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Case Report

Structural anomaly of chromosome 18 with Edward syndrome phenotype

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ABSTRACT

Edward syndrome has a median survival time of 14.5 days. Importance of this case report is in the rarity of this karyotype and prolonged survival as compared with complete trisomy 18. A 5-year-old male child with global developmental delay had brachycephaly, microstomia, narrow palatal arch, low set ears, widely spaced nipples, diastasis recti, bilateral cryptorchidism, ulnar deviation of both hands with absent distal creases, rocker bottom foot with overlapping of second and third toes. Cardiac, ophthalmological, otolaryngological evaluations, ultrasonography abdomen, and skeletal survey were normal. Computed tomography head showed mild dilatation of lateral ventricles. Karyotyping revealed 46 chromosomes with an asymmetry of chromosome 18. Pathognomonic segment responsible for Edwards phenotype is in the q arm of chromosome 18. In this patient, there was no complete trisomy 18. However, there was an abnormality in the form of asymmetry that can be due to either isochromosome 18q, translocation chromosome 18 or duplication of the critical region.

Keywords: Edward syndrome, Structural anomaly, Chromosome 18

INTRODUCTION

Edward syndrome (trisomy 18) is the second most common autosomal abnormality in live births with an incidence of 1 in 8000.[1] 50% die within 1st week and many of remaining die in next 12 months, median survival time is 14.5 days. Rarely, they can have prolonged survival.[2]

CASE REPORT

A 5-year-old male child was born of third-degree consanguineous marriage, with other two siblings being normal. Age of mother and father was 22 years and 28 years respectively. He was born at term with birth weight of 2.2 kg. History of feeding difficulty was present since birth due to microstomia and history of global developmental delay was present. The clinical features found in this case are shown against typical features of Edward's syndrome in Table 1. Figures 1 and 2 are clinical photographs of the patient. Cardiac, ophthalmological, otorhinolaryngological evaluations and ultrasonography abdomen, skeletal survey were normal. Computed tomography head revealed mild dilatation of lateral ventricles. Karyotyping revealed a total of 23 pairs (46 chromosomes) with an asymmetry of chromosome 18 as shown in Figure 3.

DISCUSSION

As we can see from the Table 1, our patient did not have all the clinical features of Edward's syndrome, and he has survived longer. This can be explained when we look at the karyotyping of this patient. Trisomy of a long arm chromosome 18 is an important factor in the development of the phenotype of Edward syndrome, as the pathognomic segment responsible for Edwards phenotype is thought to be located in the q arm.[3] In this patient, there is no trisomy 18, but there is an abnormality of chromosome 18 in the form of asymmetry that can be due to any of the following:

1. Isochromosome 18q: Isochromosome formation occurs when a chromosome divides along the

Table 1: Clinical features of present case compared with complete trisomy 18.

Features	Complete trisomy 18	Present case
General	Pre/post term, small for gestational age, hypertonia (50%)	Small for gestational age
Cranio-facial	Prominent occiput, low set, malformed auricles, short palpabral fissures, small oral opening, narrow palatal arch, micrognathia (50%), wide frontanels, microcephaly, inner epicanthal folds, ptosis of eyelid, cleft lip, cleft palate (10-50%)	Microcephaly, brachycephly, small oral opening, narrow palatal arch, low set ears, short palpabral fissures
Limbs	Clenched hands, overlapping of index finger over third finger, fifth over fourth finger, absence of distal crease on fifth, fourth, third fingers, hypoplasia of nails, ulnar or radial deviation of hand, hypoplastic thumb, rocker bottom foot, syndactyly of second and third toes (10-50%)	Ulnar deviation of both hands with absent distal creases in fingers, rocker bottom foot with overlapping of second and third toes
Trunk	Short sternum, small nipples, inguinal or umbilical hernia, diastasis recti, small pelvis (50%), broad chest with widely spaced nipples (10-50%)	Widely spaced nipples, diastasis recti
Cardiac	VSD, ASD, PDA (50%), bicuspid aortic valves, pulmonic stenosis, coarctation of aorta (10-50%)	None
Genitalia	Cryptorchidism (50%)	Cryptorchidism
Skin	Redundancy, hirsuitism of forehead and back, cutis marmorata (50%)	None
Renal	Horseshoe, ectopic kidney, double ureter, hydronephrosis, polycystic kidneys (10-50%)	None
CNS	Cerebellar hypoplasia, meningomyelocele, hydrocephalus, defect of corpus collosum	Mildly dilated lateral ventricles

CNS: Central nervous system, VSD: Ventricular septal defect, ASD: Atrial septal defect, PDA: Patent ductus arteriosus

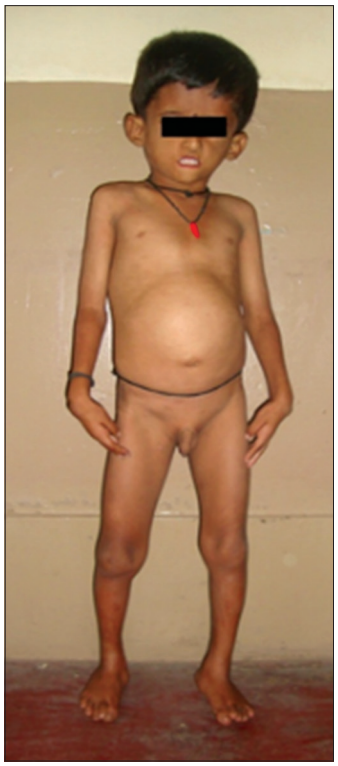

Figure 1: Clinical photograph of patient showing small mouth, ulnar deviation of both hands, widely spaced nipples, bilateral cryptorchidism, overlapping of second and third toes.

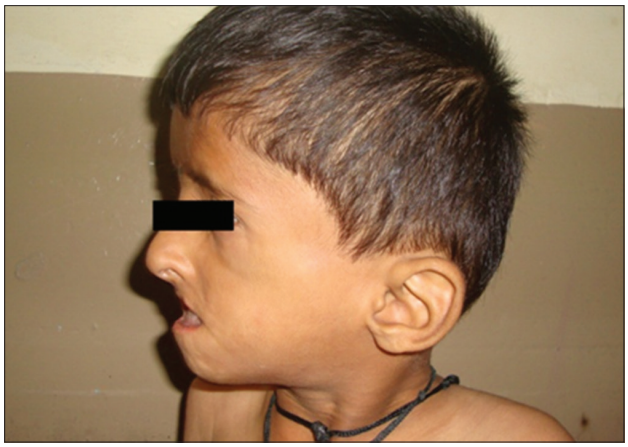

Figure 2: Low set ears in the patient.

axis perpendicular to its usual axis of division. Isochromosome will have two copies of one arm and no copies of the other.[4] Isochromosome formation can occur either during meiosis 1 or meiosis 2. Fertilization of an isochromosome bearing gamete would lead to an unbalanced karyotype. The zygote would have the information of an arm present 3 times and the other arm only once.[5] Hence, isochromosome 18q formed by deletion of the p arm and triplication of the q arm will display a range of severity from relatively mild phenotype with no internal organ malformations to the classic characteristics of Edwards syndrome.[5]

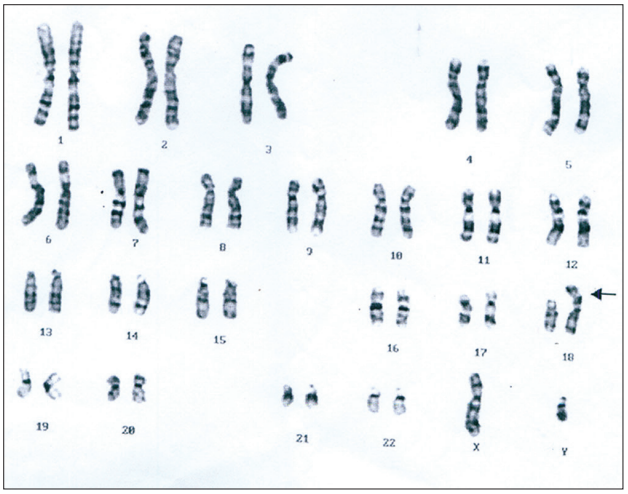

Figure 3: Karyotype revealing asymmetry of chromosome 18.

2. Translocation is resulting from non-disjunction after breaks events in both chromosomes 18. In one chromosome 18 the break occurred in the proximal portion of its long arm, in the other, a break occurred in its short arm. The large metacentric chromosome resulted when the broken long arm of one chromosome 18 joined to the other chromosome 18, which lacked only a short arm piece. The small meta-centric arose from the joining of the tiny short arm piece of one chromosome 18 to the rest of the broken long arm of the other chromosome 18.[6]
3. Duplication: Bogoshian-Sell et al. identified two regions on 18q that may work in conjunction to produce Edwards syndrome phenotype; a proximal critical (18q12.1-18q21.2) and a distal critical region (18q22.3q). Duplication of the critical region will have relatively mild Edward syndrome phenotype as in the above case in comparison to complete trisomy 18, which has a high mortality.[7]

In our patient, it is difficult to exactly pinpoint, which of the three is the cause for the milder phenotype and longer survival. Hence, further fluorescent *in situ* hybridization (FISH) studies are required to find out exactly which of these three has occurred in our patient. In our patient, we could not do FISH studies, and this is the limitation of this paper.

CONCLUSION

Importance of this case report is in the rarity of this karyotype and prolonged survival when compared to complete trisomy 18.

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