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VASCULAR DISORDERS

BRAIN BIOPSY IN CNS PRIMARY VASCULITIS

Clinical and neuropathological features of brain biopsies in 13 children diagnosed with angiography-negative, small vessel primary central nervous system angiitis (SVcPACNS) were characterized in a prospective cohort study at the Hospital for Sick Children, University of Toronto, Canada. Diagnosis was based on Calabrese criteria: 1) an acquired neurological deficit, 2) angiographic or histological evidence of cPACNS, and 3) no evidence of systemic vasculitides. Sites for lesional biopsies were identified by MRI. Nonlesional biopsies were sampled from the nondominant frontal lobe. The definition of SV vasculitis used for diagnosis of cPACNS required all of the following: 1) at least 2 layers of lymphocytes around vessel walls, 2) prominent endothelial cells in vessel walls, 3) neuronophagia, 4) parenchymal edema, and 5) no alternate diagnosis. Probable SVcPACNS required criteria (2) through (5). Patient ages ranged from 5 to 17 years. Presenting features included seizures (85%), headache (62%), and cognitive decline (54%). Elevated ESR and C-reactive protein, elevated CSF pressure and protein level, and moderate pleocytosis were frequent laboratory findings. EEG abnormalities included diffuse slowing and focal epileptiform discharges. MRI showed abnormalities attributable to cPACNS in 11 patients; 2 (15%) patients showed no evidence of vasculitis. Brain biopsy confirmed SVcPACNS diagnosis in 11 patients showing intramural lymphocytic infiltrate. Six nonlesional biopsies were also diagnostic. Lack of histological features correlated with delayed biopsy, prior steroids, or inadequate specimens.

Children presenting with new onset severe headaches, seizures, or cognitive decline should be considered for the diagnosis of SVcPACNS and brain biopsy. The biopsy should be collected before prolonged treatment with steroids. Histological features consistent with SVcPACNS include lymphocytic intramural inflamatory infiltrate, surrounding gliosis, and reactive endothelial cells. Absence of intramural infiltrate does

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not rule out the diagnosis and treatment with immunosuppression. (Eibers J, Halliday W, Hawkins C, Hutchinson C, Benseler SM. Brain biopsy in children with primary smallvessel central nervous system vasculitis. **Ann Neurol** Nov 2010;68:602-610). (Respond: Dr Benseler, Division of Rheumatology, Dept Paediatrics, Hospital for Sick Children, University of Toronto, 555 University Ave, Toronto, Ontario, M5G 1X8, Canada. Email: susanne,benseler@sickkids.ca).

COMMENT. PACNS is an immune-mediated, acquired inflammatory disease involving either small or large CNS blood vessels. In children, the disease may present acutely with seizures and refractory status epilepticus, subacutely with focal neurological deficits, or chronically with headaches and cognitive decline. In an editorial, Hunder GG and Brown RD Jr of the Mayo Clinic, Rochester, MN, and Salvarani C of Italy question whether childhood PACNS is a single disease entity. (Ann Neurol 2010;68:73-574). They report 8 adult cases with similar findings to those in children, except in adults, focal neurological abnormalities occur in all 8 (only 2 of 13 in children), seizures are absent, and ESR is normal. (Salvarini C et al. Medicine (Baltimore) 2008;87:264-271). Histological findings are also different in adult cases. Small vessel PCNSV in adults is less clearly defined than in children.

Diagnosis of cPACNS should be considered and brain biopsy performed in a child presenting with new-onset seizures, severe headaches, and cognitive decline, associated with elevated ESR, CSF pleocytosis and elevated protein, and MRI evidence of vasculitis.

PAROXYSMAL DISORDERS

COURSE OF ALTERNATING HEMIPLEGIA OF CHILDHOOD

The natural history and long-term outcome of alternating hemiplegia of childhood (AHC) was studied by questionnaire within a large cohort of 157 patients, as part of the European Network for Research on Alternating Hemiplegia (ENRAH) project. The study was largely retrospective and, for 2 years, prospective. Patients were aged from 9 months to 52 years at time of inclusion. Median age at diagnosis was 20 months. All had hemiplegic attacks, 91% had abnormal ocular movements, 86.5% reported episodes of bilateral weakness, 88% tonic/dystonic attacks, 53% epileptic seizures, 72% had chorea, and 92% mental retardation. Premonitory signs or aura were reported in 41% patients, and sleep inhibited attacks in the majority (83%) of cases. A relaxing environment (music, massage) had a beneficial effect. Children with abnormal ocular movements and hypotonia improved in adulthood, whereas the severity of other symptoms in the whole cohort did not change over the course of the illness. Gait was unsteady in 84%, and school attendance and employment were severely impacted. Seven patients died, some during severe plegic attacks or seizures. Severe hemiplegic/dystonic attacks did not increase risk of poor outcome. The natural history of AHC in individual patients was highly variable and fluctuating and, as a group, did not indicate a progressive and degenerative course. Risk of sudden death in a minority was associated with more severe neurological impairment. Various treatments were employed, all receiving flunarizine as