COMMENT. Present diagnostic criteria and guidelines for the management of pediatric PTC do not consider pediatric aspects, according to a study involving all pediatric hospitals in Germany (Tibussek D, et al. **Klin Padiatr** 2013 Mar;225(2):81-5). The annual incidence was 0.5 per 100,000 children. A wide range of vision problems included papilledema, visual loss, diplopia, visual field defect, disturbed color and stereo vision. Papilledema was absent in 10 (16.4%) of a total of 61 patients treated Jan to Dec 2008. The importance of the ophthalmological exam was emphasized.

In a study of 42 patients with average age at onset of 10.8 years (range, 12 months to 17 years), obesity was found in 11 (26%). Headache occurred in 76%. Various etiologic factors were associated, including trauma in 2, hypervitaminosis A, corticosteroid withdrawal, oral contraceptives, Guillain-Barre syndrome, urinary tract infection, varicella-zoster virus infection, and dural venous sinus thrombosis associated with otitis media. Prompt diagnosis and medical treatment are important to avoid visual loss. (Per H, et al. **Brain Dev** 2013 Jun;35(6):561-8).

An unusual case of a 13-year-old boy presented with acute paresis of the left abducens, facial and vagus nerves. Brain MRI and angiography were normal. LP revealed an intracranial pressure of 575mmH2O. Treatment with acetazolamide resulted in improvement with no sequelae (Antoun J et al. **J Fr Ophthalmol** 2013 May 31 [Epub ahead of print]).

DEVELOPMENTAL MALFORMATIONS

WILLIAMS-BEUREN SYNDROME WITH BRAIN DYSPLASIA

Investigators from Jichi and Yokohama City Universities, Japan, report a patient with the common Williams-Beuren syndrome (WBS) deletion in 7q11.23 who presented with severe cerebral and cerebellar dysplasia and progressive hypertrophic cardiomyopathy. Facial characteristics included downward slanting of the palpebral fissure, blepharophimosis, strabismus, right iris hypopigmentation, low-set ears, high-arched palate, broad nose, thick lips, wide mouth, and micrognathia. Associated abnormalities included a deep, husky voice, hearing impairment by brainstem auditory responses, hypoplastic toes with nail aplasia, and contractures of hip and knee joints. Progressive hypertrophic cardiomyopathy manifested with ventricular septal defect at birth, right ventricular hypertrophy at 1 month, and left ventricular hypertrophy and mitral valve insufficiency at age 2 months. Supravalvular aortic stenosis commonly found with WB syndrome was absent.

Brain MRI showed congenital hydrocephalus, hypoplasia of the cerebellum and brain stem, and agenesis of the corpus callosum. At 3 months of age, he developed recurrent generalized tonic convulsions daily. Laboratory findings included mild hypocalcemia, low blood sugar, and low free T4 and high TSH consistent with hypothyroidism. The patient died with heart failure at age 1 year 5 months. (Okamoto N, Yamagata T, Yada Y, et al. Williams-Beuren syndrome with brain malformation and hypertrophic cardiomyopathy. **Brain Dev** 2013 Jul 27 [Epub ahead of print]). (Response: Dr Takanori Yamagata, Department of Pediatrics, Jichi Medical University, Tochigi, Japan. E-mail: takanori@jichi.ac.jp).

COMMENT. The original reports of Williams (alt. Williams-Beuren) syndrome appeared in the journal Circulation, 1961 and 1962, with emphasis on "Supravalvular aortic stenosis." Diagnosis of Williams syndrome involves recognition of physical features and markers, followed by a confirmatory genetic test. This case report is presented as the first patient with WB syndrome to have a congenital CNS anomaly in addition to progressive hypertrophic cardiomyopathy. Neurologic symptoms previously reported include mild microcephaly, intellectual disability, and personality disorders (hyperverbal). Abnormalities in the cerebellum, right parietal cortex, and left frontal cortex are consistent with visual-spatial difficulties. Increased volume of the left auditory cortex correlates with a rhythm propensity and fondness of music. Neuropsychological, neurological, and neuroanatomical profile of Williams syndrome is compared to that of Down syndrome (Bellugi U et al. **Am J Med Genet** 1990;37(Suppl. S6):115-25). For a clinical guide to symptoms and diagnosis of Williams and other syndromes, see Millichap JG. **Neurological Syndromes.** New York: Springer; 2013. 279 p.

JOUBERT SYNDROME, A CILIOPATHY

Investigators at Neurogenetics Unit, Mendel Laboratory, Rome, and University of Salerno, Italy, review the clinical features and genetic basis of Joubert syndrome, overlap with other ciliopathies, and the multifaceted roles of primary cilia in CNS development. Joubert M. and colleagues first described a familial agenesis of the cerebellum, manifested by episodic hyperpnea, abnormal eye movements, ataxia and retardation (**Neurology** 1969 Sep;19(9):813-25). The characteristic malformation involving the cerebellum and brainstem, the MRI hallmark of the syndrome, is called the "molar tooth sign." Associated CNS defects include ventriculomegaly, meningo-encephalocele, polymicrogyria, periventricular nodular heterotopia, hypothalamic hamartoma, and corpus callosum defects. Specific Joubert syndrome subgroups are correlated with different causative genes, one known by the acronym COACH (cerebellar vermis hypoplasia, oligophrenia, ataxia, coloboma, and hepatic fibrosis). A total of 21 causative genes have been identified, all encoding for proteins of the primary cilium that has a key role in development. An increasing number of heterogeneous disorders are being causally related to mutations in ciliary genes. (Romani M, Micalizzi A, Valente EM. Joubert syndrome: congenital cerebellar ataxia with the molar tooth. **Lancet Neurol** 2013 Sep;12(9):894-905). (Response: Prof Enza Maria Valente: E-mail. e.valente@css-mendel.it).

COMMENT. Prenatal abnormal features of the fourth ventricle in fetuses with Joubert syndrome and related disorders are reported in 7 subjects, all showing the molar tooth sign using ultrasound and/or MRI. (Quarello E et al. **Ultrasound Obstet Gynecol** 2013 Jul 19 [Epub ahead of print]). The term "Joubert syndrome" now encompasses all molar tooth sign-related disorders, and the term "Joubert syndrome and related disorders" is no longer in favor. Variable clinical manifestations associated with the molar tooth sign are not distinct syndromes, but part of a wide phenotypic range characteristic of Joubert syndrome.