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


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).