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MULTIPLE XY SYNDROME: A CASE STUDY

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ABSTRACT

The present study is an account of the karyotypic analysis carried out in a three and half year old male child born to a young, healthy, non-consanguineous couple. Clinically the child had undescended testes (Cryptorchidism) with empty scrotal sac. It was an uneventful, full term delivery with no family history of congenital anomalies. Besides cryptorchidism, the child had developmental delay as well as mental retardation. Chromosome study was carried out to rule out the chromosomal cause, if any in the child having gross phenotypic anomalies. The karyotype of the child was found to be 49, XXXYY.

KEYWORDS: Cryptorchidism, Developmental Delay, Chromosome Study

INTRODUCTION

Sex chromosomal abnormalities especially that of the X-chromosome, have largely been associated with the development of reproductive system, however, abnormalities of the X and Y chromosomes have been held responsible for the birth of Klinefelter syndrome and its variant (Caldwell and Smith 1972; Robinson et al. 1979; Linden et al. 1995; Visootsak et al. 2001; Tartaglia et al. 2011). Although somatic malformations and mental retardation are more severe in the variants of Klinefelter syndrome, Majority of the cases remain undiagnosed till puberty when the clinical symptoms of androgen deficiency get manifested (Purnak et al. 2012). Children born with sex chromosomal abnormalities may have hypospadias, small phallus or cryptorchidism etc., but it is not always a feature of the Klinefelter syndrome and its variants (Lee et al. 2007; Visootsak and Graham 2006). Chromosomal evaluation is, therefore, warranted in all those children born with hypospadias, small phallus or cryptorchidism or any other abnormality of the external genitalia, so as to rule out the sex chromosomal abnormalities in these children.

MATERIALS AND METHODS

Case History

Three and half year old clinically diagnosed male child under study had phenotypic anomalies of the external genitalia (Figure 1) along with delayed neuromotor development milestone and mental retardation. To know the status of the testes, the child was subjected to abdominal ultrasonography. Though the testes were found located in the inguinal region and they had not descended in the scrotal sac (Figure 2). As a result of this, the scrotal sacs though had a rouge but they were empty from inside.

For cytogenetic study in the child under study, chromosome preparations were obtained from the cultured lymphocytes following the technique of Moorhead et al. (1960). Slides were prepared from the harvested lymphocytes using standard techniques whereas G-banding was done by using 10% trypsin following Benn and Perle (1992). Nearly 20-25 well spread metaphase plates were analyzed for ascertaining the chromosome number and a few of these metaphase plates were selected for the preparation of karyotypes using automated cytogenetic workstation (Olympus).

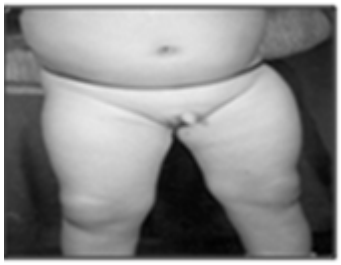

Figure 1: Abnormal Genitalia

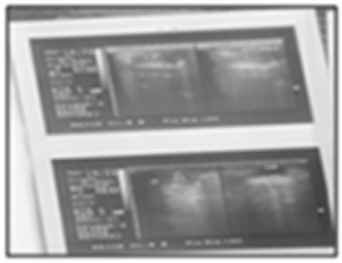

Figure 2: Abdominal Ultrasonograph Picture

RESULTS AND DISCUSSIONS

Cytogenetic study in children born with congenital anomalies, including those of the external genitalia, developmental delay and mental retardation becomes important to detect the chromosomal cause for the congenital anomalies and associated abnormalities these children are born with.

Well Spread metaphase plates were selected both for finding out the chromosome number and the preparation of karyotypes. Every metaphase plate contained 49 chromosomes i.e. 3 additional chromosomes were present in each one of the metaphase plate (Figure 3). To find out the nature of the additional chromosomes, some of the well spread metaphase plates were karyotyped.

Karyotypes prepared were found abnormal as every karyotype contained five sex chromosomes –XXXYY suggesting thereby the aneuploidy of both the X and Y chromosomes. Additional X and Y chromosomes were, therefore, held responsible for the congenital anomalies such as cryptorchidism, developmental delay and mental retardation in the child under study. On the basis of the number of X and Y chromosomes, the child was designated as a variant Klinefelter syndrome.

Klinefelter syndrome and its variants constitute a group of chromosomal disorder where one or more than one X / Y chromosome is added to the normal male karyotype, 46 XY. Although XXY is the most common karyotype, other karyotypes, though less common having been reported amongst the variants of Klinefelter syndrome are 48, XXYY; 48, XXXY; and 49, XXXYY by Caldwell and Smith (1972); Robinson et al. (1979); Bray and Hosephine (1963); Lecluse-van der Blit et al. (1974); Visootsak and Graham (2006); Linden et al. (1995).

The extra X as well as Y chromosome being responsible for the Klinefelter syndrome and its variant are also the leading cause of other phenotypic anomalies such as delayed milestone, mental retardation etc. (Kabra and Gulati 2003; Visootsak and Graham 2003). The extra X chromosome in Klinefelter syndrome and its variants has its origin either from meiotic non-disjunction in male or female gametogenesis whereas the extra Y chromosome arises during male gametogenesis. The likelihood of the extra X has been linked to the advancing maternal age (Visootsak and Graham 2003), but in the present case both the parents were below 30 years of age thus ruling out the influence of parental age on meiotic non-disjunction.

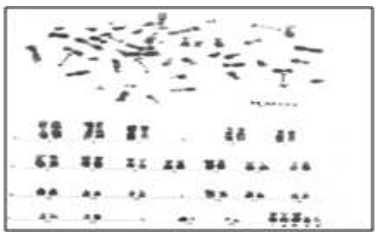

Figure 3: Complement and Karyotype

The number of extra X chromosomes do affect the physical as well as mental development as it increases with an increase in the number of X chromosome (Visootsak et al. 2001; Rovet et al. 1995). The case under study also had the delayed physical and mental development that may be attributed to the excess number of X chromosome as well as Y chromosome. Therefore, the more supernumerary sex chromosomes that exist, the more likely are the detrimental physical and mental findings (Chen 2003). Occasionally a finding of the cryptorchidism leads to the diagnosis of XXY child because XXY karyotype is nearly three times more frequent than in this group in the overall population (Topper et al. 1982; Lee et al. 2007) of the sex chromosomal abnormalities 48, XXYY, 49, XXXXY and 49, XXXYY have rarely been reported (Bray and Hosephine 1963; Lecluse-van der Bilt et al. 1974; Ratcliffe and Paul 1986; Robinson et al. 1979) and the present case is an addition to the existing data.

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