

Early genetic testing is recommended for symptomatic hyperekplexic neonates and possibly preconception counseling for those at risk for GLRB and SLC6A5 mutations. Recessive inheritance of hyperekplexia is associated with an increased risk of learning difficulties and developmental delay, particularly in speech acquisition. Severe recurrent neonatal apneas occur in approximately 50% of cases, particularly those with mutations in GLRB and SLC6A5. Stiffness, startle and stumble are the cardinal features of hyperekplexia.

DEMYELINATING DISORDERS

SINGLE CENTER EXPERIENCE OF ACUTE DISSEMINATED ENCEPHALOMYELITIS

Investigators at Department of Pediatrics, Neurology Division, Adana Medical Research Center; and Division of Child Neurology, Ankara, Turkey, retrospectively evaluated 15 children with acute disseminated encephalomyelitis (ADEM) in children from the center in Adana. ADEM was seasonal, 73.3% cases presenting in winter or spring. The majority (13/15, 86.7%) had an acute febrile upper respiratory illness 2 to 40 days before presentation. Five children had serological evidence of specific triggers: mycoplasma (2), influenza-A (H1N1) (1 child), and Epstein-Barr virus (2 children). One patient had received a combined vaccine (DTPP-Haemophilus influenzae B) 6 weeks before onset. Gait disturbance (12/15, 80%) was the most common presenting symptom, followed by altered consciousness (10/15, 66.7%), fever (7/15, 46.7%), headache (4/15, 26.7%), seizures (4/15, 26.7%), meningismus (4/15, 26.7%), and vomiting (3/15, 20%). EEG recorded in 8 patients showed generalized slowing in 3 patients and focal epileptiform discharges in 1. CT scan obtained in 14 patients showed lesions in only 3 cases, whereas MRI revealed cerebral lesions in all 15 patients (with complete resolution following treatment in 12, partial in 2). Treatment in all cases was a standard protocol of 3 to 5 days of IV methylprednisolone and IV immunoglobulin for patients with persistent deterioration. Oseltamivir and clarithromycin were administered in patients with influenza-A and mycoplasma. Follow-up evaluation ranged from 0.6 to 4 years (median 1.8 years). Neurologic symptoms and signs resolved in 13 patients; one patient had severe neurologic sequelae, and one had recurrent attacks and a final diagnosis of MS. (Erol I, Ozkale Y, Alkan O, Alehan F. Acute disseminated encephalomyelitis in children and adolescents: a single center experience. *Pediatr Neurol* 2013 Oct;49(4):266-73). (Response: Dr Erol, Division of Pediatric Neurology, Adana Teaching and Medical Research Center, Baskent University Faculty of Medicine, Adana, Turkey. E-mail: ilknur_erol@yahoo.com).

COMMENT. ADEM is an inflammatory demyelinating disease of the CNS that follows an infection or vaccination in three-quarters of the cases.

Post-vaccination ADEM. Several vaccines have been implicated including rabies, DTP, smallpox, measles, mumps, rubella, pertussis, and influenza (Huynh W et al. Post-vaccination encephalomyelitis: literature review and illustrative case. *J Clin Neurosci* 2008 Dec;15(12):1315-22). A patient presenting with bilateral optic

neuropathies within 3 weeks of “inactivated” influenza vaccination had a delayed onset of ADEM 3 months post-vaccination.

A case of ADEM is reported in a 34-month-old boy who presented with a seizure and left-sided weakness 5 days after vaccination against novel influenza A (H1N1). Following IV corticosteroids, symptoms improved and he recovered without neurologic sequelae (Lee ST et al. An adverse event following 2009 H1N1 influenza vaccination: a case of acute disseminated encephalomyelitis. **Korean J Pediatr** 2011 Oct;54(10):422-4). A PubMed search found 5 reports of ADEM following 2009 H1N1 vaccination, one occurring simultaneously with Guillain-Barre disease (Hoshino T et al. **Intern Med** 2012;51(12):1595-8). With increased demand for mandatory vaccination for health-care workers, recognition of the occasional association of ADEM with influenza vaccine should prompt early diagnosis and steroid therapy.

DEVELOPMENTAL DISORDERS

DIAGNOSTIC ALGORITHM FOR MICROCEPHALY

Investigators from Addenbrooke’s Hospital, Cambridge, UK, provide a diagnostic structure to follow when presented with a child with microcephaly. An occipital-frontal-circumference (OFC) of $>3SD$ below the age and sex expected is the definition used for microcephaly. “Primary” microcephaly is present at birth and “secondary” microcephaly develops after birth. Serial OFC measurements that follow the growth curve suggest a primary microcephaly, whereas an OFC that falls relative to the growth curve is usually a secondary microcephaly. In *primary* cases check for maternal and environmental factors including the TORCH screen, MRI, and fetal brain imaging. Cases with dwarfism and those with dysmorphic features and/or congenital anomalies may be recognized by phenotype (e.g. Cornelia de Lange syndrome- synophrys, dwarfism, limb anomalies) or may require cytogenetic testing. *Secondary* microcephaly cases may be static or progressive. The majority of chromosome disorders are associated with developmental delay and secondary microcephaly (e.g. Miller-Dieker syndrome caused by deletion of chromosome 17p13.3). Larger deletions are associated with a more severe phenotype of lissencephaly/pachygyria, and smaller deletions involve the LIS gene and a less severe form of lissencephaly. Rubinstein-Taybi syndrome is a Mendelian disorder causing secondary microcephaly and learning disorders. The diagnosis is clinical (distinctive facies, broad thumbs/big toes and postnatal growth retardation) and is confirmed by mutations in the CREBBP, EP300 or SRCAP gene.

If secondary microcephaly is associated with progressive neurologic findings, metabolic diseases should be considered. Genetic disorders such as Rett, PEHO, Cockayne, and Cohen syndromes are examples of secondary microcephaly where diagnosis by DNA testing is available. (Woods CG, Parker A. Investigating microcephaly. **Arch Dis Child** 2013 Sep;98(9):707-13). (Resp.: Dr. C. Geoffrey Woods. Clinical Genetics, Addenbrooke’s Hospital, Cambridge, UK. E: cw347@cam.ac.uk).

COMMENT. A knowledge of neurological syndromes is helpful in the differential diagnosis of microcephaly. (Millichap JG. **Neurological Syndromes : A Clinical Guide to Symptoms and Diagnosis**. New York: Springer, 2013:279).