Dominantly inherited cerebral dysplasia: arachnoid cyst associated with mild mental handicap in a mother and her son

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Abstract
We report a mother and son who each presented in infancy with hypotonia and global developmental delay. Subsequently, in both subjects, mild mental handicap was diagnosed in association with temporal lobe arachnoid cysts. Mendelian inheritance of this phenotype seems likely and macroscopic cerebral dysplasia in general may be underdiagnosed in people with familial, mild mental handicap.

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Mild mental handicap is frequently familial, but clear evidence of underlying monogenic inheritance is rarely present. In affected families, the effects of assortive mating, poor socioeconomic status, and possible polygenic influences usually combine to obscure evidence of Mendelian inheritance. Arachnoid cysts, although rarely familial, are not uncommon, occurring in up to 0.5% of cranial computed tomography (CT) or magnetic resonance images (MRI). Cysts are considered congenital, intra-arachnoid, leptomeningeal lesions that expand by CSF production. Small cysts are usually asymptomatic but larger cysts might present at any time from prenatal life through infancy and adulthood with head enlargement, symptoms of increased intracranial pressure, intracranial haemorrhage, or seizures. In this case report, we present details of a mother and her son who each have mild learning disability in association with an unusual type of inherited brain dysplasia which has the appearance of temporal lobe arachnoid cyst...
so major diagnostic significance should be attached to delayed motor milestones or atypical neurological signs present in subjects with mild mental handicap; such observations constitute an indication for detailed neuroimaging studies in affected children and adults.

Since middle cerebral fossa arachnoid cyst usually occurs sporadically and causes no symptoms, in our family it seems most likely that the CT abnormality is a non-specific macroscopic marker (in the same way that agenesis of the corpus callosum or septum pellucidum abnormality might be in other instances) of subtle, inherited cerebral dysplasia affecting neurodevelopment and learning.

There are few reports of familial arachnoid cyst: Handa et al. described two male sibs with bilateral cysts who presented in early childhood with head enlargement that was treated by surgical shunt operations. These brothers may have had normal development before their presentation, but one was mentally and physically retarded afterwards. Both parents were healthy and had normal-sized heads. Pomeranz et al. reported two male and one female sibs; both males presented in early childhood with rapidly increasing head size and underwent surgery. One had slow neurodevelopment subsequently, the other had “borderline normal” development. Their similarly affected sister was asymptomatic when she was diagnosed at the age of 5 years. Confusingly, in a diagram of the family tree, the authors indicated that the mother of these three sibs was also affected although no information was given in the text. There is one other published Japanese report of 5 year old and 3 year old brothers with arachnoid cyst.

Finally, it seems most likely that an autosomal recessive condition affected two sibs who each had large, unilateral arachnoid cyst, mental handicap, and microcephaly. Although the parents of these sibs were not known to be consanguineous, their ancestors came from the same region and had surnames in common. These rare observations of familial arachnoid cyst do not permit firm conclusions about inheritance, but underlying clinical and genetic heterogeneity seems likely. We believe that the main message which emerges from our report of concurrence of arachnoid cyst and mild mental handicap in a mother and her son is that in some cases mild learning disability may have a discernible Mendelian basis that is easily overlooked.

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