METABOLIC PIGMENTARY RETINOPATHIES

The diagnosis and management of inborn errors of metabolism associated with retinal degeneration are reviewed from the Clinique et Unité de Recherche de Génétique Médicale, the Hopital des Enfants Malades and the Opthalmologic Department et Formation Associée de Recherches Claude Bernard, Hopital Necker - Enfants-Malades - Laennec, Paris, France. Pigmented retinopathies are divided into two groups: (1) primary RP confined to the eyes; and (2) secondary RP associated with single or multiple organ system disease. Secondary RP is most often associated with nervous system involvement, morphological abnormalities, deafness, myopathy, nephropathy, and skin abnormalities. Some are well defined non-metabolic genetic syndromes and others are related to inherited metabolic disorders. In a patient presenting with retinal abnormalities the search for a metabolic disorder will concentrate on (1) errors of lipid metabolism; (2) errors of peroxisomal functions; and (3) errors of mitochondrial functions including the respiratory chain. Biochemical investigation should be considered in patients with ocular deficits that are associated with the following abnormalities: (1) neurological involvement including muscle hypotonia, seizures, peripheral neuropathies, cerebellar signs, sensorineural hearing deficit, cerebral abnormalities, mental retardation; (2) craniofacial abnormalities; (3) hepatological abnormalities; (4) renal abnormalities; (5) cardiomegaly; (6) skeletal abnormalities; (7) skin abnormalities; (8) failure to thrive; (9) hormonal disturbances; and (10) progression of symptoms. The screening procedure for metabolic disorders includes (1) peripheral blood for acanthocytes; (2) lipid pattern including lipoproteins; (3) redox status including lactic acid, pyruvate and ketones; (4) amino acid pattern; (5) organic acid pattern in the urine; (6) very long chain fatty acids and phytanic acid; and (7) enzymatic studies (Poll-The BT et al. Metabolic pigmentary retinopathies: diagnosis and therapeutic attempts. Euro J Pediatr Jan 1992; 151:2-11). (Reprints: Dr. B.T. Poll-The, Children's Hospital, "Wilhelmina Kinderziekenhuis" Metabolic Department, Nieuwe Gracht 137, NL-3512 LK Utrecht, The Netherlands.)

COMMENT. This excellent review of the metabolic retinal degenerations includes case reports of the major errors of metabolism associated with retinal degeneration including abetalipoproteinemia, neuronal ceroid lipofuscinosis, classical and infantile Refsum diseases, hydroxydicarboxylic aciduria, Sjögren-Larsson syndrome, Kearns-Sayre syndrome and peroxisomal disorders (see **Progress in Pediatric Neurology**, Millichap JG ed. 1991 pp. 470-474).

MITOCHONDRIAL CYTOPATHIES

MITOCHONDRIAL MYOPATHY WITH DNA DEPLETION

Five children with mitochondrial myopathy associated with depletion of muscle mtDNA are reported from the Departments of Neurology and Genetics and Development, Columbia University College of Physicians and Surgeons,

New York, NY and other centers in Germany, Belgium and the U.S. Symptoms manifested within or soon after the first year of life and muscle biopsies showed ragged red fibers and decreased respiratory chain activity. There was good correlation between clinical severity and degree of mtDNA depletion in muscle. An infant who died at 2 months had lactic acidosis and less than 2% of the normal level of mtDNA, while 4 children with relatively milder myopathy had no lactic acidosis and 8-34% residual mtDNA (Tritschler H-J et al. Mitochondrial myopathy of childhood associated with depletion of mitochondrial DNA. Neurology Jan 1992; 42:209-217). (Reprints: Dr. Eric A. Schon, Department of Neurology, Rm. BB324, Columbia University, 630 West 168th St., New York, NY 10032.)

COMMENT. Depletion of mtDNA is considered a distinct entity distinguished from other known mitochondrial disorders with COX deficiency or with multiple respiratory chain defects (fatal and benign infantile myopathies, Leigh's syndrome, Kearns-Sayre syndrome). The principal clinical features of patients with mtDNA depletion and mitochondrial myopathy are weakness, hypotonia and respiratory distress.

MITOCHONDRIAL MYOPATHY WITH DNA DELETIONS

Deletions of mitochondrial DNA (mtDNA) are reported in 19 of 56 patients with mitochondrial myopathy examined in the Department of Neurology and Neuromuscular Research Laboratory, Mayo Clinic, Rochester, MN. All 19 patients had progressive external ophthalmoplegia and 12 had complete or partial Kearns-Sayre syndrome. The age at onset varied from 4 to 48 years, 10 presenting in childhood. Patients with more than 50% deleted mtDNA had an earlier onset of symptoms and a higher proportion of ragged red fibers and cytochrome c oxidase negative fibers than patients with less than 50% deleted mtDNA (Yamamoto M et al. Mitochondrial DNA deletions in mitochondrial cytopathies: observations in 19 patients. Neurology Nov 1991; 41:1822-1828). (Reprints: Dr. Andrew G. Engel, Department of Neurology, Mayo Clinic, Rochester MN 55905.)

COMMENT. This paper confirms that large scale mtDNA deletions are present in a high proportion of patients with mitochondrial myopathy associated with progressive external ophthalmoplegia and that these deletions are a hallmark of Kearns-Sayre syndrome. Kearns-Sayre syndrome consists of progressive external ophthalmoplegia, pigmentary retinopathy, cardiac conduction abnormalities, and mitochondrial myopathy involving facial, cervical and limb muscles and increased CSF protein.

LEIGH'S SYNDROME WITH TWO MITOCHONDRIAL DEFECTS

A female infant with a biochemical defect of the respiratory chain and of β-oxidation and neuropathological changes typical for Leigh's disease is reported from the Department of Neurology, University of Würzburg, Departments of Pediatrics and Pathology, University of Homburg, and Department of Pediatrics, University of Freiburg, Germany. The infant was