

LHERMITTE-DUCLOS-COWDEN DISEASE

Two unrelated patients with clinical characteristics of both Lhermitte-Duclos disease and the autosomal dominant Cowden disease are reported from the Department of Neurology, University Hospital, Leiden, The Netherlands. Patient 1 was a mentally retarded woman with a large head, a high arched palate, dysarthria, mild cerebellar signs, and a single seizure at the age of 37 years. She also exhibited multiple papules on her nose, cheek, forehead and ears and on the oral mucosa. CT scan showed a nonenhancing mass in the cerebellar vermis and left cerebellar hemisphere, enlarged third and lateral ventricles, and a hypodense lesion in the centrum semiovale of the left cerebral hemisphere. A dysplastic gangliocytoma of the left cerebellar hemisphere was diagnosed at surgical resection of the tumor. Microscopic examination of skin biopsies showed trichilemmomas. Bilateral nonmalignant breast tumors were diagnosed at follow-up. The second patient had a history of tonic-clonic seizures in childhood, thyroid surgery at age 38 and he presented with cerebellar signs at 48 years of age. A dysplastic gangliocytoma was removed from the left cerebellar hemisphere. Skin lesions included papules on the face, limbs, and on the gingiva and tongue. Siblings of both patients showed the mucocutaneous lesions, thyroid disease, breast tumors, ovarian tumors, and also neurological signs including macrocephaly, mental retardation, seizures, tremor, and dysidiadochokinesia. The authors propose that Lhermitte-Duclos disease and Cowden disease are manifestations of a single phakomatosis. (Padberg GW et al. Lhermitte-Duclos disease and Cowden disease: A single phakomatosis. Ann Neurol May 1991; 29:517-523).

COMMENT. Lhermitte-Duclos disease (dysplastic gangliocytoma of the cerebellum) may present in infancy or childhood but the onset of symptoms is more usually delayed until adulthood when a slowly progressive cerebellar syndrome with hydrocephalus is a frequent complication. The characteristic skin lesions of Cowden disease are multiple facial trichilemmomas; hamartomas of other organs, including breast and ovary, occur frequently. Macrocephaly may be an early finding, and the present report suggests that neurological complications of Cowden disease may be under-reported.

VON HIPPEL-LINDAU DISEASE: FAMILIAL SYMPTOM CLUSTERS

The clinical manifestations and prevalence of von Hippel-Lindau syndrome (HLS) were reported from the Department of Medicine, Albert-Ludwigs-Universitat, Freiburg im Breisgau, Germany, and Department of Pathology, University of Zurich, Switzerland. A striking familial clustering of HLS lesions was discovered: angiomatosis retinae in 51% (47/92), haemangioblastoma of the CNS in 46% (42/92), renal lesions in 33% (30/92) and phaeochromocytoma in 24% (22/92). Of the 92 patients, 52 had 1, 31 had 2, and 9 had 3 of the 4 HLS lesions. Of 29 evaluated kindreds, 18 had renal lesions. Some features of HLS were frequently combined whereas others seemed to be almost exclusive. The patterns of lesions within individual kindreds were stable.

Vascular lesions of the syndrome (angiomas of retinae and haemangioblastoma of the CNS) occurred in most families and represented core features whereas pheochromocytoma at one end of the scale, and renal lesions, pancreatic cysts and epididymal cystadenoma at the other end of the scale, were unlikely to develop in the same family and were mutually exclusive. The authors suggest that HLS is caused from different mutations within a complex genetic locus, or additional genetic lesions, which cooperate with the HLS gene on chromosome 3p. The data point to a linear sequence of features. The calculated prevalence of the disease in the district of Freiburg, Germany, with a population of 1.909 million, was 1/38951. (Neumann HPH, Wiestler OD. Clustering of features of von Hippel-Lindau syndrome: evidence for a complex genetic locus. Lancet May 4, 1991; 337:1052-54).

COMMENT. These familial patterns of lesions are important in prognosis and the clinical management of HLS gene carriers. Patients with renal lesions are at a high risk for hemangioblastoma of the CNS, the principal cause of death in HLS patients. Patients presenting with renal disorders should be carefully monitored for the development of CNS lesions. Patients with pheochromocytoma are likely to develop angiomas of retinae but are usually spared the CNS complication.

Von Hippel-Lindau disease has been associated with loss of a region of chromosome 3 that is often deleted in renal cell carcinoma. This region contains a tumor suppressor gene whose absence is associated with the development of renal cell carcinoma, hemangioblastoma and other tumors of von Hippel-Lindau disease. Deletion of the tumor suppressor gene may allow ectopic production of erythropoietin by the intracranial hemangioblastoma. Production of erythropoietin by a recurrent intracranial hemangioblastoma in a 59 year old woman was thought to explain the erythrocytosis in this patient with von Hippel-Lindau disease. (Horton JC et al. Von Hippel-Lindau disease and erythrocytosis: Radioimmunoassay of erythropoietin in cyst fluid from a brainstem hemangioblastoma. Neurology May 1991; 41:753-754).

NEUROMUSCULAR DISORDERS

MUSCLE HYPOTONIA IN LOWE'S SYNDROME

As part of a comprehensive evaluation of 23 patients with the oculocerebrorenal syndrome of Lowe at the Section on Human Biochemical Genetics, National Institutes of Health, Bethesda, MD, concentrations of muscle enzymes and carnitine metabolism were studied in addition to special reference to growth and renal function. The diagnostic findings included congenital cataracts, neurologic involvement (cognitive impairment, areflexia, and a history of infantile hypotonia), and renal tubular dysfunction in male patients with typical facies (deep set eyes and frontal bossing). Patients ranged in age from four months to 31 years. Muscle involvement was indicated by an elevation of serum