Antigen Level May Reflect CNS Vasculitis Activity

BY KATE JOHNSON

QUEBEC CITY — Levels of von Willebrand’s factor antigen have the potential to provide a sensitive, noninvasive way to monitor disease activity in children with vasculitis involving the central nervous system. Dr. Tania Cellucci and colleagues reported at the annual meeting of the Canadian Rheumatology Association.

Knowing that CNS vasculitis is an autoimmune condition that affects the blood vessel walls, Dr. Cellucci and her colleagues at Toronto’s Hospital for Sick Children reasoned that it might impact the release of von Willebrand’s factor (vWF) antigen. So they set out to explore vWF levels in 31 consecutive pediatric CNS vasculitis patients from diagnosis through 24 months of follow-up.

The single-center cohort study ran between June 1989 and October 2008. The median age of the patients at diagnosis was 9 years, and 52% were female.

Demographic, clinical, laboratory, imaging, and histologic data were examined at diagnosis and at regular intervals throughout follow-up. Disease activity was measured at diagnosis and every 3 months thereafter using the physician global assessment visual analog scale, and levels of vWF were also measured at these intervals.

Only 10% of the cohort had secondary CNS vasculitis, whereas the remainder had childhood primary angitis of the CNS (cPACNS), the researchers reported in their poster. More than half of the cohort (58%) had angiography-negative cPACNS, indicating small-vessel disease, whereas 32% had angiography-positive (large-vessel) cPACNS, which was divided evenly between the progressive and nonprogressive form.

As expected, abnormal levels of C-reactive protein (greater than 8 mg/L) and erythrocyte sedimentation rate (greater than 10 mm/h) were not consistent across the cohort at diagnosis, occurring in 20% and 55%, respectively. Leukocytosis (WBC greater than 10 x 10⁹/L) was present in 52%. Opening pressure on lumbar puncture (greater than 20 cm H₂O) was increased in 62%, and elevated cerebrospinal fluid protein (greater than 0.4 g/L) and cerebrospinal fluid leukocytosis (greater than 5 x 10⁶/L) were present in 54% and 72%, respectively.

Abnormal magnetic resonance imaging was the most consistent finding, occurring in 94% of the cohort, with vasculitis on brain biopsy present in 71% and abnormal CNS angiogram present in 42%, they reported.

Disease activity decreased significantly and consistently from diagnosis and treatment initiation throughout the course of the study (P less than .0001), reported the researchers, although patients with angiography-negative cPACNS had consistently higher disease activity over time.

At diagnosis, the mean physician global assessment score for all patients with cPACNS was 5.7 for those with angiography-negative disease, and 6.5 for those with positive angiography. By 6 months, the mean scores for the angiography-positive patients had dropped to 1.2, whereas the mean angiography-negative score was 3.3. At 12 months, the mean score for the angiography-negative group was 1.6 vs. 0.9 for the angiography-positive group. Finally, at 24 months, the mean score for the negative group was 2.1, and 0.03 for the positive group.

Mirroring disease activity scores, levels of vWF also decreased over time in all patients (P = .0084) and mirrored disease activity scores, although they were significantly different between subtypes of cPACNS (P = .0028), reported Dr. Cel- luci. The study demonstrates that vWF is a sensitive measure of disease activity, she said.

In the example of a stable patient who suddenly develops headaches or other symptoms, a vWF level could help us figure out whether these new symptoms are due to active disease,” said Dr. Cellucci, who is a fellow in pediatric rheumatology at the University of Toronto. “If vWF is now elevated—and the patient had a high vWF at diagno- sis—then this is consistent with a disease flare and we would not need to repeat the invasive tests. If it is normal, then this suggests the new symptoms are not due to disease flare,” she said. She did not define what an abnormal vWF level might be, explaining that “all lab reports state the normal ranges for their lab and so the physician will be able to determine whether the level is abnormal or not.”

Dr. Cellucci added that an elevated vWF level can also assist in the diagnosis of pediatric CNS vasculitis, but is not specific enough in isolation. Sympto- matic patients would still need invasive diagnostic tests, but an elevated vWF would be consistent with CNS vasculitis, thus guiding the clinician in ordering the work up, she said.

Disclosures: Dr. Cellucci had no conflicts of interest to report.