Commentary

Angiitis of the central nervous system (ACNS) is a heterogeneous group of rare diseases that affect any age group and usually carry a grave prognosis. The first difficulty in diagnosing ACNS is its diverse clinical manifestations. There are neither pathognomonic clinical signs nor symptoms; the three most common clinical presentations are chronic or subacute headache, ischemic or hemorrhagic strokes and progressive encephalopathy (progressive cognitive impairment, psychiatric symptoms, seizures etc). In some cases of patients suffering from a known predisposing condition, inflammatory or other, the diagnosis can be easily attained but in most cases a complete work-up is indispensable in order to differentiate secondary from primary CNS angiitis (PACNS). In an excellent review on PACNS differential diagnosis, Birnbaum *et al*.[1] proposed the following general rules as a guide to the clinician:

- For patients less than 40 years, think of reversible vasoconstriction syndrome
- For patients older than 75, think of cerebral amyloid angiopathy
- When basal meningeal inflammation is detected on imaging, think of tuberculosis or mycosis
- Immunosuppressed patients (AIDS patients or under immunosuppressive treatment); exclude opportunistic infections and subacute bacterial endocarditis
- When inflammatory markers are elevated, think about cancer, generalized autoimmune disease or infection.

After a complete diagnostic panel that excludes all secondary causes of angiitis (for a complete list of possible differential diagnosis, a complete table can be

found in Néel *et al*.;[2] article in French but the table is accessible to English-speaking readers), PACNS emerges as a diagnosis of exclusion that can only be affirmed with certitude with a brain biopsy. Angiography has its role in diagnosis but there are reports not only of false-negative but also of false-positive results. It is a well-known fact that angiography tends to be less sensitive for small diameter arteries (less than 0.5 mm) and arteries with diameter smaller than 0.2 mm cannot be visualized; small-vessel vasculitis is therefore beyond its reach. Once considered highly specific, the finding of segmental stenosis and dilation of arteries has been also described in severe atherosclerosis, post irradiation angiopathy, infection and vasospasm and therefore should not considered pathognomonic.[3,4]

A brain biopsy remains the gold standard for diagnosis as it has been shown that in one in three patients suspected to suffer from PACNS, a biopsy proved a different diagnosis. It also has its limitations as one out of three biopsies did not provide a diagnosis.[5,6]

PACNS is a most challenging diagnosis. The present case by Bajaj *et al*.[7] highlights the main problems with diagnosing this detrimental but possibly treatable condition. Outside city context, where patients cannot be always easily followed, management is even more complicated. The authors should be praised for their persistence in obtaining brain biopsy results before reaching a diagnosis. A brain biopsy is certainly an invasive but usually necessary procedure in order to introduce an immunosuppressive treatment that is neither simple nor without side effects.[8] Since there are no randomized controlled trials for this rarely encountered disease, treatment recommendations come from expert opinion. Corticosteroids are first-line treatment with or without cyclophosphamide. Prognosis is not only dependent on disease progression but also on irreversible neurological sequelae before treatment initiation.

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