Septo-optic Dysplasia

Synonyms: de Morsier’s syndrome, pituitary hormone deficiency combined HESX1-related

Septo-optic dysplasia (SOD) is a rare, heterogeneous condition characterised by a combination of:[1, 2]

- Optic nerve hypoplasia.[3]
- Midline brain abnormalities (including absence of the corpus callosum and septum pellucidum).
- Hypothalamic-pituitary endocrine deficiencies.

Associated features include developmental delay, seizures, visual impairment, sleep disturbance, precocious puberty, obesity, anosmia, sensorineural hearing loss and cardiac anomalies.[4]

The SOD phenotype is highly heterogeneous and diagnosis is made in the presence of at least two of these three features.[5] Only about a third of patients have all three features but patients with any component of the syndrome should be screened for the other features too. The cause of SOD is unknown but viral infections, gestational diabetes, environmental teratogens, vascular or degenerative injury and genetic mutations have all been considered as possible predisposing factors.[5] Management can be complicated and can entail lifelong multidisciplinary input.

Epidemiology

This is a rare condition, in the order of 1 per 100,000 of the population.[6] A study from Greater Manchester and Lancashire has identified cases being more common where high unemployment, low income and teenage pregnancies exist.[6] The association with young mothers has been previously reported in Glasgow.[7] However, there is still a debate as to whether maternal age is significant.[5]

Genetics of SOD

Most cases are sporadic but several familial cases have been described with an increasing number of mutations in developmental transcription factors implicated, including HESX1, SOX2, SOX3 and OTX2.[8] Although it appears to be genetic in origin, it rarely runs in families.[2] This suggests that mutation is more often spontaneous than inherited.

Presentation

- Suspicions can be raised at mid-trimester ultrasound scanning and the condition can be diagnosed but it can also easily be missed.[9]
- The child may appear normal at birth or there may be problems such as poor development of male genitalia.
- Unexplained hypoglycaemia may suggest pituitary inadequacy.
- Vision testing and screening in young children may reveal the first sign of abnormality.
- Susceptibility to infection may suggest a problem and it merits investigation.
- Seizures (particularly in patients with developmental delay)[5] and/or sleep disturbances can occur.[2]

Clinical features

There is a broad spectrum of pituitary problems ranging from isolated growth hormone deficiency to panhypopituitarism.
Visual problems
- There are hypoplastic optic discs with a classical double margin.
- There may be severe sight impairment in one or both eyes; 80% of these patients are considered legally severely sight impaired.\(^5\)
- Nystagmus and astigmatism are other common features.

Neurological problems\(^5\)
- The septum pellucidum ± corpus callosum are absent in about half of patients.
- Other midline abnormalities may affect the fornix, the septum pellucidum, the corpus callosum, and cerebellum.
- Developmental delay can occur.
- A majority of patients have some psychomotor impairment.
- Associations with autism have been described.

Hormonal problems
- The most consistent clinical feature is short stature associated with poor or absent growth hormone. Weight and head circumference are normal for size.
- Lack of growth hormone and other pituitary hormones can make individuals susceptible to neonatal hypoglycaemia. There may also be hypernatraemia.
- Other pituitary hormones are often deficient and there may be diabetes insipidus, although the posterior pituitary or neurohypophysis has a different embryological origin from the anterior pituitary of adenohypophysis.
- Hormonal imbalance can lead to a precocious puberty \(^2\)
- NB: if there is illness, the lack of adrenocorticotrophic hormone (ACTH) can precipitate an adrenal crisis and sudden death.

Other problems
- Thermoregulation may be deficient.

Classification according to MRI findings\(^{10}\)
A series of 55 patients was divided into four groups based on septum pellucidum and hypothalamic-pituitary axis appearance on MRI scan:
- In group 1 both were normal.
- In group 2 there was abnormal septum pellucidum and normal hypothalamic-pituitary axis.
- In group 3 there was normal septum pellucidum and abnormal hypothalamic-pituitary axis.
- In group 4 both were abnormal.

None of the patients in group 1 had endocrine dysfunction compared with 22% in group 2, 35% in group 3 and 56% in group 4. Group 2 was the most common to experience precocious puberty.

Investigations
- Brain imaging with MRI is an important investigation and an MRI to measure the size of the optic nerves can confirm the diagnosis.\(^{11}\) MRI will indicate the degree of structural abnormality and this indicates the likely endocrine abnormality.
- Tests of pituitary function may show hypopituitarism.
- Developmental assessment is likely to show delayed development.

Management
A lifelong multidisciplinary approach is required to optimise growth and development and to lead as normal life as possible.\(^2\)
- Growth hormone may be administered.
- If ACTH is deficient, the correct dose of cortisone to permit health and growth is a delicate balance.
- Management of puberty requires judgement. It may involve induction of puberty or delaying it if premature.
- Psychomotor retardation complicated by poor vision requires specialist help.
- A lifelong multidisciplinary approach is important to optimise growth and development.\(^2\)

Prognosis
Early detection and treatment reduces disease-related morbidity, and can be life-saving.\(^{12}\)

Further reading & references
- Septo-optic Dysplasia; Online Mendelian Inheritance in Man (OMIM)
- Septo-Optic Dysplasia; National Institute of Neurological Disorders and Stroke

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