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Holoprosencephaly and Klinefelter Syndrome

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Holoprosencephaly (HPE) is a malformation that arises during the first 4 weeks of embryonic development (blastogenesis)^[1] caused by a failure or incomplete division of the prosencephalon into cerebral hemispheres. This defect is frequently associated with other facial anomalies such as anophthalmia, cyclopia, proboscis, midface clefting, hypertelorism, single maxillary central incisor, and absence of olfactory nerves or corpus callosum. It is a causally heterogeneous field defect caused by: 1) chromosome aberrations in particular trisomy 13^[2], partial deletion of the long arm of the chromosome 7, triploidy (69, XXY)^[3] and other recessive, dominant, or X-linked genes^[2] multifactorial causes. Klinefelter syndrome is the most common sex chromosome abnormality in men and boys, with a reported prevalence of 0.1% to 0.2% in the general population and of up to 3.1% in the infertile male population^[4]. Since the first report in 1942, Klinefelter syndrome has been characterized by small, firm testes and varying symptoms of androgen deficiency including gynecomastia, hypogonadism, infertility^[5] immaturity of external genitalia. Although additional X chromosomes are predominantly inactivated, the entire chromosome region is not inactivated, and inactivated region of the additional X chromosome is likely to be responsible for the clinical features^[6].

A male neonate was born at full term (38 weeks of gestation). His mother was nullipar and his Apgar scores were 5 and 7 at 1 and 5 min, respectively. He was the first child of healthy and nonconsanguineous parents. The family history

was negative for abortion and genetic abnormalities. The pregnancy was uneventful. The antenatal ultrasonography revealed microcephaly and cleft deformity.

Assessment after birth showed body weight of 3200g (25-50percentile), head circumference of 29.5cm (<10 percentile) and body length of 50cm (25-50percentile). His parents were both healthy, with the ages of his father and mother 25 and 30, respectively.

On physical examination, phenotypic abnormalities including bilateral cleft lip/palate and low-set ears, hypotelorism, exophthalmos, one sided nostril in nose without columella, absence of premaxilla, underdeveloped septum and vomer (arhinia) with microcephaly were observed (Fig. 1). The other physical and laboratory findings were normal in the cardiac, ventricular, and genitourinary systems. In the neurologic evaluation he has generalized epilepsy that are controlled with 15 mg Phenobarbital BID. His genitalia were normal without ambiguity, and both testes were palpable outside the inguinal rings. Cytogenetic analysis was conducted and the karyotype of peripheral blood lymphocytes was 47,XXY/46,XY. The head CT scan revealed colpocephaly and overriding in parietooccipital sutures (Fig. 2). Klinefelter syndrome may remain largely undiagnosed, unless there are typical clinical features and cytogenetic abnormalities. Most 47,XXY neonates appear normal at birth, and

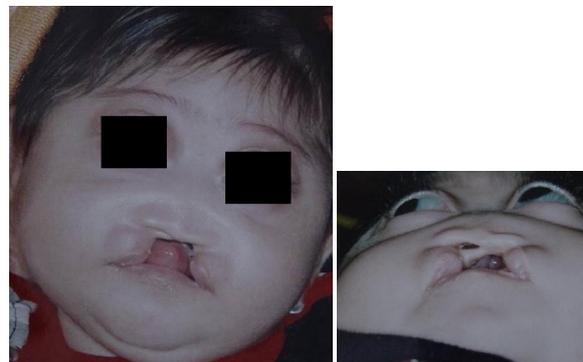


Fig. 1: Phenotypic abnormalities in frontal (left) and basal (right) view of a child with holoprosencephaly and klinefelter syndrome

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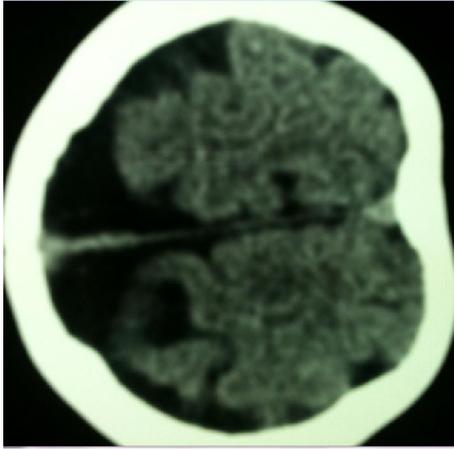


Fig. 2: brain CT scan of the holoprosencephalic child with klinefelter syndrome



Fig. 3: Postoperative view of the holoprosencephalic child after repairing his cleft lip and cleft palate

boys with Klinefelter syndrome have variable phenotypic features without obvious facial dysmorphism^[5]. There are three major variants of Klinefelter syndrome including 48,XXX^Y;48,XXYY; and 49,XXXXY^[7].

Phenotypic abnormalities which may be observed in variant Klinefelter syndrome include: microcephaly with short stature, hypertelorism, flat nasal bridge, fifth-finger clinodactyly, bifid uvula, heart defect, radioulnar synostosis and genu valgum^[7]. To the best of our knowledge, cleft palate has been described in only one case with the 49XXXXY/46XY karyotype and one case with 48XXXXY/46XY karyotype^[8]. Therefore cleft palate might be a rare clinical presentation of the variant Klinefelter syndrome. Cleft palate is a common birth defect and is considered to be a multifactorial condition in which genetic predispositions interplay with environmental factors^[9]. We describe a case of variant Klinefelter syndrome with 48XXXXY/46XY mosaicism and cleft palate. There were 2 cases of cleft palate with variant types of Klinefelter syndrome reported in the past. Our case entered in cleft workup after initial managements and genetic studies. We repaired his cleft lip and cleft palate in 2.5 and 12 months respectively (Fig. 4). One sided nostril and short clumella were reconstructed in combination with revision surgery. He was admitted in children hospital several times because of respiratory infections and his dismorphic face such as exophthalmia and midface growth retardation which needs to several surgeries to repair in the future. To conclude it seems that cleft palate might

be a rare clinical presentation of the variant Klinefelter syndrome.

Key words: Holoprosencephaly; Klinefelter's Syndrome

References

1. Opitz JM. Entwicklungsstörungen des Menschen. *Monatsschr Kinderheilkd* 1991;139(5):259-72.
2. Lehman CD, Nyberg DA, Winter TC 3rd, et al. Trisomy 13 syndrome: prenatal US finding in a review of 33 cases. *Radiology* 1995;194(1):217-22.
3. McGahan JP, Nyberg DA, Mack LA. Sonography of facial features of alobar and semilobar holoprosencephaly. *AJR Am J Roentgenol* 1990;154(1):143-8.
4. Philip J, Lundsteen C, Owen D, et al. The frequency of chromosome aberrations in tall men with special reference to 47, XYY and 47,XXY. *Am J Hum Genet* 1976;28(4):404-11.
5. Lanfranco F, Kamischke A, Zitzmann M, et al. Klinefelter's syndrome. *Lancet* 2004;364(9430):273-83.
6. Wakako O, Yasuhiro T, Atsushi N, et al. Mosaic tetrasomy 9p case with the phenotype mimicking klinefelter syndrome and hyporesponse of gonadotropin-stimulated testosterone production. *Kobe J Med Sci* 2007;53(4):143-50.
7. Visootsak J, Aylstock M, Graham JM Jr. Klinefelter syndrome and its variants: an update and review for the primary pediatrician. *Clin Pediatr(Phila)* 2001;40(12):639-51.
8. Mina H, Hyoun Ch Cho, Lee KM, et al. Cleft Palate in a Rare Case of Variant Klinefelter Syndrome With 48,XXX^Y/46,XY Mosaicism. *Cleft Palate Craniofac J* 2009;46(5):555-7.
9. Aldred MA. Cleft lip and palate: new genetic clues. *Trends Mol Med* 2001;7(12):539-40.