

G.S. Medical College and K.E.M. Hospital, Bombay for granting permission to publish this case report.

#### REFERENCES

1. Alford CA. Chronic congenital and perinatal infections. *In: Neonatology, Pathophysiology and Management of the Newborn*, 3rd edn. Ed. Avery GB. Philadelphia, J.B. Lippincott Co, 1987, pp 874-916.
2. King A, Claude M, Rodin P. Congenital syphilis. *In: Venereal Diseases*, 4th edn. Tonbridge, Whitefrairs Press, 1986, pp 104-132.
3. Robinson RCV. Congenital syphilis. *Arch Derm* 1969, 99: 599-610.
4. Fiumara NJ, Lessells S. Manifestations of late congenital syphilis. *Arch Derm* 1970, 102: 78-83.
5. Caffey J. Infections. *In: Pediatric X-ray Diagnosis*, Vol 2, 7th edn. Chicago, Year Book Medical Publishers, 1978, pp 1407-1442.
6. King A, Claude M, Rodin P. Syphilis. *In: Venereal Diseases*, 4th edn. Tonbridge, Whitefrairs Press, 1986, pp 1-14.

---

## 48 XXXY Variant of Klinefelter Syndrome

**G.L. Gupte**  
**S.V. Kotvaliwale**  
**P.V. Mahajan**  
**A.S. Kher**  
**S.P. Kanade**  
**8.A. Bharucha**

In 80% of the cases, the karyotype in Klinefelter syndrome is 47 XXY. In the

---

*From the Genetic Clinic, Department of Pediatrics, Seth G.S. Medical College and K.E.M. Hospital, Parel, Bombay 400 012; and Genetic Diagnostic Centre, 203, Bombay A/C Market, Bombay 400 034.*

*Reprint requests: Dr. Burjor A. Bharucha, Professor of Pediatrics, K.E.M. Hospital, Parel, Bombay 400 012.*

*Received for publication: November 30, 1992;  
Accepted: November 4, 1994*

remaining 20% chromosomal variants including mosaicism is seen. Among the variants, 48 XXXY is the commonest observed<sup>1</sup>. The most significant effect of the additional X chromosomes on the phenotype is an increase in somatic malformations and mental retardation<sup>(2)</sup>. Dysmorphic features are very mild in 47 XXY, but are multiple and widespread in 49 XXXXY while 48 XXXY represents the intermediate level of the spectrum<sup>(2,3)</sup>. The abnormality is rare and features overlap with many chromosomal syndromes, notably Down's syndrome. This communication documents 48 XXY variant of Klinefelter syndrome.

### Case Report

An 11 month old boy born of a non-consanguineous marriage was referred for delayed milestones and blindness. Paternal and maternal ages were 25 and 21 years, respectively. A detailed history including family history of infertility, mental handicap, past abortions and

still births was recorded which was noncontributory. Height and weight percentiles, upper segment to lower segment ratio, hand and foot lengths, interpupillary distance, internipple distance, stretched penile length and testicular length were recorded. External eye examination, fundoscopy, brainstem evoked response audiometry (BERA), skeletal X-rays, ultra sonography of the abdomen, buccal smear for Barr body, karyotype of the peripheral blood leucocytes and dermatoglyphics were done. Developmental age assessment was done by the Clinical Psychologist.

He had delayed milestones, short stature, hypoplasia of the supraorbital ridges, bushy eyebrows, medial flare of the eyebrows, hypertelorism, inner epicanthal folds, upward slant to the palpebral fissures, left divergent squint, low set ears, micrognathia, high arched palate, thin upper lip, micromelia of hands and the feet, bilateral simian

crease, clinodactyly, low dermal ridge count on hands, small penis, small undescended testes and a hypoplastic scrotum. Developmental age was 6 weeks. Fundii were normal. BERA did not reveal any hearing loss. X-ray of the hands demonstrated short middle phalanx of the fifth finger and X-ray of the pelvis revealed coxa valga. There was no evidence of radioulnar synostosis or elbow dysplasia. Ultra sonography of the abdomen revealed small testes in the inguinal canals.

Two X chromatin masses were observed in the interphase nuclei on the buccal smear. Karyotype revealed a uniform pattern of 48 XXXY in all the metaphases (*Fig. 1*).

#### Discussion

The dysmorphic features seen in this child overlap with those of Cornelia de Lange, mosaic Down syndrome, 3 duplication deficiency syndrome and

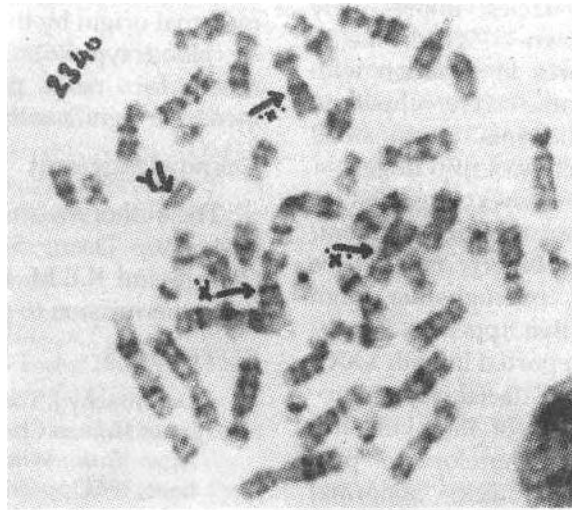


Fig. 1. Presence of three X chromosomes and single Y chromosome indicated by arrows

Klinefelter syndrome. Dysmorphic features common with Cornelia de Lange syndrome were short stature, microcephaly, bushy eyebrows, high arched palate, micrognathia, low set ears, micromelia of the hands and the feet, simian crease, undescended testes and small penis. However, long curly eyebrows with synophrys, hypoplastic nipples and characteristic lips and mouth, seen in all cases of de Lange syndrome were not observed in our patient(3). Since many of the phenotypic characteristics seen in this patient and in the de Lange syndrome are also seen in 3 duplication deficiency syndrome (duplication of the q 21-25 deletion p25-pter)(3,4), it was considered in the differential diagnosis. Mental and developmental retardation is a feature of both these conditions. Dysmorphic features in common with mosaic 21 trisomy were short stature, microcephaly with upslanting palpebral fissures, epicanthal folds, low set ears, clinodactyly, simian crease and small penis. Many poly ,X syndromes have facies impressively resembling Down syndrome(3). Dysmorphic features in common with Klinefelter syndrome were upper to lower segment ratio, small penis, small testes and clinodactyly of fifth finger.

The unusual features observed in this patient, but not reported in literature were bushy eyebrows, medial flare of the eyebrows, micrognathia, high arched palate and thin upper lip. Somatic malformations reported in both XXXY and XXXXY include facial asymmetry due to abnormalities of the skull and jaw, epicanthus, hypertelorism, protruding lip, short neck, abnormal elbows due to radio ulnar synostosis, other abnormalities of the radius and

ulna, clinodactyly, coxa valga and abnormalities of feet and toes. These abnormalities are similar in XXXY and XXXXY, but are much common in the latter. Radioulnar synostosis or other abnormalities of the radius and ulna were not observed in this patient; an otherwise frequent finding in many Poly-X syndromes(3). While reporting on two cases of 48 XXXY, Ferrier *et al.* commented on the inability to assign a specific set of dysmorphic criteria(5). The features seem to be intermediate in severity between XXY and XXXXY, which is in keeping with the view that every extra X chromosome imposes greater malformation(3,5).

The most likely explanation for 48 XXXY is non-disjunction occurring at both the first and second meiotic divisions of oogenesis. The result is an XXX ovum which is then fertilized by a Y bearing sperm. The absence of another cell line effectively rules out post-zygotic non-disjunction. The three X chromosomes have been proved to be of maternal origin by the parental study of Xg blood types(6). The risk of recurrence for next pregnancy is not increased significantly.

#### Acknowledgement

The authors wish to thank Dr. (Mrs) P.M. Pai, Dean, Seth G.S. Medical College and K.E.M. Hospital for granting us permission to publish this report.

#### REFERENCES

1. De Grouchy J, Tourleau G. Clinical Atlas of Human Chromosomes, 2nd edn. New York, Wiley Medical Publications, 1984, pp 392-395.
2. Emery AH, Rimoin LD. Principles and Practice of Medical Genetics, Vol 1, 1st

- edn. London, Churchill Livingstone, 1983, pp 208-209.
3. Jones KL. Smith's Recognizable Patterns of Human Malformation, 4th edn. Philadelphia, W.B. Saunders Company, 1988, pp 66-72.
  4. Goodman RM, Gorlin RJ. Atlas of the Face in Genetic Disorders, 2nd edn. St Louis, C.V. Mosby Company, 1977, pp 404-405.
  5. Ferrier PE, Ferrier SA, Pescia G. XXXY Klinefelter syndrome in childhood. Amer J Dis Child 1974, 127: 104-105.
  6. Greenstein RM, Harris DJ, Luzatti L, Cann HM. Cytogenetic analysis of a boy with XXXY syndrome-origin of the X chromosome. Pediatrics 1970, 45: 677-686.
-