Microcephaly

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low-osmolality and nonionic agents, which are much closer in osmolality to serum, have been developed.

Katayama et al prospectively compared the rates of adverse reactions in 337,647 patients receiving either low- or high-osmolality contrast media. The overall incidence of reaction in those who received low-osmolality contrast media (LOCM) was only 3.1%, compared with 12.7% in those who received high-osmolality contrast media (HOCM). Moreover, a lower incidence of reactions was observed with LOCM in each subgroup, categorized by severity of reaction, age of patient, and presence of underlying risk factors. The reason HOCM continues to be used at all today is the much higher cost of LOCM.

The effect of steroid pretreatment on the incidence of contrast reactions has been studied with both LOCM and HOCM. Lasser and coworkers found an overall reduction in the rate of reactions for both types of agent when steroids were given 12 to 24 hours in advance. Wolf et al compared the rates of reactions in those receiving HOCM with and without steroid pretreatment. Additionally, they looked at the incidence of reactions occurring in those receiving HOCM with steroid pretreatment compared with those receiving LOCM and no pretreatment. The rate of reactions was reduced when steroids were given before HOCM. However, an even lower rate of reactions was seen in patients who received LOCM alone.

In the pediatric population, factors other than statistical likelihood need to be addressed. Any reaction causing distress to a child may result in motion, rendering the radiologic study nondiagnostic. Moreover, vomiting poses an increased risk of aspiration in young patients, particularly when they have been sedated.

In summary, the use of intravenous iodinated contrast during radiologic examination can be accompanied by a variety of adverse reactions with multifactorial etiology. In those who are at higher risk, the likelihood of reaction can be decreased through use of low-osmolality, nonionic contrast and through pretreatment with steroids and antihistamines.

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IN BRIEF

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Microcephaly is characterized by a head circumference that is below the normal range. The diagnosis is made by measuring the largest circumference of the head, using the glabella and the occipital protuberance as reference points.

Head circumference reflects brain volume, with a small skull usually reflecting a small brain. Furthermore, the smaller the head, the less likely that intelligence will be normal. Avery et al reported that the incidence of moderate-to-severe mental retardation among infants who have a head circumference from 2 to 3 standard deviations (SD) below the mean is 33%, while among infants who have a head circumference more than 3 SD below the mean, the incidence is 62%. Thus, measurement of head circumference is a useful and readily obtainable means of evaluating the neurologic status of a newborn. However, this measurement is not reliable in infants who have abnormally shaped heads, as with craniosynostosis. Nor is microcephaly always associated with mental retardation; exceptions include familial small heads and growth retardation secondary to physiologic disturbances such as malabsorption or congenital heart disease.

Nellhaus set the standard graphs for the normal term newborn head circumference in 1968. Head circumference differs slightly between male and female infants at birth, with means of 35 cm and 34 cm, respectively. At birth, the brain has achieved approximately 25% and at 1 year of age about 75% of its adult volume. During the first 3 months of life, the head should grow at a rate of 2 cm/mon, from 4 to 6 months of life at 1 cm/mon, and from 6 to 12 months at 0.5 cm/mon. This growth pattern results in a mean head circumference of about 46 cm at 1 year of age.

A head circumference 3 SD or more below the mean is the generally accepted criterion for identifying infants who have microcephaly. To set 2 SD below the mean as the cutoff would define 2.5% of the population as microcephalic; 3 SD is more in keeping with the estimated incidence of 1 to 2 cases per 1000 deliveries.

Factors that can interfere with accurate measurement of head circumference include scalp edema, cephalohematoma, and molding; measurement may be unreliable until the third or fourth day of life. Of importance, too, is the influence of skull shape on head circumference. Circular skulls can accommodate a normal intracranial volume within a smaller head circumference than can skulls that have a large occipital-frontal diameter.

Microcephaly can be divided into two categories: congenital and acquired. Congenital microcephaly, resulting from anomalous induction and migration of brain tissue, can be associated with chromosomal abnormalities, autosomal recessive disorders, transplacentally transmitted infections, prenatal exposure to drugs and toxins, and maternal phenylketonuria. The forebrain is affected most severely, leading to characteristic features that include a sloping forehead and a small anterior fontanelle. Another related abnormal-

ity may be lissencephaly, the absence of cerebral convolutions, which is a hallmark of Miller-Dieker syndrome and is associated with defects of the short arm of chromosome 13. Either macrogyria, characterized by broad gyri and shallow sulci, or polymicrogyria also can be associated with congenital microcephaly.

Acquired microcephaly may result from infection late in the third trimester or during the perinatal period, from perinatal hypoxic-ischemic insults, or from metabolic derangements such as hypothyroidism or aminoaciduria. In such infants the head circumference is normal at birth; their microcephaly, resulting from postnatal impairment of brain growth, becomes apparent after several months.

Any child identified as having microcephaly deserves a thorough evaluation, beginning with serologic studies, as well as appropriate cultures, for TORCH infections and syphilis. Such transplacentally transmitted infections also may make themselves apparent by other typical abnormalities, including petechiae, hepatosplenomegaly, chorioretinitis, and intracranial calcifications. Other studies to consider, depending on the clinical presentation, are computed tomography, magnetic resonance imaging, and metabolic screening. With dysmorphic features, chromosomal analysis is worthwhile.

The prognosis for infants who have microcephaly varies significantly, depending on the underlying cause. Those whose microcephaly is part of a wider pattern of malformation, as with trisomies 13 and 8, or syndromes such as Meckel have a poor prognosis. So, too, do infants whose brain growth has been impaired by transplacental infection. In some situations, on the other hand, damage to the brain and subsequent microcephaly can be mitigated or even prevented: Prompt and expeditious delivery of a fetus in distress, aggressive management of maternal phenylketonuria, and early identification of hypothyroidism with appropriate replacement therapy all can improve the prognosis of an affected neonate dramatically. Familiarity with the variety of etiologies that can contribute to microcephaly and early recognition of an abnormal pattern of head growth can make interventions possible that will improve a child's outcome.

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Comment: Another congenital infection that, unfortunately, belongs on Dr Rios' list is human immunodeficiency virus (HIV). In some inner cities, HIV has become the most common infectious agent causing microcephaly. This is an instance in which we have the opportunity, at best, to prevent disease and, at least, to improve outcome. Routinely offering serologic testing to pregnant women can make primary prevention possible; treatment with zidovudine reduces mother-to-child transmission of HIV by two thirds. For those children born infected, early identification with polymerase chain reaction testing offers the chance for therapy with an expanding array of antiretroviral agents that can improve the quality and length of life.

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Editor, In Brief

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