Large-vessel Involvement and Varicella Zoster Virus Vasculopathy in Giant Cell Arteritis–related Stroke: Something to Keep an Eye On

To the Editor:

We have read with great interest the original article written by de Boysson, *et al*[1]. This multicenter retrospective study highlighted the vasculitic-related risk of stroke in patients with newly diagnosed giant cell arteritis (GCA) and how it was related to ophthalmic ischemic impairment and to lower systemic inflammatory markers (i.e., lower acute-phase proteins level and lower risk of anemia) in comparison with GCA patients without stroke. Concerning this, in our cohort of 82 patients with a GCA diagnosis according to the 1990 American College of Rheumatology criteria, 6 (mean age at diagnosis 73.5 ± 8.89 yrs; 5 women, 83%) experienced stroke at GCA diagnosis (7.3%). In all these patients, GCA diagnosis was confirmed by temporal artery color Doppler sonography, demonstrating a ≥ 1 mm thick perivascular hypoechoic ring surrounding the main temporal arteries. In 2 of the patients, the temporal artery biopsy results were consistent with GCA. Half of them reported ophthalmic symptoms, such as amaurosis fugax and diplopia, and among these patients, one developed unilateral sight loss. Our data were consistent with and confirm de Boysson, *et al*'s brilliant analysis.

Considering the peculiar cranial localization of the vessel wall inflammation, the lower inflammatory variables and the higher hemoglobin levels, together with less frequent constitutional symptoms and/or polymyalgia rheumatica, we would be led to believe that these patients have a localized inflammation, or better, a different pattern of inflammation; the literature data seem to confirm the second hypothesis. Indeed, peculiar tissue cytokine profiles have been related to different disease patterns[2]. In confirmation of this, in 3 out of 4 patients (75%) with GCA-related stroke, 18F-fluorodeoxyglucose positron emission tomography demonstrated the presence of an occult large-vessel vasculitis. In the fourth patient, color Doppler sonography revealed the presence of a hypoechoic subclavian and axillary arteries wall thickening consistent with vessel inflammation.

Regarding the therapeutic approach, de Boysson, *et al* underlined the absence of standard recommendations for the treatment of GCA-related stroke. An intriguing finding during the past few years is that varicella zoster virus (VZV) infection could lead to GCA[3]. VZV is a known cause of cerebrovascular accidents, such as transient ischemic attack and stroke[3], and extracranial VZV could have a role in the GCA pathogenesis[4], even if it is not considered sufficient to trigger the disease alone[5]. VZV vasculopathy is a productive virus infection and therefore antiviral treatment with acyclovir is generally recommended[3]. According to Nagel, *et al*[6], additional antiviral treatment may confer benefit to patients with GCA whose temporal artery biopsies contain VZV antigen.

Although we do not have wide experience in this field, it could be interesting to analyze all the biopsy specimens from patients with GCA-related stroke, GCA patients without history of stroke, and from postmortem age-matched control individuals for VZV antigen and correlate its presence with a peculiar clinical manifestation pattern. Further, treatment trials should be performed to assess the usefulness of antiviral drugs.

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