Clinical Phenotype and Complications, Endocrinopathies and Neuroimaging Findings in a Case Series of SOD

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BACKGROUND

• Septo-optic dysplasia (SOD) is a highly heterogeneous condition with a variable phenotype, defined as two or more features of the clinical triad:
  i) optic nerve hypoplasia,
  ii) midline brain defects and
  iii) pituitary hormone abnormalities.

• Rare congenital anomaly with incidence of 1 in 10,000 live births, equally prevalent in males and females, associated with younger maternal age and primigravida.

• Most instances of SOD are sporadic, a number of familial cases have been described with an increasing number of mutations in developmental transcription factors including HESX1, SOX2, SOX3 and OTX2 being implicated in its aetiology.

OBJECTIVE

• To describe the clinical spectrum, biochemical and neuroimaging features, as well as to identify possible genotype – phenotype correlations in a series of 8 patients diagnosed with SOD.

PATIENTS AND METHODS

• Eight (6 male) consecutive patients, diagnosed with SOD in a Regional Paediatric Endocrinology Service

• Retrospective review:
  • Clinical diagnostic features
  • Tests of pituitary function
  • Neuroimaging
  • Ophthalmologic assessment
  • Genetic tests
  • Evolving pituitary hormone insufficiencies and treatment

RESULTS

DIAGNOSIS

• 50% of cases had all 3 diagnostic features and 50% 2 out of 3
• Neonatal diagnosis in 5/8 (62.5%) cases
• Maternal age < 25 years in 4/8 (50%) cases
• Primigravida mothers in 6/8 (75%) cases

CLINICAL FEATURES

Moderate/severe visual impairment (62.5%)
Developmental delay (62.5%)
Endocrine disorders (62.5%)
Seizures (62.5%)

Neuroimaging

Midline brain defects identified in 7/8 (87.5%) patients
Hypophyseal optic nerves and chiasm was described in 7/8 (87.5%) patients

Endocrinopathies

Growth
5 patients were Growth Hormone deficient (1 panhypopituitarism).

GH therapy - 2/5 patients experienced normal height velocity (-0.97 – 1.14 SDS) and normal BMI.

Puberty
Only 2 of these children (boys) were at age of normal puberty. Both had normal onset and normal LHRH testing despite GH and ACTH deficiency in one and no endocrinopathy in second boy.

REFERENCES

Fig. 1 Typical SOD features on MRI Brain: A - Absent septum pellucidum on coronal T2, B - EPP at superior end of stalk on sagittal T1, C - Tiny optic nerves, D - Thin infundibulum.

Fig. 2 Genotype – Phenotype correlations

ENDOCRINOLOGIES

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CONCLUSIONS

• This case series confirms that the phenotypic heterogeneity in SOD is high.
• Genetic screening was negative, in keeping with previous series.
• The acute complication of sudden onset hydrocephalus is novel and has not been described to date.
• These complex patients with a life threatening condition require careful clinical management.

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Fig. 2. Genotype – Phenotype correlations

ASPF/CC agenesis septum pellucidum/corpus callosum, SE schizencephaly, PH pituitary hypoplasia, EPP ectopic posterior pituitary, NP normal pituitary, ONH optic nerve hypoplasia