gene also have been linked to

mycobacterial infections. We report a novel association between MBL deficiency and strongyloidiasis, aspergillus mycetoma, and spindle cell tumor.

A 66-year-old Hispanic man presented to our Allergy/Immunology clinic with complaints of nasal congestion and difficulty breathing for 2 years. His symptoms had been refractory to previous intranasal steroids, multiple antibiotic courses, and antihistamines. His medical history was notable for a spindle cell tumor and several opportunistic infections, including a pulmonary *Mycobacterium*