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Normal children with large heads—benign familial megalencephaly

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SUMMARY Fifteen normal children with large heads (circumference >0·5 cm above the 98th centile) were studied. CAT scans were performed to exclude hydrocephalus, and ventricular size was compared with that of hydrocephalic children. In 11 of the 13 families in which the parents' heads were measured, one parent (10 fathers and one mother) was found to have a large head, as had 6 of 17 siblings. Head circumference at birth was large in 7 of 10 babies and rate of head growth was excessive in 8 of 13. Skull *x*-ray showed suture diastasis in 7 infants. These families have a benign familial megalencephaly. It is important to recognise this so as to avoid unnecessary investigation and anxiety about normal children with large heads.

A large head—macrocephaly—may be due to hydrocephalus, megalencephaly, a space-occupying lesion, or a thick skull. A large brain—megalencephaly—is associated with some cerebral degenerative disorders, as well as with other conditions—for example neurofibromatosis and achondroplasia—which are usually recognised by associated physical stigmata. Isolated megalencephaly while described in some gifted individuals—for example Byron, Turgenev, Bismarck—is generally considered to be associated with fits and retardation (Laurence, 1964).

Nelson and Deutschberger (1970) related the IQ at 4 years to head circumference (HC) at one year in 9379 children. They found that those with HCs >0·5 cm above 98th centile had a slightly higher mean IQ than children with heads of average size. One family in which father and son had large heads, normal intelligence, and normal computerised axial tomography (CAT) was reported by Asch and Myers (1976). Four other normal male relatives also had large heads. DeMyer (1972) reported 18 children with large heads and normal ventricular size on pneumoencephalography (AEG), but only 5 of these were of normal stature and neurologically normal. One of these had normal relatives with large heads.

When considering whether children with large heads are normal or not it is important to exclude hydrocephalus; Laurence and Coates (1967) showed that some children with untreated hydrocephalus had average intelligence. CAT enables us to identify normal children with large heads who do not have hydrocephalus, so we studied the head growth, skull *x*-rays, CAT appearances, and head size of such children.

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Method

Graphs (Nellhaus, 1968) were used to obtain standards for HC. Of 26 children who were investigated for large head size and found not to have hydrocephalus, 3 were mentally retarded and 8 had a HC only just above the 98th centile. Thus 15 children were investigated (14 CAT, 1 AEG) who fulfilled our criteria, having HCs >0·5 cm above the 98th centile and being of normal stature and developmentally and neurologically normal.

Results

Of the 15 children 11 were boys. The HC at birth was known for 10 of them and 7 were >98th centile (36·5 cm for girls, 37·5 cm for boys). Two of the children with large heads at birth were delivered with Kielland's forceps and a further child had a difficult normal delivery. The expected rate of head growth was calculated from the HC chart; in 8 children this was found to be faster than normal, 5 were growing at a normal rate, and 2 were not seen in the first 2 years of life. Four of the children had been noticed to be hypotonic in early life, one had a squint, and one speech delay.

Skull *x*-ray. All children had skull *x*-rays performed between one month and 5 years. These were examined

independently by two radiologists. Seven of the children were thought by both, and a further 4 by one, to show suture diastasis. Cranial capacity was estimated by the method of Gordon (1966) and was >95th centile in 14 cases and on the 95th centile in one. The volume related better to the HC than to the measurements of ventricular size on CAT. One child (Case 14) had a very thick dense skull vault with a low width/length ratio and a high height/width ratio.

CAT scan appearance. 14 of the 15 children had CAT scans. The ventricular size was measured in two ways. The bifrontal and bicaudate diameters of the frontal horn of the lateral ventricle were measured at the level of the basal ganglia (as described by Hahn and Rim, 1976) and compared with brain diameter at the same site to give a ratio (cerebroventricular index). The upper limit of normal in adults for the bifrontal ratio is 39·3% and for the bicaudate ratio 23·1%.

Cerebroventricular indices in the 13 normal children with large heads are shown in Fig 1 (group A) (ventricles too small to measure in one) and compared with 8 otherwise normal children whose HC was on the 98th centile (group B), and 12 children later treated for hydrocephalus (group C). Fig. 1 shows that the indices are within the normal adult range, apart from Case 10 (Fig. 2).

As the body of the lateral ventricles is often more dilated than the frontal horns, the area of the ventricles at the level of the above measurements and at the next higher cut was measured with a planimeter and compared with the area of the brain at the respective cut to give a ratio of ventricular to brain area at two levels. These area ratios are shown in Fig. 3. The measurements of the normal large-headed children are within the same range as those with heads on the 98th centile and, with one exception, do not overlap those with hydrocephalus. This child with hydrocephalus had relatively small

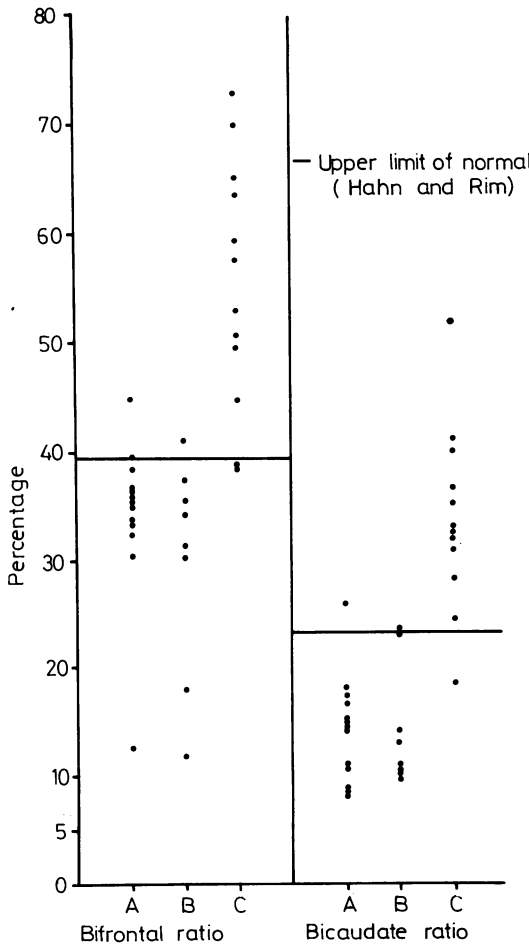

Fig. 1 *Cerebroventricular indices on CAT in (A) normal megalencephalic children; (B) normal children with HC on 98th centile; (C) hydrocephalic children.*

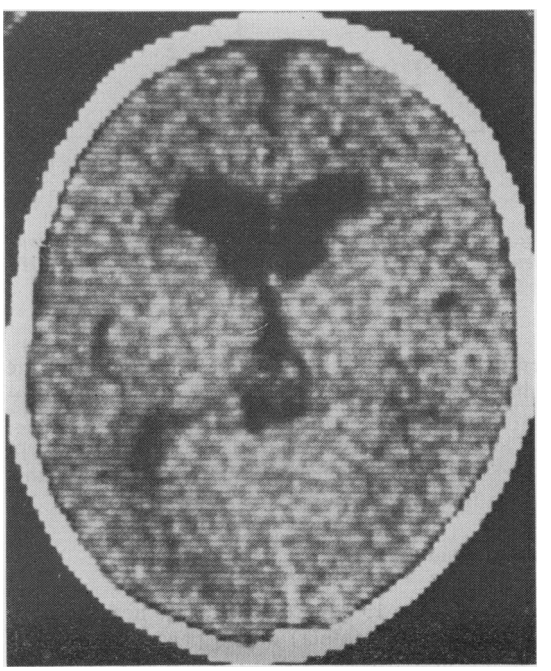

Fig. 2 *Case 10. CAT scan. Cerebroventricular indices above the upper limit of normal.*

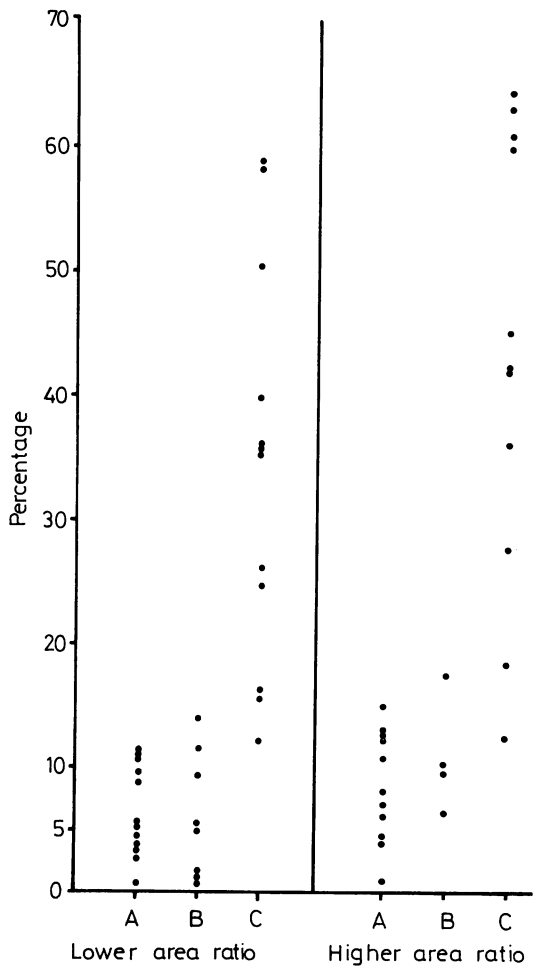

Fig. 3 *Ratio of ventricle and brain areas (A) normal megalencephalic children; (B) normal children with HC on 98th centile; (C) hydrocephalic children.*

ventricles although he had marked dilatation of the subarachnoid space and evidence of raised intracranial pressure.

Thus the normal children with large heads, except Case 10, had ventricular measurements which came within the normal range.

Family head size (Table)

Parents. Of the 15 children with large heads, 11 (10 fathers and one mother) of the parents had heads >98th centile (males >58·5 cm, females >58 cm). Only 2 children had parents with head circumferences within the normal range. Three parents were not available to be measured, one child having been adopted.

In families where the history was negative, one child (Case 13) had had viral meningitis at age 5 months and the other (Case 14) had a somewhat thick skull. The HCs of parents of 11 children in the hydrocephalus group were all <98th centile.

Siblings. Of the 11 children who each had one parent with a large head, 9 had 17 siblings (11 boys and 6 girls). Six (4 boys, 2 girls) of these had HCs >0·5 cm above the 98th centile for age. Two siblings also had hydrocephalus, of whom one had gross ventricular dilatation and was stillborn. Necropsy showed widespread old and new haemorrhage of undetermined aetiology. The other child with hydrocephalus was a twin to one of the index cases; he had a normal HC at birth which rapidly increased, and at 9 weeks AEG showed a communicating hydrocephalus which was treated with a ventriculo-atrial shunt. Of the 2 children whose parents did not have large heads, one had 2 sisters with normal sized heads and the other had a sister whose head was not measured.

Second-degree relatives. Of the 11 parents with large heads, 6 had their own parents' heads measured, and in 3 the grandfather's head and in one the grandmother's head was large. Four of the parents with large heads had siblings, in 2 the HC was normal, in one it was large, and one was not measured.

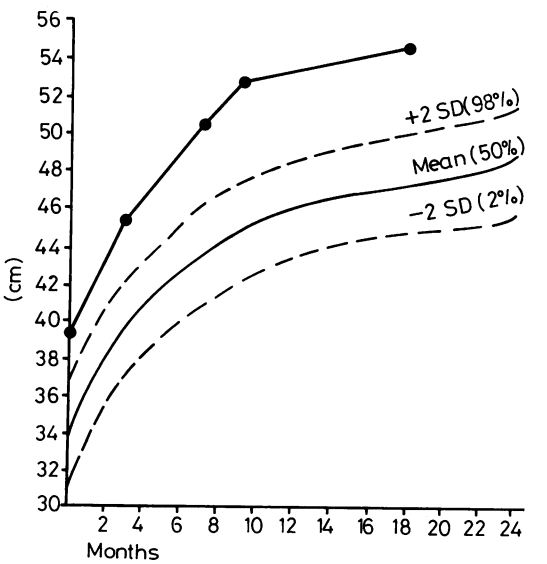

Fig. 4 *Case 6. Head circumference from birth to 18 months.*

Table *Head sizes of relatives of 15 normal children with large heads*

Case	Mother		Father		Sisters		Brothers			Grandmother		Grandfather		Siblings	
	Large (n=1)	*Normal (n=13)*	*Large (n=10)*	*Normal (n=2)*	*Large (n=2)*	*Normal (n=6)*	*Large (n=4)*	*Normal (n=5)*	*Hydro-cephalus (n=2)*	*Large (n=1)*	*Normal (n=4)*	*Large (n=3)*	*Normal (n=3)*	*Large (n=1)*	*Normal (n=2)*
1		1	1							NM		1			
2		1	1			1				NM		NM		NM	
3		1	1				1		1	NM		NM			
4		1	1				2				1	1			
5		1	1					3		NM		NM		Not known	
6		1	1				1			1			1	1	
7		1	1		1	1		1			1		1		1*
8		1	1		1			1			1		1		
9*		1	1			1			1	NM		NM			
10*		1	1								1	1			1*
11	1		NM			1				NM		NM		Not known	
12		1	NM												
13		1		1	NM										
14*		1		1		2									
15*	Adopted														

NM = Not measured, *female

The following case illustrates some of these points.

Case report

A baby boy (Case 6) born at 39 weeks' gestation by Kielland's forceps for deep transverse arrest. Birthweight 4·25 kg, length 57 cm, HC 39·5 cm. He was followed up from birth and investigated at 9 months when HC was diverging (Fig. 4) and skull *x*-ray (Fig. 5) showed suture diastasis, skull volume 1390 ml (normal 925–1050). CAT scan (Fig. 6) showed bifrontal ratio 35·5, bicaudate ratio 16·6, lower ventricular area 9·0, and upper ventricular area 12·6. At 18 months the child is walking and saying several words, and development appears normal. Fig. 7 shows the family tree. Father (HC 61 cm), the elder brother (57 cm at 3 years), paternal uncle (60·2 cm), and grandmother (60·4 cm), all have large heads. The grandmother said she never seemed able to find hats to fit her.

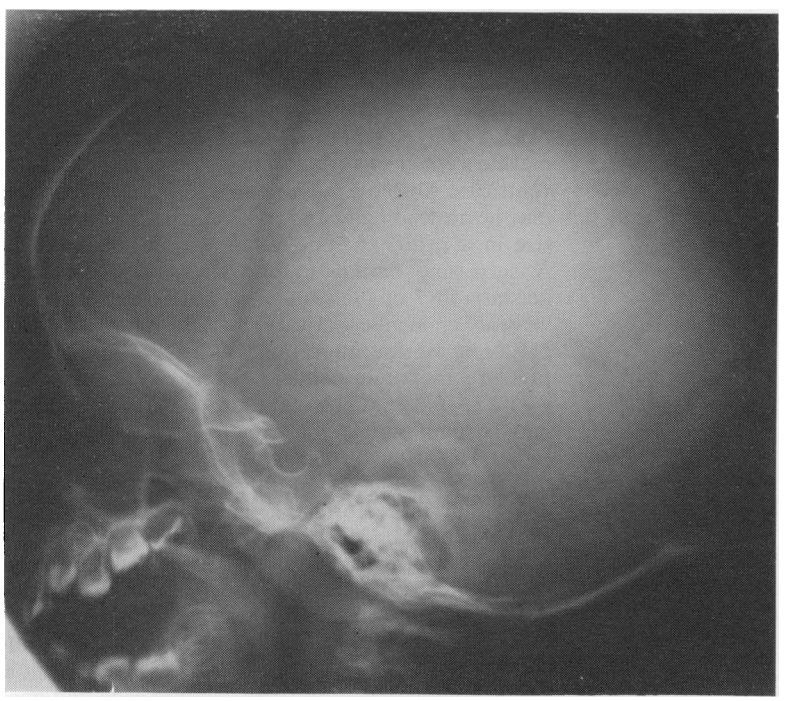

Fig. 5 *Case 6. Skull x-ray age 9 months.*

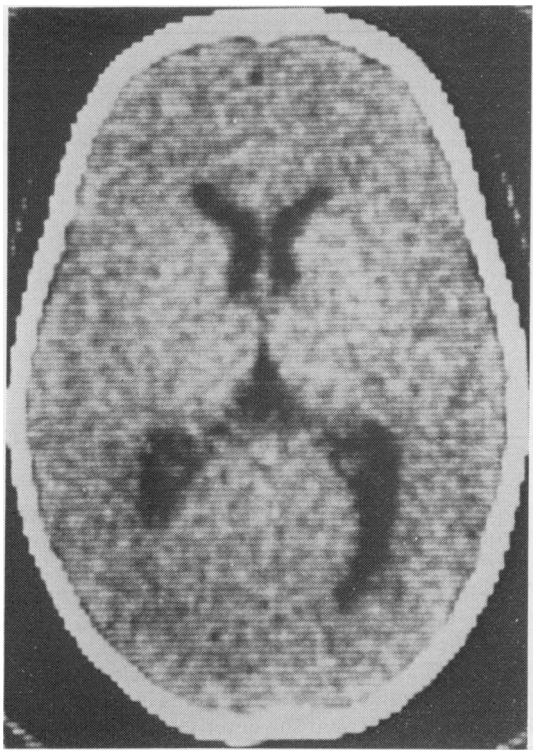

Fig. 6a *Case 6. CAT scan, cut 2A.*

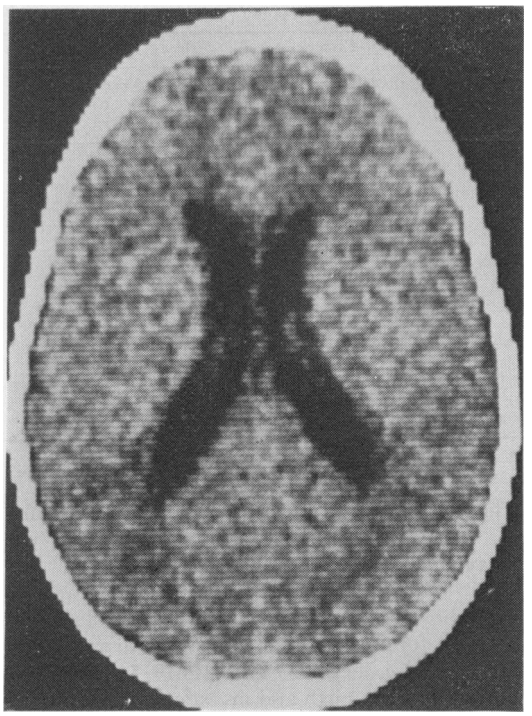

Fig. 6b *Case 6. CAT scan, cut 2B.*

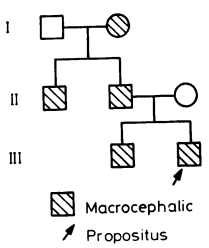

Fig. 7 *Case 6. Family tree.*

Discussion

All the 15 normal children with large heads had ventricular measurements on CAT scan which were within the normal range, except Case 10 in whom lateral ventricular measurements on low cuts (2A) were high (although well below most hydrocephalic babies). However measurement of the lateral ventricular area by planimetry was nearer the mean for the large-headed children. Nellhaus (1972) measured ventricular size by AEG and carotid angiography in 5 children with 'benign idiopathic megalencephaly' and found that the ventricles were in proportion with the cerebral mantle. Harwood-Nash (1977) stated that the CAT appearance of megalencephaly was that of normal or mildly dilated ventricles. Absolute measurements of ventricular size may be misleadingly high and comparison with brain size in a ratio, as done here, is more meaningful. A surprising finding in our series was of suture diastasis in 7 of the skull *x*-rays. This supports the view of Schönenberg (1973) that mild suture diastasis may not be an indication of raised intracranial pressure in young children. Conversely, he found that 12 of 39 infants with proved hydrocephalus had normal sutures.

The HC at birth was large in 7 of 10 babies. This may lead to difficulty during labour and delivery, and result in cerebral damage (Lorber and Bhat, 1974) with secondary mental retardation or neurological abnormality. Rate of head growth was increased in 8 of 13 children in whom it was measured giving the appearance of divergence from the centile lines. This was also seen in 2 of DeMyer's (1972) tall children with large heads.

The finding that 11 of these children each had one

parent with a large head and that 6 of 17 siblings also had large heads supports the suggestion of an autosomal dominant pattern of inheritance. The family described by Asch and Myers (1976) had 6 members in three generations with macrocephaly (all male). The family described by DeMyer (1972) had 4 confirmed and a further 4 suspected members with megalencephaly (4 female, 4 male) in three generations. Platt and Nash (1972) reported 4 normal children each having one parent with a large head but they did not give details. In our series there is a predominance of males 27:6 and the affected members in the family described by Asch and Myers (1976) were all males.

In two of our families one member had hydrocephalus. In one there was evidence of haemorrhage. In the other there was a communicating hydrocephalus. Schreier *et al.* (1974) described a family in which 2 members had hydrocephalus and 10 were normal with large heads. Three of these were investigated by echoencephalography which showed ventricles of normal size in one and at the upper limit of normal in two.

Thus 11 of our children have a benign familial megalencephaly which appears to be more common in males. The HC may or may not be large at birth and rate of growth may be excessive. Some of the children were hypotonic as infants but development was generally normal. Skull *x*-ray may show mild suture diastasis. CAT scan will usually clearly distinguish these children from those with hydrocephalus, although the ventricles may be at the upper limit of normal size.

It is concluded that in the absence of evidence of raised intracranial pressure or factors which might predispose to hydrocephalus or intracranial space-occupying lesion, the finding of a large head in an otherwise normal child should lead to the measurement of both parents' HC and, if one parent's head is large, the child should be observed rather than having further investigations, although CAT would reassure both doctors and parents.

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