

SHORT PAPER

A very rare entity of diabetes insipidus associated with Edwards Syndrome

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Summary

Edwards syndrome is the second most commonly seen trisomy. It was first described by John Hamilton Edwards in 1960. Although most cases result in termination or foetal loss, live births have been documented in 5%. Edwards syndrome is characterized by multisystem anomalies, of which holoprosencephaly (HPE) is observed in 4–8% of cases. The clinical findings correspond to the degree of HPE malformation. Convulsions and endocrinopathies are among the severe clinical findings. The most common endocrinopathies are central diabetes insipidus (DI), hypothyroidism, hypocortisolism and growth hormone deficiency. The coexistence of holoprosencephaly and DI in Edwards syndrome was discussed under the light of literature.

1. Introduction

Trisomy 18, which is also known as Edwards syndrome, is the second most common trisomy after Down syndrome. Although the incidence of trisomy 18 was first estimated to be 1/6000–1/8000, due to early termination and foetal losses, this ratio is thought to actually be higher (1/2500–1/2600) (Edwards *et al.*, 1960; Crider *et al.*, 2008). Trisomy 18 cases usually result in intrauterine loss. Only 5% are live born and among these cases 95% die within the first 6 months. However, 5–10% survive more than a year (Carey, 2005). The vast majority of cases are diagnosed with intrauterine ultrasonography. The postnatal diagnosis is fairly easy due to the classic clinical findings that include intrauterine growth retardation, microcephaly, low and malformed ears, micrognathia, small mouth, short sternum, classic hand sign and rocker bottom feet. The most common cardiac anomalies are ventricular septal defect (VSD), patent ductus arteriosus (PDA) and aortic coarctation. Renal anomalies, cranial malformations and vertebral and ocular anomalies can also be seen (Jones, 2006). The most common cranial malformations include cerebellar hypoplasia, agenesis of the corpus callosum,

polymicrogyria, spina bifida and holoprosencephaly (HPE) (Jones, 2006). The incidence of HPE is 5–12/10000 where forebrain and mid-facial defects are most common. Malformation resulting from the inadequate development of the cerebral hemispheres is known as HPE. The clinical findings depend on the degree of the defect. Of the clinical findings, convulsions and endocrinopathies are in the forefront due to their effects on morbidity and mortality. Common endocrinopathies include central diabetes insipidus (DI), hypothyroidism, hypocortisolism and growth hormone deficiency (Dubourg *et al.*, 2007). We wanted to highlight the rarity of DI secondary to HPE in Edwards syndrome.

2. Case report

A 35-week-old baby boy born to a 22-year-old healthy mother as a second child was spontaneously delivered vaginally. The mother had not been routinely followed up during pregnancy and multiple anomalies were observed on pre-delivery obstetric ultrasonography. After delivery, the cyanotic baby did not cry and having Apgar scores of 3 and 5 at the first and fifth minutes was intubated and transferred to the newborn intensive care unit. His birth weight was 1850 g (3–10 percentile), height was 42 cm (3–10 percentile) and his head circumference was 27 cm (<3 percentile).

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Fig. 1. Patient, 2-day-old boy. Note a wide forehead, malformed and low ears, hypertelorism, microcephaly, microphthalmia, micrognathia, short neck, syndactyly on the left hand, an accessory finger on the right hand, nail dystrophy, bilateral cryptorchidism and omphalocele.

Physical examination findings included a wide forehead, malformed and low ears, hypertelorism, microphthalmia, micrognathia, short neck, syndactyly on the left hand, an accessory finger on the right hand, bilateral simian lines, bilateral cryptorchidism, omphalocele and a single artery and vein in the umbilical cord (Fig. 1). On postnatal day 5 his laboratory findings were as follows: a serum sodium (Na) of 167 mEq/l, serum and urine osmolality of 345 and 158 mOsm/kg, respectively, a urine density of 1006, urinary sodium excretion of 80 mmol/l, serum antidiuretic hormone (ADH) level of 0.9 pmol/l (normal reference range; 2–8 pmol/l) and polyuria (5.5 cc/kg/h). All other pituitary hormone levels were found to be normal. The patient was diagnosed with central DI and was given desmopressin 20 $\mu\text{g}/\text{m}^2/\text{day}$ (Minirin[®] nasal spray 10 mcg/0.1 ml) in two doses. Serum and urine osmolality were found to be 282 and 301 mOsm/kg, respectively and the serum sodium level was 138 mEq/l. Cranial ultrasonography examination revealed HPE (Fig. 2). The cranial MRI showed



Fig. 2. Cranial ultrasound scan showing holoprosencephaly.

agenesis of the corpus callosum, lissencephaly, lateral monoventricle and HPE. Phenobarbital was administered when the patient had myoclonic convulsions and multifocal epileptiform activity was detected on electroencephalography. Abnormal results were acquired with an otoacoustic emission test. On cardiological evaluation, a 4/6 systolic murmur was noted and with echocardiography tetralogy of Fallot, VSD, atrial septal defect, PDA and pulmonary stenosis were observed. His genetic analysis result was 47, XY+18 inv(9). The electrolyte values and urinary output were normal, but owing to the severity of the cardiac defects, the patient died from cardiopulmonary insufficiency.

3. Discussion

Although many multisystemic anomalies coexist in trisomy 18 cases, HPE is of importance as it is one of the factors that increases mortality. Studies have stated that HPE occurs in 4–8% of trisomy 18 cases (Kagan *et al.*, 2010). The cause of HPE is not known. Maternal diabetes, intrauterine infections (syphilis, toxoplasmosis, rubella, herpes and cytomegalovirus) and drugs (alcohol, aspirin, lithium etc.) are the most common risk factors. HPE can also be seen with chromosomal anomalies, monogenetic diseases and as part of syndromes as was the case with our patient (Chang, 2003). The most common clinical findings are microcephaly, psychomotor retardation, seizures, growth hormone and other pituitary hormone deficiencies, hypertonia, sensorineural hearing loss, optic nerve hypoplasia and hypotonia. Since HPE is a midline brain defect, it affects the development of the hypothalamic and pituitary glands, which causes endocrinal disorders. Posterior pituitary dysfunction is more common than anterior dysfunction. Diabetes insipidus is the most common endocrinal pathology (Ko & Kim, 2010). In a 117 case study by Hahn *et al.* (2005) they observed hypothyroidism in 11%, hypocortisolism in 7%, growth hormone deficiency in 5% and DI in 70%. Even though central DI is common in HPE, multiple pituitary hormone deficiency is rare (Traggiai & Stanhope, 2002). In our case, except for central DI, hormonal parameters were found to be normal. In HPE, as a result of an abnormal hypothalamic-infundibular region, central DI can develop due to defects in the supraoptic and paraventricular nuclei of the hypothalamus. Although the posterior pituitary gland was normal on MRI, the presence of DI suggested the likelihood of hypothalamic osmoreceptor insensitivity. Another hypothesis is that the gene causing cerebral malformations secondarily affects hypothalamic neuron development (Kourti *et al.*, 2008).

We believe that the central DI in our case developed secondarily to HPE. In this case report, we wanted to draw attention to central DI that develops secondarily to the rarely occurring HPE in Edwards syndrome. To the best of our knowledge, this clinical manifestation had not been previously reported.

4. Declaration of interest

No conflicts of interest and no financial support were declared in relation to this article.

5. Supplementary material

To view supplementary material for this article, please visit <http://dx.doi.org/10.1017/S0016672313000165>.

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