Rituximab for Primary Angiitis of the Central Nervous System: Report of 2 Patients from the French COVAC Cohort and Review of the Literature

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To the Editor:

Primary angitis of the central nervous system (PACNS) is a rare and severe inflammatory disease affecting the vessels of the brain and sometimes spinal cord. Diagnosis relies on (1) a neurologic deficit that remains unexplained after complete examination; (2) CNS vascular abnormalities on conventional cerebral angiography (CCA) or histopathology; and (3) the exclusion of other differential diagnoses such as reversible cerebral vasoconstriction syndrome or systemic vasculitides. Neurologic manifestations usually worsen or relapse in the absence of treatment. Corticosteroids are the cornerstone of therapy and with severe disease are often combined with an immunosuppressant, mainly cyclophosphamide (CYC). Few patients are refractory to this treatment and/or relapse. To date, only limited information exists on potential rescue and alternative treatments, including rituximab (RTX).

We describe 2 adult patients with PACNS who showed improvement with RTX and corticosteroids.

**Case 1.** In a 42-year-old man, progressive cerebellar ataxia developed over a couple of months; then left hemiparesis and binocular diplopia developed. Brain magnetic resonance imaging (MRI) revealed multiple lesions of the cortical and deep subcortical white matter, thalami, cerebellum, and cervical spine. Most lesions and meninges were enhanced after gadolinium injection (Figures 1A, B). Cerebrospinal fluid (CSF) examination revealed protein concentration 600 mg/l and leukocyte count 60/mm³. An open-wedge biopsy revealed a vascular wall lymphocytic infiltrate (Figure 1C). Complete examination (Table 1) was negative for differential diagnoses. Oral prednisone (70 mg/day) was administered with

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**Figure 1.** Images for Patient 1. (A, B) Magnetic resonance imaging (MRI) gadolinium-enhanced T1 sequences of brain and cervical spinal cord, respectively, showing lesions in cerebellar lobes as well as vermis, pons, subcortical white matter of anterior temporal lobes and cervical spine at C2 and C4 levels (arrows). C. Histopathology findings of brain biopsy (immunohistochemical staining of CD4+ and CD20+ cells) showing a lymphocytic infiltrate, predominantly CD4+ T cells, of the vessel wall. Staining for amyloid deposits was negative. D. MRI gadolinium-enhanced T1 sequence of brain demonstrating a reduced number of lesions after treatment with rituximab.
Table 1. Investigations performed in our 2 patients diagnosed with primary angiitis of the central nervous system.

<table>
<thead>
<tr>
<th>Category</th>
<th>Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard laboratory tests</td>
<td>Complete blood count, blood electrolytes, serum creatinine level, liver tests, C-reactive protein level, blood coagulation tests, serum protein electrophoresis, thyroid-stimulating hormone level, urine analysis.</td>
</tr>
<tr>
<td>Immunological tests</td>
<td>Antinuclear antibodies, anti-dsDNA antibodies, antineutrophil cytoplasm antibodies, antidermatolipin antibodies, lupus anticoagulant screening, antiphospholipid antibodies, rheumatoid factor, complement exploration (C3, C4, CH50)</td>
</tr>
<tr>
<td>Infection screening tests</td>
<td>Blood: Hepatitis B and C virus, HIV, cytomegalovirus, Epstein-Barr virus, toxoplasmosis, Q fever, syphilis, borreliosis, rickettsiosis including Lyme Cerebrospinal fluid: PCR for herpes simplex virus and varicella-zona virus, culture</td>
</tr>
<tr>
<td>Other investigations</td>
<td>Whole-body CT, duplex carotid ultrasonography, transthoracic echocardiography, FDG-PET scan for patient 1, somesthetic evoked potentials for patient 1</td>
</tr>
</tbody>
</table>

RTX was given (375 mg/m²/week for 4 weeks), followed by azathioprine. Monthly intravenous CYC, but at 5 months, ataxia and upper-limb paresis worsened and the number of lesions on repeat MRI had increased. Neurological status improved 1 month after RTX completion, with reduced paresthesia and ataxia. Repeat brain and spine MRI showed fewer lesions (Figure 1D), without relapse at the 12-month followup post-RTX.

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REFERENCES

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