Thunderclap Headache Usually Not CNS Vasculitis

BY NANCY WALSH
New York Bureau

PARIS — A severe headache with near-instantaneous onset—a "thunderclap" headache—is likely to represent a reversible cerebral vasoconstrictive process rather than central nervous system vasculitis, Dr. Leonard H. Calabrese said at the annual European Congress of Rheumatology.

The reversible cerebral vasoconstriction syndrome (RCVS) has been associated with a variety of conditions, including pregnancy, head trauma, and exposure to drugs such as nasal decongestants, selective serotonin reuptake inhibitors, and cannabis.

"RCVS can be readily diagnosed if you understand the clinical picture, but despite remarkable progress in understanding this condition in the past 5 years, it is still misdiagnosed and mismanaged as CNS vasculitis," said Dr. Calabrese, who holds the R.J. Fasenmeyer Chair of Clinical Immunology at the Cleveland Clinic.

CNS vasculitis requires a brain biopsy for diagnosis, and treatment involves extended immunosuppression. Neither is typically necessary in RCVS.

The rapid-onset headache of RCVS, developing over 1-2 minutes, is the hallmark of the condition and can occur with or without other neurologic signs and symptoms. It is more common in women and often develops in the wake of sexual activity, exercise, coughing, or the Valsalva maneuver and is "the worst headache of the patient's life," he said.

Headache associated with CNS vasculitis, in contrast, is indolent and progressive and typically is associated with episodes of neurologic dysfunction.

Angiographic findings in the two conditions can be indistinguishable, with multiple areas of stenosis and beading, but the abnormalities are reversible, usually within 3 months, in RCVS.

In contrast, although few follow-up angiographic studies have been done in patients with CNS vasculitis, the data that exist suggest that resolution does not occur.

Analysis of spinal fluid is essential for the patient with thunderclap headache to rule out not only CNS vasculitis but also subarachnoid hemorrhage. The fluid should be within normal limits, with only a few cells and a little protein, Dr. Calabrese said.

"However, we do not advocate biopsy with the classic presentation of RCVS—female patients, pristine spinal fluid, and thunderclap headache," he said.

But if the pretest probability for RCVS is low and vasculitis seems more likely, with a more insidious onset of headache, abnormal spinal fluid, or other abnormalities such as elevated acute phase reactants, biopsy may be warranted.

The headache associated with RCVS can abate but may recur within a week or two, and unfortunately may be accompanied by stroke, seizures, or other sequelae, he said.

In one recent prospective series of 67 patients, complications included cortical subarachnoid hemorrhage in 22%, intracerebral hemorrhage in 6%, and reversible posterior leukoencephalopathy in 9% (Brain 2007;130:3091-4101). Treatment thus far has been guided by observational data and experience, because no trials of any therapy have been conducted. "Some patients have recovered with no treatment whatsoever, but we often use calcium channel blockers, in conjunction with glucocorticoids if stroke is present," he said.

The reason for using glucocorticoids in RCVS—which is not an inflammatory condition, but rather is thought to be an endothelial disease with increased expression of adhesion molecules—is that in experimental models of induced vasoconstriction, their use represents the most potent pharmacologic intervention, he explained. ■

No Need to Rule Out Cancers in Newly Diagnosed AAV

BY BRUCE JANCIN
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PARIS — Patients with newly diagnosed antineutrophil cytoplasmic antibody–associated vasculitis do not have an increased rate of underlying malignancies, according to the findings of a large Danish case-control study.

"The overall message of our study is that as a clinician you don't have to screen your patients with newly diagnosed [antineutrophil cytoplasmic antibody (ANCA)–associated vasculitis] for any underlying cancer on a routine basis," Dr. Mikkel Faurschou said at the annual congress of the European League Against Rheumatism.

"There has been speculation that cancer might somehow trigger the [ANCA-associated vasculitis]. Our conclusion is that we cannot confirm that. We don't believe that [ANCA-associated vasculitis] is sometimes a paraneoplastic condition," added Dr. Faurschou, a rheumatologist at the National University Hospital, Copenhagen.

He reported on 293 ANCA-associated vasculitis (AAV) patients and 2,930 age- and gender-matched controls. The comprehensive Danish Cancer Registry was used to gather data on the occurrence of cancer before the diagnosis of AAV or prior to the same date among controls.

Twenty-six AAV patients had one or more cancers diagnoses at any site prior to diagnosis of their vasculitis, as did 194 controls prior to their cutoff dates. These rates were statistically similar.

In analyzing specific cancer types, the Danish investigators found that only one type of malignancy—testicular cancer—was significantly more common in AAV patients than in controls. However, although the odds ratio of 6.4 sounds impressive, this amounted to a mere two cases in the AAV group, compared with three cases in controls. Given these small case numbers, coupled with the fact that neither of the cases of testicular cancer in AAV patients occurred within 2 years prior to diagnosis of the vasculitis, it's quite unlikely that the malignancies served as a direct trigger in the pathogenesis of the AAV, Dr. Faurschou explained in an interview.

Earlier studies citing an increased risk for internal malignancies and documenting the screening costs caused a stir in rheumatology circles.

The only type of malignancy that was detected more commonly within 2 years prior to diagnosis of AAV than in controls was nonmelanoma skin cancer. There were 5 cases in the AAV patients and 12 in controls during this time frame, for an odds ratio of 3.9. The finding suggests the possibility that ANCA-associated vasculitis and nonmelanoma skin cancer share a genetic predisposition is worthy of further investigation. Alternatively, it may be the case that AAV patients are somehow immunologically dysfunctional, since nonmelanoma skin cancer is known to be associated with immunodeficiency, the rheumatologist observed.

An earlier report by investigators at the University of Birmingham (England) concluded the risk of malignancy is increased prior to diagnosis of AAV and that cancer should be considered part of the differential diagnosis in patients presenting with AAV (Rheumatology 2004;43:1532-5).

Moreover, German investigators who found an increased rate of renal cell carcinoma in patients recently diagnosed with ANCA-associated vasculitis recommended routinely looking for internal malignancies in such patients (Ann. Rheum. Dis. 2004;63:1183-5). These two prior reports have caused a stir in rheumatology circles because of their assertion that an extensive and costly work-up using abdominal ultrasound, CT, and other tools to rule out cancer is warranted in AAV patients. ■