Hospital Topics

Septo-optic Dysplasia

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Summary

Four children are described who had hypoplastic optic nerves, absent septa pellucida, and various types of endocrinological dysfunction. The importance is stressed of recognizing this syndrome and of following up the growth of the patient, because now that human growth hormone is available the short stature of some blind children may be susceptible to treatment.

Introduction

The association of abnormalities of the optic nerves, optic chiasm, and optic tracts with anomalies of the midline structures in the brain was first reported in 36 cases by de Morsier in 1956[1]; the condition was called "septo-optic dysplasia." Attention was drawn to the presence of pituitary dysfunction in this condition by Hoyt *et al.*, in 1970.[6] Since then we have seen four children with septo-optic dysplasia, of whom three were of short stature and lacked the ability to secrete growth hormone. Since treatment with growth hormone is now available[3] we thought it timely to draw attention to a syndrome which is one cause of short stature in blind children.

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Patients and Findings

Details of the patients and results of investigations are given in Tables I and II. All patients showed the major features of septo-optic dysplasia: (1) blindness with searching nystagmus; (2) hypoplasia of one or both optic discs (Fig. 1); (3) normal electroretinogram with abnormal visually-evoked cortical responses; and (4) absence of the septum pellucidum and dilata-

FIG. 1—Fundal photograph in Case 3 showing hypoplastic disc with typical double rim and sparse retinal vessels and paucity of normal branching pattern.

TABLE I—*Clinical Details and Ophthalmic and Radiological Findings*

Case No.	Sex	Date of Birth	Age at Examination (Years)	Height Centile[4]	Height Velocity Centile[5]	Optic Discs	Electro-retinogram[7]	Visually-evoked Responses[7]	Air Encephalogram
1	F.	31/1/68	2·7	10th	50th	Bilateral hypoplasia	Normal	Absent	Absent septum pellucidum. Dilated chiasmatic cistern. Slender optic nerves visible
2	F.	2/3/67	4·5	40th	<3rd	Left disc hypoplastic	Normal	Absent left eye	Absent septum pellucidum. Dilated chiasmatic cistern. Slender optic nerves visible
3	F.	2/9/66	5·4	<3rd	<3rd	Right disc hypoplastic	Normal	Absent right eye	Absent septum pellucidum. Dilated chiasmatic cistern. Slender optic nerves visible
4	F.	17/11/63	7·2	<3rd	<3rd	Bilateral hypoplasia	Normal	Absent	Absent septum pellucidum. Dilated chiasmatic cistern

TABLE II—*Results of Endocrinological Investigations*

Case No.	Peak Growth Hormone Levels (μIU/ml) to:		Adrenal Function Tests	Thyroid Function Tests
	Insulin-induced Hypoglycaemia	Bovril[8]		
1	—	>40	—	—
2	1·5	5·8	Plasma cortisol in hypoglycaemia rose from 6·4 μg to 14·0 μg/100 ml. Tetracosactrin test: plasma cortisol rose from 6·8 μg to 16·8 μg/100 ml.[9]	Serum thyroxine 5·0 μg/100 ml. Serum TSH 3·0 μUI/ml and rose to 21·5 after administration of TSH-releasing hormone intravenously
3	7·1	—	Plasma cortisol in hypoglycaemia rose from 16·6 μg to 26·8 μg/100 ml	Serum thyroxine 7·5 μg/100 ml
4	2·8	6·2	Tetracosactrin test: plasma cortisol rose from 4·0 μg to 16·4 μg/100 ml.[9] Four-day ACTH stimulation test normal	Serum protein-bound iodine 7·1 μg/100 ml

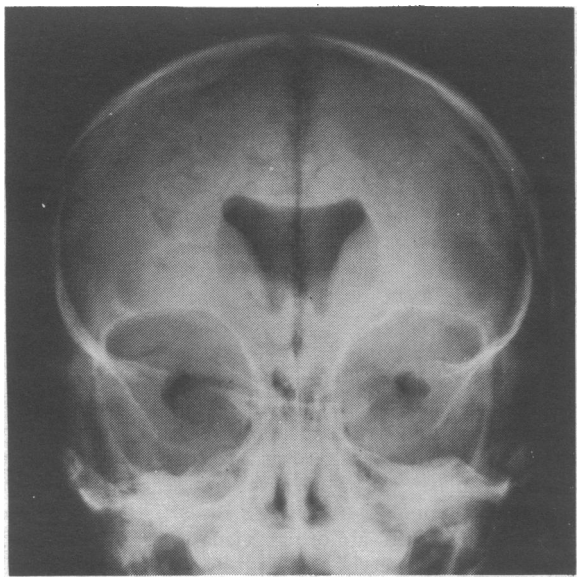

FIG. 2—Lumbar air encephalogram in Case 2. Anteroposterior view showing absence of septum pellucidum.

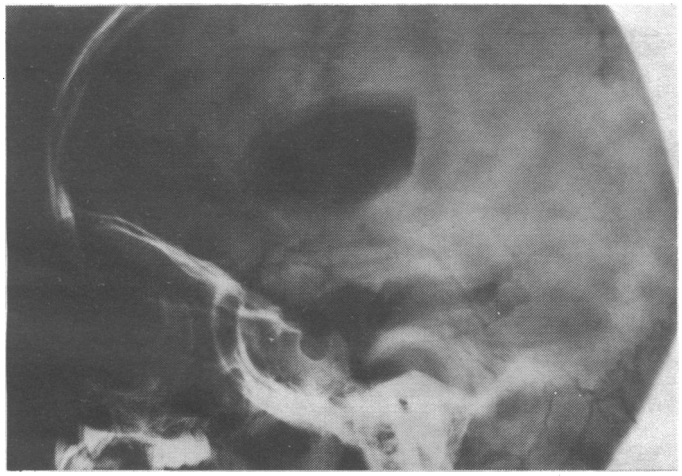

FIG. 3—Lumbar air encephalogram in Case 2. Lateral view showing absence of septum pellucidum and dilated chiasmatic cistern.

tion of the chiasmatic cistern on air encephalography (Figs. 2-4). Slender optic nerves may be demonstrable (Fig. 5).

One patient (Case 1) presented for investigation of blindness; she had grown and appeared to be growing normally. Another (Case 2) presented with hypoglycaemia and unilateral blindness; at the time of investigation she was of normal stature but she later failed to grow at the normal rate. Cases 3 and 4 were referred because of short stature.

No endocrine abnormalities were shown in the youngest patient (Case 1), one (Case 2) had evidence of panhypopituitarism, and the remaining two (Cases 3 and 4) had "isolated" growth hormone deficiency. None of the patients showed evidence of posterior pituitary dysfunction.

Discussion

Septo-optic dysplasia is a developmental disorder. At six weeks of gestation (15 mm crown to rump) a thickening begins to develop in the dorsal part of the anterior wall of the neural tube within which the septum pellucidum eventually forms at about 18 weeks (145 mm).[4] Differentiation of ganglion cells in the eyes also occurs at about six weeks, and the absence of ganglion cells in the eyes of anencephalic fetuses with hypoplasia of the optic nerves suggests a failure of such differentiation in that condition.[5] In septo-optic dysplasia both these processes must have miscarried. Pathological study of the condition shows agenesis of the septum pellucidum and malformation of the fornix, which does not become attached to the corpus callosum.[1] In addition there may be enlargement of the optic ventricle associated with hypoplasia of the optic nerves. No environmental factor has been found to account for this.

Abnormalities of endocrine function presumably result from an extension of the midline abnormality into the hypothalamus. This results in the abnormal dilatation of the chiasmatic cistern seen on air encephalography. Three of these children showed evidence of deficiency of growth hormone production, but only one had other clearly delineated abnormalities of hypothalamic-pituitary function. The age of the

FIG. 4—Midline tomogram showing normal anterior end of third ventricle.

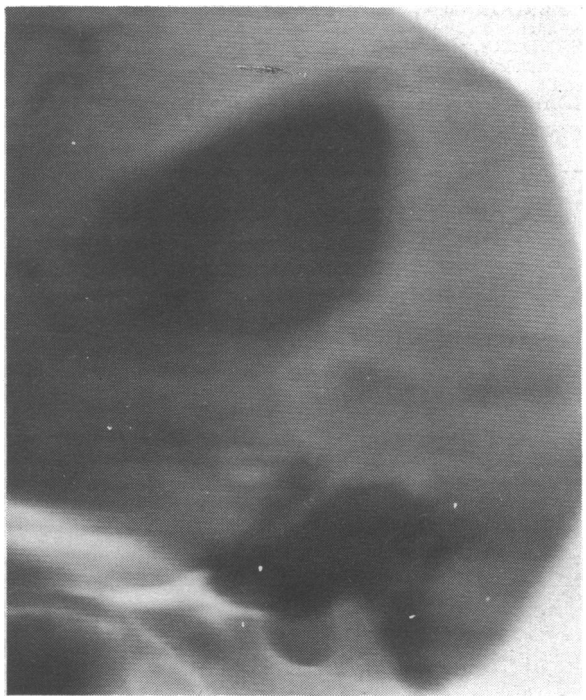

FIG. 5—Tomogram 4 mm to left of midline showing slender optic nerve.

children may however, have affected the clinical presentation. The youngest patient appeared to be growing well and to have normal endocrine function, but the older children manifested progressively more severe endocrine and growth problems. In Case 2 there was evidence that the growth rate was declining. In Case 3 measurements taken at the referring hospital indicated that growth velocity was probably normal between the ages of 2·7 and 3·3 years but that it diminished progressively thereafter. Case 4 "appeared to grow normally along the 25th percentile until the age of 1½ years. After this the growth curve flattened out, and she has hardly grown since the age of 3½." This raises the question whether there may be a progresssive disability—or whether lack of growth hormone may in fact not manifest itself immediately after birth.

The delayed onset of retarded growth in this series suggests that the main responsibility for early diagnosis rests in the interpretation of the ophthalmoscopic findings. The appearance of the disc, with its inner hypoplastic margin and an outer halo which probably represents the normal extent of the disc, is typical of the syndrome. Further experience suggests that there may be also be a paucity of retinal vessels. Fundoscopy and electrodiagnostic tests in blind children may suggest the syndrome, but confirmation can be obtained only by air encephalography. The characteristic findings are absence of the septum lucidum and dilatation of the chiasmatic cistern. Slender optic nerves may also be present, but we have not succeeded in showing the optic ventricle described by de Morsier[1] and demonstrated in one patient by Hoyt *et al.*[2]

Long-term follow-up of blind children with this syndrome is needed in order to make sure that they grow normally. We propose to treat the children of short stature in this series with growth hormone, and recent experience leads us to expect a satisfactory response.

References

1 de Morsier, G., *Schweizer Archiv für Neurologie und Psychiatrie*, 1956, 77, 267.
2 Hoyt, W. F., Kaplan, S. L., Grumbach, M. M., and Glaser, T. S., *Lancet*, 1970, 1, 893.
3 Tanner, J. M., Whitehouse, R. H., Hughes, P. C. R., and Vince, F. P., *Archives of Disease in Childhood*, 1971, 46, 745.
4 Ellenberger, C., and Runyan, T. E., *American Journal of Ophthalmology*, 1970, 70, 960.
5 Walton, D. S., and Robb, R. M., *Archives of Ophthalmology*, 1970, 70, 960.
6 Tanner, J. M., Whitehouse, R. H., and Takaishi, M., *Archives of Disease in Childhood*, 1966, 41, 454, 513.
7 Harden, A., and Pampiglione, G., *Lancet*, 1970, 1, 805.
8 Jackson, D., Grant, D. B., and Clayton, B. E., *Lancet*, 1968, 2, 13.
9 Barnes, N. D., Joseph, J. M., Atherden, S. M., and Clayton, B. E., *Archives of Disease in Childhood*, 1972, 47, 66.

For Debate . . .

Bile Acids: A pH Dependent Antibacterial System in the Gut?

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Summary

Bile acids are secreted in the bile in the form of conjugates and many species of intestinal bacteria can rapidly deconjugate them. Studies have shown that an unconjugated bile acid may have bactericidal and bacteriostatic effects, which are pH dependent. It is proposed that unconjugated bile acids may be involved in a homoeostatic mechanism, preventing bacterial growth in the small intestine.

Introduction

The small intestine has a recognized bacterial flora that is both qualitatively and quantitatively different from the flora of the caecum and colon[1]. Investigation of the mechanisms that limit bacterial proliferation in the bowel has recently stimulated interest because the functional consequences of bacterial overgrowth in the small intestine are known to cause symptoms associated with malabsorption of fat[2–4] and of vitamin B_{12}[5] and abnormalities of protein metabolism.[6] We report a bactericidal effect observed when strains of *Clostridium welchii* or of *Bacteroides* spp., some of which were obtained from human faeces, were grown in the presence of the bile salt taurocholic acid, a normal component of human bile. Normal faeces of healthy adults in Britain contain about 10^4 *Cl. welchii* and about 10^{10} *Bacteroides* spp./g wet weight.[7]

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Methods

Strains of *Cl. welchii* or of *Bacteroides* spp. (Table I) were grown in fluid media (Oxoid Brewer medium or Oxoid nutrient broth with glucose 0·5%) in anaerobic jars containing hydrogen with 10% CO_2. Brewer medium contains 0·5 g glucose/100 ml. In most experiments sodium taurocholate was added to the medium at a concentration of 4 mmol/l. Parallel cultures were set up in medium without taurocholate. The effect of cholic acid (the product of bacterial deconjugation of taurocholate) was

TABLE I—*Test Strains of Bacteria**

Strain	Description
Cl. welchii:	
L2A	A classical type-A strain (reference strain)
C24	β-haemolytic, from human ileostomy fluid
CX	β-haemolytic, from human faeces
N.C.T.C.8359	A typical food-poisoning strain, Hobbs type 1
Bacteroides spp.:	
N.C.T.C.7155	*B. necrophorus* (reference strain)
N.C.T.C.9343	*B. fragilis* (reference strain)
G.N.A.B.3	From an infected wound
G.N.A.B.7	From infected wound
G.N.A.B.9	From human faeces
G.N.A.B.10	From human faeces

*N.C.T.C. = National Collection of Type Cultures; G.N.A.B. = Gram-negative anaerobic bacillus.