

MANGANESE POISONING IN ALAGILLE'S SYNDROME

An 8 year old girl with Alagille's syndrome who developed dystonia secondary to manganese toxicity is reported from the Pediatric Department, Hershey Medical Center, Hershey, PA. She had developed a mild sensory neuropathy secondary to vitamin E deficiency which was corrected. MRI revealed hyperintense lesions in the globus pallidus bilaterally on T1 weighted images. A CT scan was normal. The serum manganese was 27 ug/l (normal less than 3). Treatment with ursodeoxycholic acid resulted in a normal serum manganese level. The dystonia cleared within 2 months of therapy. (Barron TF et al. Manganese neurotoxicity in Alagille's syndrome: a case report. Ann Neurol Sept 1992; 32:453 (abstr).)

COMMENT. Long exposure to inhalation of manganese has been known to be associated with neurological syndromes. The present case is unusual because the manganese toxicity was dietary in origin and caused by an impairment of the normal excretion of manganese through the biliary tree. Also, the symptoms were reversible. Wilson's disease was considered and excluded.

Alagille D. and colleagues described a syndrome of hepatic duct hypoplasia associated with characteristics facies, vertebral malformations, retarded physical, mental and sexual development and cardiac murmur (J Pediatr 1975;86-63). He also published on the clinical aspects of neonatal hepatitis (AMJ Dis Child 1972; 123:287). The above case of Alagille's syndrome was characterized by paucity of intrahepatic bile ducts with chronic cholestasis and pulmonic stenosis. Toxicity from dietary sources of manganese appears to require a prolonged period of exposure before neurological symptoms develop.

COCAINE AND THE DEVELOPING BRAIN

The effects of cocaine on corticogenesis in the developing murine brain were examined at the University of Louvain Medical School, Brussels, Belgium, and the Massachusetts General Hospital, Boston, MA. Two groups of 5 pregnant mice were injected with 20-40 mg/kg/day of cocaine hydrochloride from the 8th day of gestation until term. Examination of brains of embryos from embryonic day 15-18, post-natal pups from birth to 10 days, and adults showed disturbances of corticogenesis and brain growth and reductions in the number of live pups per litter. Neocortical architecture was disrupted and various steps of gliogenesis were altered. Interference with neurogenesis in the germinative zone could be attributed to cocaine-induced recurrent ischemia and inhibition of DNA synthesis (Gressens P, Kosofsky BE, Evrard P. Cocaine-induced disturbances of corticogenesis in the developing murine brain. Neuroscience Letters 1992; 140:113-116). (Correspondence: Professor P. Evrard, Laboratoire de Neurologie du Developpement, Av. Hippocrate 10/1303, B-1200 Brussels, Belgium.)

COMMENT. An estimated 10-15% of pregnant mothers deliver infants who have been exposed to cocaine in utero. Some develop behavioral impairments and structural brain abnormalities at birth (Kosofsky BE.

NIDA research monograph 1991). In a separate series of experiments the same authors injected rat pups ages 8, 15 and 28 days and adult rats with cocaine 30 mg/kg. As early as 8 days, a 5-6 fold induction of striatal mRNA was evident before cortical-immediate early gene-induction was demonstrable. Cocaine induced alterations in gene transcription during critical developmental periods may alter CNS form and function and may relate to the gestational timing of the cocaine exposure (Kosofsky BE et al. Neuroanatomical consequences of exposing developing brain to cocaine: a rodent model. Ann Neurol Sept 1992; 32:426 (abstract)).

NEURO CUTANEOUS SYNDROMES

SEIZURES AND IQ IN TUBEROUS SCLEROSIS

The relationship of seizures to intellectual disability was examined in 104 patients with tuberous sclerosis ascertained from the total population of the West of Scotland and reported from the Royal Hospital for Sick Children, Yorkhill, Glasgow, Scotland. Detailed analysis of the seizures was confined to the 52 patients who were born after the 1st of July, 1966: 4 (8%) had no seizures and normal intelligence. Of the 48 patients with seizures, 18 (35%) had normal intelligence, 6 (12%) had moderate intellectual disability, and 24 (45%) had severe intellectual disability. Seizures were significantly associated with intellectual disability. No patient who developed seizures after the age of 5 years was intellectually impaired. Most individuals with intellectual disability presented with infantile spasms or other seizures under 1 year of age, or had multiple seizure types. A higher incidence of intellectual disability was found among individuals who had more than 1 seizure type. Also, children with TS whose first seizure is febrile have a high risk of developing intellectual disability (Shepherd CW, Stephenson JBP. Seizures and intellectual disability associated with tuberous sclerosis in the West of Scotland. Dev Med Child Neurol Sept 1992; 34:766-774). (Correspondence: Dr. C.W. Shepherd, Craigavon Area Hospital, Portadown, Northern Ireland BT63 5SQ.)

COMMENT. Several papers on tuberous sclerosis were presented at the 6th Congress of the International Child Neurology Association, November, 1992, Buenos Aires, Argentina. Laan LA et al. Rotterdam, found vigabatrin in therapy of resistant epilepsy with tuberous sclerosis to be valuable, if given early in childhood. Calderon-Gonzalez R et al. of Monterrey, Mexico, found 7 of 27 children (26%) with TS had infantile autism evident by 3.5 years of age. Rett syndrome was associated with tuberous sclerosis in 2 patients reported by Philippart M of Pomona, California. Curatolo P et al. of Rome, Italy reported topographic spike mapping of the EEG in TS which showed that "generalized" spike-and-wave discharges were of focal origin (Pediatr Neurol Sept/Oct 1992; 8:344-411).