



# Headache, Bilateral Carotid Stenosis, and Hypoglossal Palsy Revealing Granulomatosis with Polyangiitis: An Innovative Application of Vessel-Wall MRI

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Dear Editor,

Granulomatosis with polyangiitis (GPA) is a systemic small-vessel anti-neutrophil cytoplasmic antibodies (ANCA)-associated vasculitis. The most-frequent manifestations of GPA in the central nervous system (CNS) are lymphocytic meningitis and the involvement of multiple cranial nerves.

A healthy 54-year-old female patient presented with unusual left-sided headache with a 2-month history, which responded to corticotherapy administrated for bilateral serous otitis media, although causing slight hypoacusia. A neurological examination revealed left-sided tongue palsy. Blood tests revealed an elevated erythrocyte sedimentation rate of 92 mm/h, thrombocytopenia ( $370 \times 10^3/\text{mm}^3$ ), and positivity for anti-PR3 c-ANCA antibodies. Magnetic resonance angiography showed bilateral superior cervical stenosis and initial petrous-segment stenosis associated with an infiltrative process in the upper cervical perivascular spaces and leptomeningitis in contrast-enhanced sequences (Fig. 1A and B). Vessel-wall MRI (VW-MRI) sequences (3D T1-weighted turbo spin echo with variable angle before/after contrast) confirmed the presence of an infiltrating posterior parapharyngeal process in the upper cervical perivascular space encasing the carotids (Fig. 1C and D), but without plaques with typical eccentric and focal gadolinium enhancement suggestive of atherosclerosis. The integrity of the VW and the absence of methemoglobin and pseudoaneurysms did not support bilateral carotid dissection, while the presence of an extravascular process compressing the vessels did not support reversible cerebral vasoconstriction syndrome. Only extracranial involvement (i.e., no carotid T abnormalities) excluded Moyamoya disease. The large size of the involved vessel and the past medical history allowed the reasonable exclusion of other etiologies such as drug- and radiation-induced vasculopathies.

(18)F-fluorodeoxyglucose positron-emission tomography revealed an asymptomatic pulmonary hypermetabolic nodule (Supplementary Fig. 1A and B in the online-only Data Supplement). The temporal artery histology was normal, and fibroscopy revealed granulomas and the presence of giant cells (positivity for CD68 and CD34 antibody staining) in the Eustachian tube (Supplementary Fig. 1C and D in the online-only Data Supplement). These findings supported a diagnosis of GPA according to the 2017 European League Against Rheumatism Criteria (nine items, with five or more needed for a diagnosis). Unilateral headache and bilateral carotid stenosis with an inflammatory state could have evoked giant-cell arteritis (GCA), but VW-MRI showed a granulomatous infiltrate encasing carotids but no vasculitic process of the large vessels like in GCA.

The patient was treated by high-dose corticotherapy (initially 1 mg/kg/day orally, tapered to 0.4 mg/kg/day by month 3, and 5 mg/kg/day by month 15) and intravenous cyclophosphamide (15 mg/kg every 2 weeks for three doses followed by maintenance doses every

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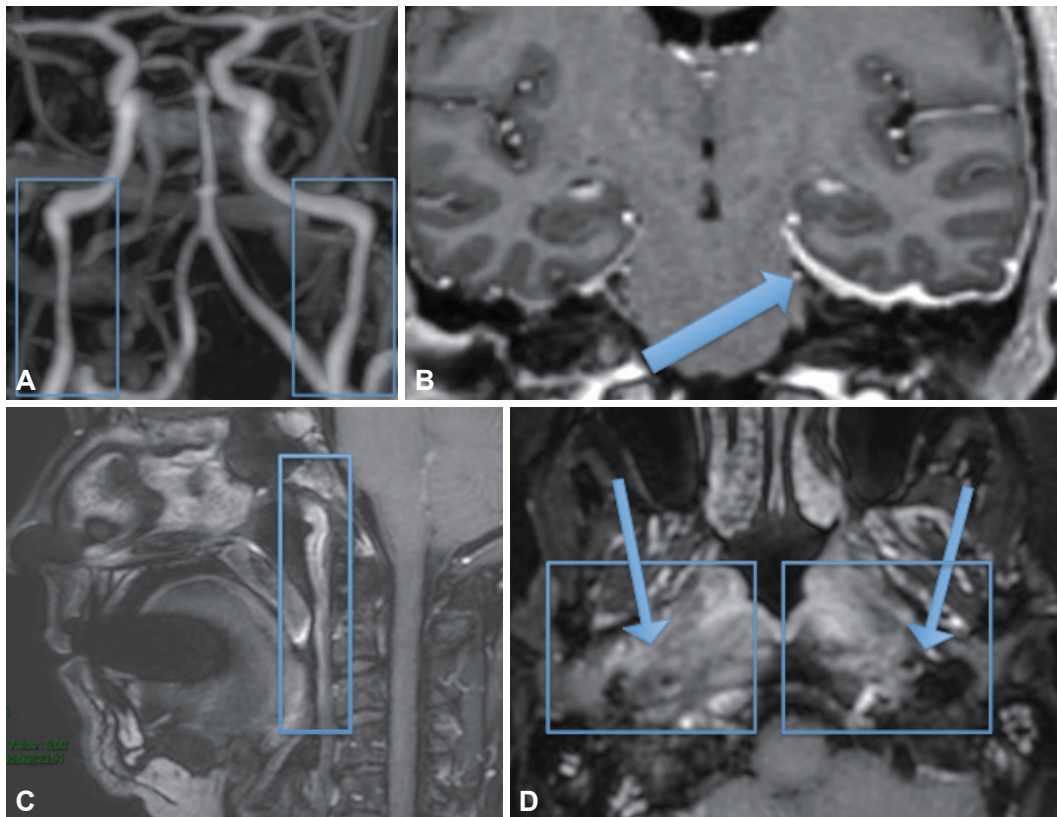
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**Fig. 1.** A: Magnetic resonance angiography showing bilateral superior cervical stenosis and initial petrous-segment stenosis (blue panels). B: Temporal lobe leptomeningitis in contrast-enhanced sequences (blue arrow). C and D: 3D T1-weighted turbo spin echo with variable-angle sequence confirms an infiltrating posterior parapharyngeal infiltrative process in the upper cervical perivascular space encasing the carotids (coronal-panels-and transverse views-panels and arrows).

3 weeks). This intervention led to partial remission after five pulses: the Birmingham Vasculitis Activity Score decreased from 6 to 4, the size of the cervical lesion decreased in VW-MRI, inflammatory markers normalized, and the titer of anti-PR3 c-ANCA antibodies decreased from 9.8 U/l to 3.6 U/l at the 3-month follow-up. Nevertheless, pachymeningitis and headache persisted. Rituximab was initiated (1 g on day 1 and 1 g on day 14), which resulted in complete remission with the resolution of pachymeningitis 3 years later.

The reported prevalence rate of neurological involvement in GPA has ranged from 22% to 54%.<sup>1</sup> It is mainly represented by peripheral neuropathy (10.6–28.6%)<sup>2</sup> rather than CNS involvement (7–11%)<sup>1</sup> or cranial nerve palsy (2–10%).<sup>2</sup> According to Drachman,<sup>3</sup> pathogenic mechanisms of CNS lesions include granulomatous tissue spreading from nasal or paranasal cavities and contiguously invading the CNS; remote granulomatous intracerebral lesions of the brain, meninges, cranial nerves, or parietal bones; and spinal cord or cerebral small-vessel vasculitis. In 30% of cases, CNS involvement may result from a combination of these three pathogenic mechanisms.<sup>3</sup> The pathogenesis of cranial neuropathies is often unclear, but a combination of vasculitic and local granulomatous processes

is supposed.<sup>4</sup> In our patient, a retropharyngeal granulomatous mass led to 12th cranial nerve palsy by continuity, in parallel with leptomeningitis causing stabbing headache, indicating that two GPA-related pathogenic mechanisms were present simultaneously. Although there are several series of frequent 12th cranial nerve involvement,<sup>5</sup> there has been only one case report of isolated 12th cranial nerve palsy in the setting of GPA,<sup>6</sup> which was due to an infiltrating retropharyngeal lesion causing syncope and tongue atrophy.

We defined the inflammatory nature of perivascular infiltrative lesion using VW-MRI, which is a noninvasive technique that is increasingly being used for discriminating between several intracranial vascular pathologies.<sup>7</sup> This technique makes it possible to explore the meninges, brain parenchyma, and VW enhancement simultaneously, thereby reducing the risks and inconvenience associated with digital subtraction angiography and biopsy. This is the first report of VW-MRI making a substantial contribution to detecting the extracranial involvement of GPA, and it highlights the potential role of VW-MRI in the differential diagnosis of vasculitis and during the follow-up period.

## Supplementary Materials

The online-only Data Supplement is available with this article at <https://doi.org/10.3988/jcn.2021.17.1.137>.

## Author Contributions

Conceptualization: Pasquale Scoppettuolo, Frédéric Vandergheynst. Data curation: Pasquale Scoppettuolo, Isabelle Delpierre, Serge Goldman. Formal analysis: Noémie Ligot, Gilles Naeije, Frédéric Vandergheynst. Methodology: Noémie Ligot, Isabelle Delpierre, Serge Goldman. Resources: all authors. Supervision: Gilles Naeije, Frédéric Vandergheynst. Validation: all authors. Visualization: all authors. Writing—original draft: Pasquale Scoppettuolo. Writing—review & editing: Gilles Naeije, Frédéric Vandergheynst.

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## Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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None

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