Joubert's syndrome

Synonyms: Joubert-Boltshauser syndrome, cerebelloparenchymal disorder IV, familial cerebellar vermis agenesis, cerebello-oculo-renal syndrome. [1]

Joubert's syndrome is a rare autosomal recessive condition characterised by partial or complete absence of the cerebellar vermis, leading to neonatal breathing abnormalities, jerky eye movements, hypotonia, ataxia, impaired equilibrium, and mental handicap. [2]

Epidemiology

The incidence of Joubert's syndrome has been estimated to range between 1/80,000 and 1/100,000 live births, although this may be an underestimate. [3]

Genetics

Joubert's syndrome is transmitted as an autosomal recessive trait (genetic heterogeneity - chromosome 9 is a possible candidate [4]). Mutations in five genes have been identified, including AHI1, NPHP1 and RPGRIP1L. [5] [6]

Recurrence risk is 25% in most families, although X-linked inheritance should also be considered.

Presentation

Onset is in early infancy with abnormally rapid breathing, jerky eye movements, mental retardation, hemifacial spasms, seizures and ataxia:

- Eyes: abnormal eye movements, chorioretinal coloboma, ptosis, and retinal dysplasia.
- Mouth: tongue tumours and protrusion.
- Hand and foot: polydactyly.

- Neurological: hypotonia, hypoplasia or aplasia of the cerebellar vermis, occasional occipital meningo-encephalocele, hemifacial spasms and ataxia.
- Gastrointestinal: duodenal atresia or fibrosis.
- Renal: cystic kidneys.
- Mental and motor retardation.
- Behavioural problems: self-mutilation.
- Neonatal apnoea followed by episodic hyperpnoea which may improve and subsequently disappear.

Investigations

- The diagnosis of Joubert's syndrome is confirmed with MRI, which shows classic neuroradiological finding of a complex midbrain-hindbrain malformation known as the 'molar tooth sign' (MTS), originating from the association of cerebellar vermis hypoplasia, horizontally-oriented and thickened superior cerebellar peduncles and a deepened interpeduncular fossa ('molar tooth sign'). [2] [7]
- Detection of the MTS should be followed by a diagnostic protocol to assess multi-organ involvement.
- MRI findings also include dilated cisterna magna, occipital meningo-encephalocele, Dandy-Walker malformation, hypoplasia of the corpus callosum, retrobulbar cystic mass.
- Abdominal ultrasound may show cystic kidneys.
- Genetic testing is not currently available but the physical abnormalities may be detected at antenatal ultrasound. A fetal MRI scan at between 20 and 22 weeks of gestation has been shown to be an effective method of antenatal diagnosis. [8]

Differential diagnosis

Other autosomal recessive ataxias, eg Friedreich's ataxia, ataxia-telangiectasia. [9]

Associated disorders

Leber's amaurosis (blindness with normal optic fundi and brain and kidney abnormalities) may be associated.

Management

- Treatment is symptomatic and supportive and will include physiotherapy, and occupational and speech therapy.
- The parents will need a great deal of support.

Prognosis

- This depends on the degree of malformation or agenesis of the cerebellar vermis.
- Some will have a mild form with mild physical disability and good mental development.
- In others, there may be severe physical disability, moderate mental retardation and death in infancy or early childhood.

Further reading

- Parisi MA; Clinical and molecular features of Joubert syndrome and related disorders. Am J Med Genet C Semin Med Genet. 2009 Nov 15;151C(4):326-40.

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