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TUMORS OF THE NERVOUS SYSTEM:

NEUROFIBROMATOSIS

The diagnostic criteria, associated problems, genetics, pathogenesis, clinical evaluation and treatment of neurofibromatosis type I in childhood are reviewed from the Department of Pediatrics, Northwestern University Medical School and Children's Memorial Hospital, Chicago, Illinois. The National Institutes of Health Consensus Development Conference identified seven components of the syndrome, two or more required for the diagnosis: 1) six or more cafe au lait macules, 2) two or more neurofibromas or one plexiform neurofibroma, 3) freckling in axillary or inguinal region, 4) optic glioma, 5) two or more Lisch nodules, 6) osseous lesion such as sphenoid dysplasia or pseudoarthrosis and 7) a first degree relative with NF-1. Other malignancies that occur in association with NF-1 include neurofibrosacroma, leukemia, xanthogranulomas, neuroblastoma, rhabdomyosarcoma and Wilms tumor. The full scale IQ is relatively low, but usually within the normal range. A visual perceptual disability occurs in 60 to 90% of the patients. The degree of intellectual deficit increases in direct proportion to the clinical severity. NF-1 and the Noonan syndrome may occur together. The localization of the NF-1 gene to chromosome 17 and the identification of linked markers has opened the door to prenatal and presymptomatic diagnosis of NF-1 and linkage analysis will soon be possible in families in which there are two or more affected members. Nearly 50% of persons with NF-1 do not have an affected parent and 50% are new mutations. Neurocristopathy, a generalized disorder of cells of neural crest origin, is the hypothesis for pathogenesis of NF-1. Histamine containing mast cells are found in high concentrations in peripheral neurofibromas and may be a factor in promotion of neurofibroma growth.

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Screening for optic gliomas by MRI is justified because of a high incidence (15%). Radiation therapy is the standard approach for optic glioma in children older than 5 years. Adverse effects include hypopituitarism, growth failure, cognitive deterioration, cataracts and secondary malignancies. Chemotherapy, if proven effective, would be preferable. Many optic gliomas are nonprogressive. Hormone treatment for precocious puberty associated with optic glioma may be efficacious. Related neurofibromatosis syndromes include neurofibromatosis type 2, segmental neurofobromatosis and familial cafe-au-lait spots. Patients with multiple cafe-au-lait spots may not have any of the other stigmata of NF-1. The gene for neurofibromatosis type 2 with bilateral acoustic neurofibromatosis has been linked to chromosome 22. (Listernick R., Charrow J. Neurofibromatosis Type I in childhood. J Pediatr June 1990; 116:845-853).

COMMENT: To this excellent review of NF-1 we may add a note concerning the simultaneous occurrence of neurocutaneous syndromes and a first report of a case of NF-2 and tuberous sclerosis in the same patient.

Neurofibromatosis I and tuberous sclerosis may occur simultaneously. This association is rare and the report by Schull and Crowe (Neurology 1953; 3:904-909) is the only case accepted by Gomez M (Tuberous Sclerosis, Raven Press, New York, 1988). Two patients reported by Vouge M et al (Neuroradiology 1980; 20:99-101) had clinical manifestations of neurofibromatosis I and also subependymal or intranuclear calcifications in the brain identical to the tubers of tuberous sclerosis.

I have recently evaluated a 14 year old girl with the simultaneous occurrence of neurofibromatosis type 2 and tuberous sclerosis. She presented with flaccid weakness and wasting of the left upper limb and electromyographic evidence of brachial plexopathy affecting primarily the upper and middle trunks. Examination of the skin showed a large depigmented patch over the right deltoid region, a small shagreen patch over the left lumbar region and a large pigmented area under the left axilla. The diagnosis of tuberous sclerosis was based on the skin lesions and typical calcifications shown in the CT scan of the head. The child had one seizure within 24 hours of a booster DPT immunization at 18 months. The diagnosis of neurofibromatosis type 2 was suggested by an MRI of the cervical spine showing enlargement of neural foramina C5-6 on the left side and was confirmed by a gadolinium MRI performed by Dr. Gomez at the Mayo Clinic. He also uncovered a right acoustic neuroma and a small meningioma at the level of C1. The weakness and wasting of the left arm was explained by a plexiform neurofibroma. In addition the patient had a familial macular degeneration. She had inherited the neurofibromatosis from her father who had bilateral acoustic neuromas and other neurofibromata. No one in the family

was known to suffer from tuberous sclerosis and examination of the mother was negative (Millichap J G, Gomez MR Neurofibromatosis II and tuberous sclerosis: Simultaneous occurrence in a 14 year old girl Ped Neur Briefs 1990;4:50-51).

EPIDERMOID TUMORS

Six patients with histologically proven epidermoid tumors are reported from the neurosurgical service, Brigham and Women's Hospital and Children's Hospital, Harvard Medical School, Boston, Mass. All patients were adults between 22 and 52 years of age at the time of diagnosis. Symptoms had been present for more than one to five years and the methods of presentation included seizures in two, ataxia (3), headaches (3), dysmetria (3), left-sided hearing loss (1), visual loss (1) and papilledema (1). The locations of the tumor were variable; cerebellar hemisphere in two, left temporal lobe (2), left cerebral hemisphere (1) and suprasellar cistern (1). Surgery was successful in all patients. None had symptoms related specifically to the tumor in childhood; one had been treated for bulimia for 17 years and another had meningitis at ten years of age. CT demonstrated a hypodense, smoothly contoured, extra axial paramedial mass with a lower density than cerebrospinal fluid. MRI showed an irregularly, but sharply marginated, mass with homogeneous density, variable enhancement with gadolinium, lack of edema in adjacent normal structures, extensive insinuation into cisternal and other cerebrospinal fluid spaces and a high signal intensity on proton-weighted images. Multiplanar magnetic resonance imaging was extremely helpful in showing the full extent of the lesion and its relation to other structures (Panagopoulos K P et al. Intracranial epidermoid tumors. A continuing diagnostic challenge Arch Neurol July 1990; 47:813-816).

COMMENT: Epidermoid, adamantinoma, cholesteatoma, and pearly tumor are terms used interchangeably to refer to this entity. Epidermoid tumors are congenital and arise from misplacement of ectoderm. They are usually benign and slow growing but malignant change may occur. The tumors may be very large at the time of diagnosis, with considerable mass effect but minimal edema. The MRI allows the distinction of an epidermoid from an arachnoid cyst. The MRI or CT is not diagnostic but the MRI is more likely to elucidate the extra axial-nature of the tumor and is preferred. Spinal epidermoid tumors may complicate a lumbar puncture performed 1 to 20 or more years previously. Symptoms are slowly progressive and manifested by back and leg pains progressing to gait difficulties. (Shaywitz BA. J Pediatr 1972; 80:638).

AV MALFORMATIONS: RADIATION THERAPY

Clinical and radiologic follow-up of 86 patients with symptomatic, but surgically inaccessible, cerebral arteriovenous malformations treated with stereotactic heavy charged particle Bragg-peak radiation is reported from the Divisions of Neurosurgery