Coexisting Edward syndrome and Klinefelter syndrome

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Case report

A 40 year old woman, admitted to the Colombo South Teaching Hospital at term, delivered a baby boy with intrauterine growth retardation (IUGR-birth weight 2.16kg), microcephaly (head circumference 31cm) and normal length (46cm). He had hypertelorism, elongated head, narrow bifrontal diameter, prominent occiput, low set dysplastic ears, micrognathia, long thin limbs, overlapping fingers, hypoplastic nails, clinodactyly, bilateral talipes equinovarus (TEV) deformity, rocker bottom feet and bilateral cryptorchidism with normal size phallus (Figures 1A-1E).

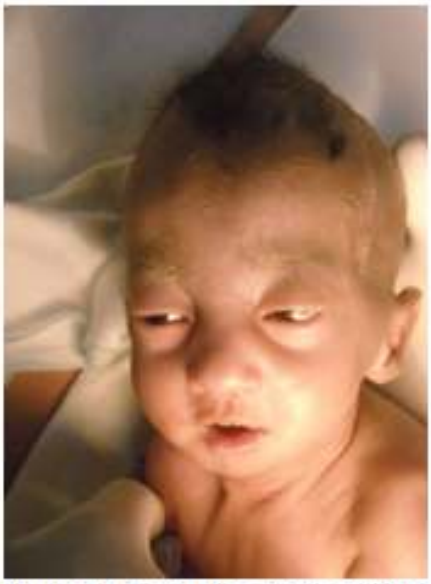

Figure 1A: ***Facial dysmorphism***

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Figure 1B: ***Overlapping fingers***

Figure 1C: ***Limited hip abduction & TEV***

Figure 1D: ***Dysplastic low-set ear***

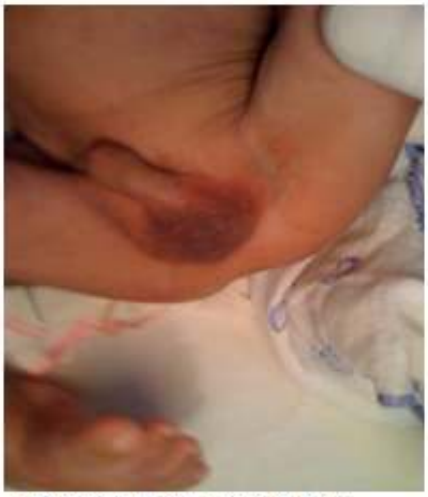

Figure 1E: ***Cryptorchidism***

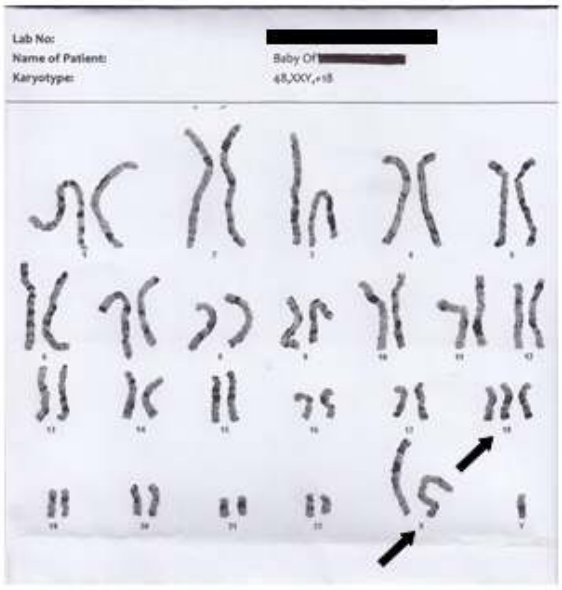

Figure 2: ***Karyotyping – 48 XXY+18***

Table 1

Comparison of clinical features of Edward syndrome, Klinefelter syndrome and present case[4]

	Edward syndrome	**Klinefelter syndrome**	**Present case**
Head/Skull	prominent occiput, long skull, small biparietal diameter of skull	brachycephalic	prominent occiput, long skull, small biparietal diameter of skull
Ears	dysplastic, low-set	normal or slight dysplasia	dysplastic, low-set
Eyes	narrow palpebral fissures, ptosis microphthalmia, hypotelorism /hypertelorism,	Unremarkable	Hypertelorism , narrow palpebral fissures
Nose	broad nasal bridge	Unremarkable	broad nasal bridge
Mouth	small mouth, micrognathia, narrow high palate, short upper lip	Unremarkable	micrognathia
Growth	IUGR, short stature, microcephaly	Normal length at birth, taller than XY males, normal head circumference	IUGR, microcephaly, normal length
CVS	VSD, PDA, single umbilical artery	Unremarkable	VSD, PDA
Abdomen/GIT	inguinal/umbilical hernia, Meckel diverticulum, diaphragmatic hernia	Unremarkable	Normal
Renal	horseshoe kidney, hydronephrosis, hydroureter	Unremarkable	normal
Neurological	Severe psychomotor retardation	psychosocial adjustment problems	Severe psychomotor retardation
Musculoskeletal	clinodactyly, overlapping fingers, small narrow pelvis, limited hip abduction, rocker bottom feet, TEV	altered body proportion (US/LS < 1), long limbs, vertebral collapse with osteoporosis, mild elbow dysplasia, scoliosis, clinodactyly, radioulnar synostosis	long limbs, overlapping fingers, small narrow pelvis, limited hip abduction, rocker bottom feet, clinodactyly, TEV
Genitalia	cryptorchidism, micropenis	cryptorchidism, normal penis	cryptorchidism, normal penis
Outcome	poor: often die of cardiac or respiratory problems	relatively good, normal life span, incomplete virilization	Poor, died at 4 months

He had a systolic murmur with persistent respiratory distress and chest radiographic evidence of cardiomegaly. 2D echocardiogram revealed a large ventricular septal defect (VSD), a double outlet right ventricle and a moderate size patent ductus arteriosus (PDA) with moderate pulmonary hypertension. Ultrasound scans of the brain and the abdomen were normal. Karyotyping revealed a chromosomal pattern of 48 XXY+18 confirming coexistent Edward and Klinefelter syndromes in this baby (Figure 2)

He needed prolonged hospital stay due to recurrent infections, heart failure and severe failure to thrive, finally succumbing at four months of age in spite of maximal medical and supportive care. Parents were provided genetic counseling.

Clinical features of Edward syndrome, Klinefelter syndrome and the present case are shown in Table 1.

Discussion

Aneuploidy is the presence of abnormal numbers of a particular chromosome. Down syndrome (+21) is the commonest aneuploidy encountered in clinical practice. Rarer aneuploidies include Edward syndrome (+18), Patau syndrome (+13), Turner syndrome (45X0) and Klinefelter syndrome (47XXY).

Double aneuploidy is the coexistence of two aneuploidies involving two different chromosomes in one person. These combinations can be either two different autosomes (48+18+21, 48+13+21, 48+13+18) or an autosome and a sex chromosome (48 XXY+21, 48 XYY+18, 46 X0+21). Occurrence of double aneuploidies is rarer than single aneuploidies and hence their exact incidence is not known[1]. Majority of these pregnancies are terminated as miscarriages[2]. In one study 2.18% of miscarriages had double aneuploidies[3]. These miscarriages usually contain nonviable trisomies of chromosomes 2, 8, 15, 16[2] whereas live born double aneuploidies bear combinations of sex chromosomes and autosomes of 13, 18, 21[2].

Coexistent Edward and Klinefelter syndromes are caused by double aneuploidy of chromosome 18 and sex chromosome X (48 XXY +18). Up to date only 14 cases have been reported worldwide[1]. To our knowledge this is the first reported case of Edward and Klinefelter syndrome in Sri Lanka.

When these two conditions coexist clinical features of Edward syndrome predominate[4] and it is difficult to diagnose Klinefelter syndrome clinically without karyotyping. In our case all features including dysmorphism, cardiovascular, neurological and musculoskeletal are compatible with Edward syndrome while cryptorchidism and clinodactyly are common to both conditions. Only clinical features favouring Klinefelter syndrome were normal stature at birth, long limbs and normal penile length.

Extra chromosomes in aneuploidies are mostly maternal in origin and usually associated with advanced maternal age[2]. Furthermore, in double aneuploidies non-disjunction events involving 2 chromosomes can occur in different cell divisions either meiosis I or II[1,3]. Even though the parental origin of extra chromosomes and the level of cell division involving non disjunction are unknown in our case there is a clear association with advanced maternal age.

References

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