fertilized products, could give rise to effective dizygous twins.

**Summary**

The presence of unequivocal Down’s syndrome in dizygotic twins of opposite sex is recorded. To our knowledge, this has been documented only once before, and at that time no chromosomal analyses were available for confirmation.

We wish to thank Dr. F. P. Hudson, who initially referred this family to our genetic counselling clinic, for permission to publish details of this case.

**REFERENCES**


D. W. FIELDING* and S. WALKER

Institute of Child Health, Alder Hey Children’s Hospital, and Cytogenetics Unit, University of Liverpool, Liverpool.

*Correspondence to Dr. D. W. Fielding, Alder Hey Children’s Hospital, Eaton Road, Liverpool L12 2AP.

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**Septo-optic Dysplasia with Growth Hormone Deficiency (De Morsier Syndrome)**

The association of hypoplasia of the optic discs with absence of the septum pellucidum was described by De Morsier (1956). Few examples have been described outside the ophthalmological literature until recently, but it is now becoming apparent that the condition is not as rare as was once considered. It is now recognized that growth retardation is a feature of the condition, and it is the purpose of the present report to describe an example of septo-optic dysplasia with the classical features of the syndrome and an associated growth hormone deficiency in a female child.

**Case Report**

The patient was born after a normal pregnancy at term to an 18-year-old primipara. The birthweight was 2-84 kg. She was reported to have been jaundiced for a month after birth, but she was not seen by a paediatrician at that time. No investigations were carried out. Initially her progress was considered normal. Blindness was discovered at the age of 7 months when she was referred to hospital for the first time because she was unable to see.

Examination at this time showed a left-sided hemiplegia. There appeared to be no vision. Hearing was normal. She was unable to sit up spontaneously and her sitting balance was poor, but in spite of this she handled objects well and could play with a rattle.

Ophthalmoscopic examination under anaesthesia showed abnormal discs on both sides. On the right side the vessels all appeared on the temporal side of the disc. The disc had a deep pale cup and there was fine pigment stippling surrounding it. On the left side there was a small coloboma present, and fine pigmentary disturbance surrounding the optic nerve head.

The patient was treated with regular physiotherapy, and the mother instructed to afford the child as much stimulation as possible to compensate for the lack of vision. She quickly caught up developmentally and at the age of 10 months she was sitting unsupported. She spoke at the age of 2, and walked unsupported at the age of 3. Her hemiparesis improved steadily with physiotherapy and by the time she was 2 this had disappeared completely.

Initially she appeared to grow normally and at the age of 3 years 9 months her height was 91·5 cm just at the 3rd centile. From then on she stopped growing. This was first noted when she was admitted to hospital at the age of 5½ with a fractured skull. She was then extensively investigated at the Torbay Hospital and at the Royal Devon and Exeter Hospital. Obvious causes for growth retardation due to intercurrent disease, such as chronic infection and malabsorption, were excluded, nor did there appear to be any obvious endocrine cause; there was a normal response to tetracosactrin stimulation.

**TABLE**

**Growth Hormone Levels After Stimulation with Bovril and Insulin-induced Hypoglycaemia (units = HGH micro units/ml)**

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Bovril (Royal Devon)</th>
<th>Bovril (G.O.S.)</th>
<th>Insulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (fasting)</td>
<td>1-3</td>
<td>3-3</td>
<td>2-8 (58)</td>
</tr>
<tr>
<td>15</td>
<td>6-9</td>
<td>3-9</td>
<td>1-6 (27)</td>
</tr>
<tr>
<td>30</td>
<td>6-9</td>
<td>3-9</td>
<td>1-3 (28)</td>
</tr>
<tr>
<td>45</td>
<td>6-1</td>
<td>5-1</td>
<td>1-8 (31)</td>
</tr>
<tr>
<td>60</td>
<td>6-1</td>
<td>5-1</td>
<td>1-9 (34)</td>
</tr>
<tr>
<td>90</td>
<td>8-5</td>
<td>6-2</td>
<td></td>
</tr>
<tr>
<td>120</td>
<td>3-3</td>
<td>6-2</td>
<td></td>
</tr>
<tr>
<td>150</td>
<td>3-3</td>
<td>3-3</td>
<td></td>
</tr>
</tbody>
</table>

*Note: Bracketed figures refer to blood glucose levels (mg/100 ml).*
Plasma 11-oxyhydrocorticosteroids before tetracosactrin 13·0 $\gamma$/100 ml. Plasma level 5 hours after 0·5 mg tetracosactrin 44·0 $\gamma$/100 ml. Human growth hormone studies were carried out using Bovril stimulation (Table, column 1). This response was considered poor, but as there was evidence of some growth hormone being present, an expectant attitude was maintained for another year.

When a year later, at the age of 7, she still had not grown, it was decided to refer her to the late Dr. D. G. Cottom for admission to The Hospital for Sick Children, Great Ormond Street, for further investigations. She was a blind, growth-retarded child, who had a wandering nystagmus. There was a lumbar lordosis, but otherwise, formal clinical examination was normal.

Investigations showed growth hormone deficiency after stimulation with Bovril and insulin-induced hypoglycaemia. The results are shown in the Table. All other tests of endocrine function were normal, confirming the findings at Torbay and the Royal Devon and Exeter Hospitals.

Electrodiagnostic tests. Electretinogram (ERG) showed a fairly large amplitude response, with no loss of function of outer retinal receptor elements. Visual evoked responses (VER) showed no consistent response, indicating probable complete loss of function of the visual pathways to the brain.

Neuro-ophthalmology (M. D. Sanders). There was a sluggish pupillary reaction to light. There were random ocular movements with a searching nystagmus. There was hypoplasia of the optic disc (Fig. 1), and this together with growth retardation made the diagnosis of septo-optic dysplasia almost definite.

Lumbar air encephalogram. The posterior fossa and the third ventricle were normal. The lateral ventricles were slightly enlarged and there was absence of the septum pellucidum (Fig. 2). The suprasellar cisterns were large (Fig. 3).

Discussion

Septo-optic dysplasia is a malformation of the anterior midline structures of the brain, including agenesis of the septum pellucidum, a primitive optic ventricle, and hypoplasia of the chiasma, optic nerves, and infundibulum. As described,

Fig. 1.—Retinal photograph, showing the characteristic double disc margins, with an outer ‘true’ margin shown by choroidal pigment, and an inner ‘hypoplastic’ margin containing the hypoplastic, pale nerve tissue.
the syndrome now includes growth retardation as a frequent concomitant.

Absence of the septum pellucidum is a well-known cerebral anomaly. Though it is seen as part of major brain malformations (e.g. holoprosencephaly), it is more usually found as an isolated congenital anomaly not associated with any recognizable clinical picture. Reeves (1941) described absence of the septum pellucidum and an optic nerve anomaly occurring together in the same patient, but De Morsier (1956) was the first convincingly to prove an association. In a series of 36 patients with absent septum pellucidum, he found 9 with abnormalities of the optic nerve. He suggested that the name ‘septo-optic dysplasia’ be applied to these patients.

At this stage, growth retardation was not recognized as part of the syndrome, but Hoyt et al. (1970) reported a growth-retarded child with hypoplastic optic discs in whom air encephalography revealed absence of the septum pellucidum. They next found 8 growth-retarded children with hypoplastic optic discs, and air encephalograms on three of these has shown the same defect. At the same time, Ellenberger and Runyan (1970) described a growth-retarded adult with septo-optic dysplasia. Sanders et al. (1970) reported seeing a number of children with blindness or near blindness from birth, small optic discs, and slow development without evidence of hypopituitarism. They drew particular attention to the characteristic ‘double disc’ appearance of the optic fundi, and also stressed the importance of the electrodiagnostic tests.

The child described fulfils all the criteria of septo-optic dysplasia. She has the characteristic and diagnostic appearance of her optic fundi, and is growth retarded with a proven growth hormone deficiency. The diagnosis was confirmed by air encephalogram. We wish to draw particular attention to the characteristic clinical features of the syndrome, and to support the contention of Hoyt et al. (1970) that the diagnosis can be made on clinical grounds alone without resorting to neuroradiological investigations.

The outlook for life of the condition appears to be good. With regard to growth, she has been entered on the growth hormone trial (M.R.C.), and it can be anticipated that she will have a good response (Tanner et al., 1971).

Summary

A 7-year-old girl is described with septo-optic dysplasia. This consists of hypoplastic optic discs with a characteristic double margin, and absence of the septum pellucidum. In addition, she was growth retarded, and shown to be growth hormone deficient. The diagnosis can be made clinically, and the syndrome is not as rare as was once believed.
We wish to thank Dr. M. D. Sanders for the neuro-ophthalmological opinion and for the retinal photographs.

References


R. J. Harris and L. Haas* The Hospital for Sick Children, Great Ormond Street, London, and Torbay Hospital, Torquay, Devon.

*Correspondence to Dr. L. Haas, Torbay Hospital, Torquay TQ2 7AA, Devon.

Malignant Nonchromaffin Parangangioma

This case is reported because of its rarity at this age, and also because of the response to cytotoxic drugs.

Case Report

A 5-year-old boy who had previously enjoyed good health was referred to hospital with a complaint of cough for one month. His family doctor had also heard a cardiac murmur. The cough was irritating and nonproductive. Examination confirmed the presence of the murmur, early systolic in timing, and heard loudest at the 2nd and 3rd left interspaces and in the left scapula region. Clinical examination of the chest revealed no abnormality; the only other physical sign being a small hard lymph node in the right supraclavicular region.

A chest x-ray showed collapse of the left lower lobe and widening of the mediastinum. He was admitted in February 1970 with a working diagnosis of tuberculous hilar lymph nodes giving rise to compression of the bronchus.

Investigations showed Hb 12.4 g/100 ml; WBC 11,000, normal differential; ESR 33 mm/hr; Heat test, negative; ECG, a moderate degree of left ventricular hypertrophy; blood pressure 100/60 mmHg, both arms and legs; catecholamine excretion levels within normal limits; IVP no abnormality.

During the next 10 days the clinical signs altered; initially collapse of the left lower lobe became more obvious, and then obstructive emphysema of the whole of the left lung appeared. On 9 February 1970 bronchoscopy was performed (Mr. D. J. Waterston). This showed a normal right main bronchus but the left main bronchus contained easily bleeding granulation tissue. Biopsy was taken from this, and the lymph node in the neck was also removed.

Histology. The tumour was composed of rounded groups of cells bounded by reticulin and collagen fibrils. The cells were large and had granular cytoplasm. The nuclei were large with marked nuclear pleomorphism and mitotic figures. There was necrosis of individual cells scattered through the tumour.

The patient was treated at St. Bartholomew's Hospital by irradiation (2500 rads in 30 days to neck and mediastinum), with relief of symptoms, but the cough returned after one month and x-ray showed a large mass in the region of the left main bronchus. Thoracotomy revealed collapse of the left lower lobe, and inoperable tumours at the hilum and at the tracheal bifurcation.

On 22 April 1970 treatment with intravenous vincristine, 2 mg/m² was started. On 10 June, intravenous cyclophosphamide 300 mg/m² was added. Injections were given fortnightly until September, when the chest was radiologically clear, and thereafter monthly. The cardiac murmur had disappeared by February 1971. In the following September he had varicella and rubella, but in October he appeared well. He had gained 3650 g in weight and grown 8 cm in height since falling ill 21 months before. When last seen in February 1972 he was well.

Discussion

The ganglia and parangangioma in relation to the autonomic nervous system both derive from neural crest cells. The former are part of the sympathetic chain while the latter have either (1) chromaffin-positive and endocrine-secreting, or (2) chromaffin-negative and functioning as neuro- or chemoreceptors (Haber, 1964). The nonchromaffin parangangioma have also been called 'chemodectoma' by Mulligan (1950) for this reason. Boyd (1937) described the embryology and phylogegetic development from nerves supplying the gills, which explains the distribution around nerves and vessels derived from branchial arches.

Smithers and Gowing (1965) reviewed 28 cases of chemodectoma in the region of the aortic arch; of these, 11 had survived some years after surgical excision. The others had died with varying degrees of complications attributable to the tumour. Both multicentric origin and metastatic spread have been reported (Smithers and Gowing, 1965;
Septo-optic dysplasia with growth hormone deficiency (De Morsier syndrome).

R J Harris and L Haas

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