Gonadal Dysgenesis Due to Isochromosome Formation of Long Arm of X Chromosome

Asish Kumar Basu*, Rudrajit Paul**, Ramtanu Bandyopadhyay***, Srabani Chakrabarti****

Abstract

Isochromosome involving the long arm of X chromosome is a rare structural rearrangement of the X chromosome, leading to Gonadal dysgenesis. These patients present as phenotypic females with amenorrhea and growth failure. Often other associated features like endocrine abnormalities and skeletal deformities are found. They are chromatin positive cases and are only diagnosed by karyotyping. Hashimoto’s thyroiditis is a rare association with isochromosome X.

Introduction

Isochromosome involving the long arm of X chromosome is a structural rearrangement of the X chromosome accounting for 15% cases of Gonadal dysgenesis. These patients present as chromatin positive cases. These cases often present with amenorrhea. A case of Gonadal dysgenesis due to isochromosome of X is reported here.

Case Report

An 18 year old girl attended endocrinology OPD for evaluation of primary amenorrhea. She had a history of hypothyroidism. She had stunted growth compared to the peers. She was born out of a non-consanguinous marriage and there was no similar family history of primary amenorrhea. Physical examination revealed unambiguous female phenotype with short stature (142 cm; less than 3rd percentile for age). There were short 4th metatarsals, with mild Ptosis of right eye. There were no evidences of shield chest, webbing of neck or cubitus valgus. Her breast development was tanner stage 5 and axillary and pubic hair was tanner stage 3 / 4 (Figure 1). Examination of cardiovascular system revealed no evidence of bicuspid aortic valve or coarctation of aorta; there were no signs of wasting, chronic disease, tuberculosis, or hemolytic anemia. She also had a firm goiter with clinical features of hypothyroidism.

Laboratory investigations revealed: hemoglobin 10 gm/dl, Fasting Blood Sugar and Post Prandial Blood Sugar were normal. Serum fT3, fT4 and TSH were 0.8 ng/ml, 3.6 microgm/dl and 24 μU/ml (normal: 0.34 -4.25) respectively, consistent with primary hypothyroidism. Anti- TPO was present in >1:400 dilution and FNAC from thyroid gland showed features consistent with hashimoto thyroiditis. Serum LH and FSH levels were 42 mIU/ml (normal: 2-15) and 70 mIU/ml (normal: 3-20) respectively determined by radioimmunoassay. Serum GH levels following insulin hypoglycemia revealed no abnormality. Pelvic sonography revealed bilateral streak gonads and hypoplastic uterus. Buccal smear was positive for sex chromatin. The karyotype was 46, XXqi i.e. an X chromosome consisting of two long arms and no short arms (Figure 2). This was found in all the cells studied. The karyotype analysis of the parents was normal.

Discussion

Patients with long arm X isochromosome invariably present with short stature and streak gonads as in our case. Some
of them may menstruate, although most patients like ours, present with primary amenorrhea. The somatic stigmata of Turner’s syndrome are less evident. Features that are commonly present include short stature, overweight, scant secondary sexual characteristics, sterility, strabismus, nevi and cubitus valgus. Coarctation of aorta and lymphedema of the hands are conspicuously absent, as in the present case. Slight webbing of neck has been occasionally reported. Hashimoto thyroiditis, impaired glucose tolerance and inflammatory bowel disease have been reported to occur more frequently in patients with long arm X isochromosome. Our patient had hashimoto thyroiditis with clinical hypothyroidism which is a rare association with isochromosome X with Gonadal dysgenesis.

**Conclusion**

In cases of Gonadal dysgenesis it is important to carry out karyotyping and endocrine evaluation to know the underlying pathology. This helps in proper hormonal therapy and also genetic counseling.

**References**