HEADACHE DISORDERS

LANGERHANS CELL HISTIOCYTOSIS AND FRONTAL HEADACHE

A most recent case record of the Massachusetts General Hospital involved a clinicopathological presentation of a 15-year-old boy admitted with frontal headache, right retro-orbital pain, and a retro-orbital mass that proved to be a Langerhans' cell histiocytosis involving the right sphenoid sinus and orbit. Episodes of pain and headache began 3 weeks before admission and occurred two or three times weekly, lasted one or two hours, were not associated with photophobia or vomiting, and were relieved by ibuprofen. Eight days before admission he had visual impairment in the right eye, and diplopia provoked by looking down and to the left, a trochlear nerve and superior oblique muscle lesion. MRI showed an enhancing right retro-orbital mass that extended into the right sphenoid, posterior ethmoid and right cavernous sinuses, and involved the internal carotid artery. CT revealed a destructive lesion in the right sphenoid bone and optic canal. Visual acuity was 20/100 in the right eye, the optic disks were normal, and downward gaze was impaired in the right eye. A biopsy of the sphenoid sinus revealed aggregates of histiocytic cells and numerous eosinophils. Immunohistochemistry of histiocytes for CD1a was positive and confirmed a Langerhans' cell histiocytosis, with intracytoplasmic Birbeck granules. Treatment with dexamethasone was immediately beneficial, and following the diagnostic biopsy, stereotactic radiation therapy was used for 6 weeks, with improvement in double vision and control of headaches. Differential diagnoses suggested were neoplasm, possible eosinophilic granuloma, and non Hodgkin's lymphoma, probably T-cell or lymphoblastic lymphoma. (Harris NL et al. Clinicopathological exercise, MGH case record. Langerhans' cell histiocytosis and retro-orbital mass. N Engl J Med February 14, 2002;346:513-520).

COMMENT. Langerhans'-cell histiocytosis may present with headache and neurologic symptoms and signs of a mass lesion involving the sphenoid sinus and orbit, without other systemic manifestations.

MIGRAINE AND AUTONOMIC NERVOUS SYSTEM DYSFUNCTION

Tests of autonomic nervous system (ANS) function were administered to 80 adult patients with migraine (28 with disabling headaches) and 85 matched controls, in a study at the Thomas Jefferson University Hospital, Philadelphia, PA, Johns Hopkins School of Hygiene and Public Health, Albert Einstein College of Medicine, and Montefiore Medical Center, Bronx, NY. During headache-free intervals, resting diastolic, but not systolic, blood pressure was elevated in migraineurs with disabling headaches compared to nondisabled patients and controls. Pulse rate variability during deep breathing, and the Valsalva maneuver ratio, a measure of change in heart rate, were significantly lower in disabled migraineurs cf nondisabled and controls. Blood pressure response to psychological stress was not different in the 3 groups. Migraineurs with disabling headaches may be susceptible to impaired autonomic nervous responses. The link between migraine and abnormal autonomic function is unclear. The dysfunction of the ANS may increase the tendency to headaches by lowering the threshold to migraine triggers. (Shechter A, Stewart WF, Silberstein SD, Lipton RB. Migraine and autonomic nervous system function. A population-based, case-control study. Neurology February (1 of 2) 2002;58:422-427). (Reprints: Aaron Shechter, Jefferson Headache Center, Department of Neurology, Thomas Jefferson University Hospital, 111 S 11th

Street, Suite 8130, Philadelphia, PA 19107).

COMMENT. Autonomic symptoms, including nausea, vomiting, diarrhea, pallor, flushing, and diaphoresis, are common during acute migraine headaches. Studies of autonomic nervous system (ANS) function provide variable results, some suggesting hypofunction, some hyperfunction, and some a dysregulation, the result of an imbalance of sympathetic and parasympathetic nervous sytems in migraine. The present results favor a hypofunction of the ANS in adult migraineurs, and a lowering of the threshold to migraine triggers is proposed as one possible mechanism. The degree of ANS dysfunction is related to the severity and disabling nature of the headaches.

In children with migraine equivalents, recurrent abdominal pain and cyclical vomiting are symptoms of autonomic nervous system dysfunction. Typical migraine headaches may coexist and often develop in adolescence and adulthood. The degree of nausea and vomiting exacerbates the disability of migraine sufferers and influences the route of administration of medications. (see Progress in Pediatric Neurology III, PNB Publishers, 1997;pp176-178).

SEIZURE DISORDERS

DRUG RESISTANCE PROTEINS AND REFRACTORY EPILEPSY

Expression of multi-drug resistance gene-1 P-glycoprotein (MDR1) and multidrug resistance-associated protein 1 (MRP1) in refractory epilepsy was studied at the Epilepsy Research Group, Institutes of Neurology and Child Health, University College, London, and Radcliffe Infirmary, Oxford, UK. The epilepsy causes were dysembryoplastic neuroepithelial tumors (DNTs) in 8 cases, focal cortical dysplasia (FCD) in 14, and hippocampal sclerosis (HS) in 8. Lesional tissue from therapeutic resections was compared immunohistochemically with normal adjacent tissue. Reactive astrocytes in pathological tissue expressed MDR1 and MRP1 in all DNT and FCD cases,.and in 5 of 8 HS cases. In 5 FCD cases, dysplastic neurons also expressed MRP1. Accentuation of reactivity was noted around lesional vessels in FCD and DNTs. MDR1 and MRP1 may transport antiepileptic drugs (AED), and the overexpression of these drug resistance proteins in lesional tissue from patients with refractory epilepsy may lower the interstitial concentration of AEDs in epileptogenic lesions, a possible explanation for the mechanism of drug resistance. (Sisodiya SM, Lin W-R, Harding BN, Squier MV, Thom M. Drug resistance in epilepsy: expression of drug resistance proteins in common causes of refractory epilepsy. Brain January 2002;125:22-31). (Respond: Dr SM Sisodiya, Epilepsy Research Group, Institute of Neurology, University College London, Queen Square, London WC1N 3BG, UK).

COMMENT. MDR1 and MRP1, known mediators of AED resistance, may be demonstrated in epileptogenic tissue glia from refractory epilepsy patients, and also in some lesional dysplastic neurons in FCD. These drug resistance proteins are absent in normal human glia and normal neurons. The overexpression of these drug resistance proteins in epileptogenic tissue is an explanation for the refractory epilepsy, and a possible target for the development of new AEDs.

The distribution of glutamate transporters (EAATs) in the hippocampus of patients with AED resistant temporal lobe epilepsy has been studied at University Medical Center, Utrecht (Proper EA et al. Brain Jan 2002;125:32-43). Decreases in EAAT1 and EAAT2-immunoreactivity (IR) were observed in CA4 and dentate gyrus of hippocampal sclerosis cases, and increased EAAT2-IR in the non-HS group.