

Interstitial Deletion of Chromosome 10 with Microgenitalia and Gynecomastia

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Abstract

We describe an 18 year old male with an interstitial deletion. This was characterized by dysplasia of the genital organs, absence of axillary hair and sparse pubic hair and a female like physique with bilateral gynecomastia. Other clinical findings included severe mental retardation and minor anomalies, both of which were consistent with other reports. A review of the literature revealed 12 other cases of interstitial deletion of chromosome 10, 3 of which exhibited features of abnormal male sexual development. We conclude that there is an association between chromosome 10 and abnormal male sex development.

Introduction

The primary event in the determination of male and female sex is dependant on the presence or absence of the sex determining region of the Y chromosome (SRY). Recently a number of cases with chromosomal aberrations

and impaired sexual development have suggested the existence of genes, located on the X chromosome and other autosomes, that are necessary for male sexual determination. Impaired male sexual development and monosomy of 9p has been reported in a number of cases (Ogata et al. 1997). Similarly terminal 10q deletions appear to be associated with abnormal male genital development (Wilkie et al. 1993). Here we describe a patient with a de novo interstitial deletion of (10)(q21) presenting with hypogonadism. The features of other reported interstitial

10q deletion cases are reviewed. The proband was born at 39 weeks to a 32 year old mother and a nonconsanguineous 33 year old father. The patient has 2 older brothers both of whom are physically and mentally normal. The pregnancy and delivery were normal except for slight cyanosis which was noted postpartum. Birth weight was 3300g, length was 50 cm and head circumference was 33 cm. In the neonatal period a right torticollis was noticed which resolved without intervention after 6 months. Acquisition of developmental milestones was

retarded. Head control was achieved at 6 months, first steps at 24 months and first spoken word at 24 was treated conservatively and by the age of 10 it had resolved completely. The patient also has a history of febrile convulsions which were first noticed at two and which continued until age 10.

On physical examination at 18 years, his weight was 55 kg, height 162 cm and head circumference 55 cm. Multiple craniofacial dysmorphia were noted. Head shape was plagiocephalic with frontal bossing. Ears were large and low set and strabismus divergens was noticed. He had a broad nasal bridge, a beaked and bulbous nose with small nostrils and a large and prominent philtrum. Other facial features included a cupid-bow upper lip, micrognathia and a flat maxilla (Fig. 1c). The patient presented with microgenetalia. Penile length was short measuring 4cm in length. Bilateral testis were less than the size of the tip of the small finger. There was no facial or axillary hair and pubic hair was sparse. He had a female like physique with rounded shoulders and bilateral gynaecomastia. Bilateral genu valgum and pes planus along with genu recurvatum of the left knee were noticed in the lower limbs. Upper limbs were slightly hypotonic and had mild muscle weakness. CT scan revealed small bilateral areas of calcification in the periventricular region of the frontal lobe. EEG recorded a basic rhythm of 8-9 Hz with many theta waves intermingled.

The patient presented as a pleasant, cheerful and sociable man. He communicated in two word sentences and had relatively good

comprehension. He scored 20 on the Tanaka-Binet IQ test which is the Japanese equivalent of the Binet test. Presently he lives at home with his parents and attends a sheltered workshop. He is independent in all activities of daily living and in the use of public transport.

CYTOGENETIC AND MOLECULAR ANALYSIS

Chromosome analysis performed on 30 peripheral blood lymphocytes by the G banding technique revealed an interstitial deletion of 10q chromosome in all 30 cells. By high-resolution G-Banding the breakpoints were identified (Fig.2) and we can describe the karyotype thus: 46,XY,del(10)(q11.23q22.1).

The parental chromosomes were normal. Permission was not granted to analyse his brothers chromosomes. Two FISH methods were performed. The first method used the probe HK1 and described the following karyotype 46,XY,del(10)(q11.23q22.1).ish del(10)(HK1-).

The second method used the probe wcp10 and described the following karyotype 46,XY,del(10)(q11.23q22.1).ish del(10)(HK1-,wcp10+).

The SRY gene was amplified by polymerase chain reaction, cloned and sequenced and found to be normal.

Endocrine investigation was consistent with gonadal failure with a raised FSH of 17mIU/ml (normal range 2.9-8.2mIU/ml). LH was 5.0mIU/ml (normal range 1.8-5.2mIU/ml). In response to a standard LH releasing hormone test LH rose markedly to 43mIU/ml. Basal

testosterone level was 561ng/dl (normal range 250-1100ng/dl).

Discussion

We have described an 18 year old male with an interstitial deletion of 10q associated with psychomotor retardation, hypotonia, microgenitalia and dysmorphia. Some 12 cases of interstitial 10q deletion have been described and are summarised in table 1. Common findings include psychomotor retardation, hypotonia, malformation and displacement of ears, telecanthus or hypertelorism and heart murmurs or defects. A comparison of these 12 cases and our case failed to show sufficient consistent features to suggest a recognizable clinical syndrome. Similarly no correlation could be found with the size of the chromosome deletion and increasing severity of their clinical presentation and/or major malformations. Six cases including this case involve the q11 region, with only 2 features common to all 6 - hypotonia and low set and/or malformed ears.

The production of the male phenotype is dependant on the presence of 2 hormones from the testis - antiMullerian hormone which is produced by the Sertoli cells and dihydrotestosterone produced by the Leydig cells which results in virilisation of the external genitalia. This case presented with micropenis and small testis . Endocrinological results were consistent with gonadal failure . These findings suggest that the fault lay in the development of the gonads post production of antiMullerian hormone and testosterone and occurred after the critical period where insufficient androgen

production resulted in decreased virilisation of the external genitalia.

Recently a number of cases have highlighted the role of genes on both the X chromosome and autosomes in the determination of male sex. Four known cases of interstitial deletion of chromosome 10, including this case, have reported abnormalities in male sexual development. Van de Vooren et al.(1983) present a 5 year old male with bilateral cryptorchidism , Ray et al. (1980) present a 1 year old boy with a small penis and Farrell et al.(1993) describe a 9 month old male with a small penis. Similarly, terminal deletions of chromosome 10 have been consistently associated with abnormal male genital development ranging in degree from complete sex reversal to micropenis and cryptorchidism (Wilkie et al. 1993, Zatterale et al. 1984, Teyssier et al. 1992). From this study we conclude that interstitial deletions of chromosome 10 are also associated with abnormal male genital development and add to the growing body of evidence which suggests a role for autosomes in the complex process of sexual development.

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