Case Report

A case of primary amenorrhea with 46+XY genotype from Kashmir Valley

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Primary amenorrhea is one of the common reproductive disorder affecting females. It leads to the absence of menarche in the reproductive age group in females and/or complete absence of reproductive organs. There are many causes which lead to PA, including genetic aberrations which are the leading factors.

Key words: Amenorrhea, genotype, Karyogram

Introduction

Primary amenorrhea (PA) is defined by the absence of attainment of menarche by the age of 16-18 years. PA occurs in 1-3% of women in the reproductive age group. Various factors such as anatomical, genetic and hormonal factors reported to influence PA. We report the 46+XY genotype case of PA with tall thin stature coupled with male dominant facial features.

Case Report

A 19-year-old female student residing in central urban district of Kashmir was referred to our genetic counseling center by the local Gynecologist. The patient had been diagnosed with failure to reach menarche and PA. Her height was 5.8 ft and weight 54 kg. Secondary sexual characters of the patients were also under developed, with breast buds instead of well-developed ones. Interview with the patient revealed the female gentile organs. Furthermore, patient was a product of consanguineous marriage – both parents were paternally related [Figure 1]. The patient was the first among four children arisen from the marriage and only one to survive the gestation period prior to three consecutive abortions. The facial features of the patient were similar to those of male individuals with high rise brows, prominent fore head and jaw line. The patient was advised to undergo regular ultrasonographic (USG) examination. USG of the patient revealed the complete absence of the uterus and small atretic ovaries [Figure 2]. It also revealed mullarian agenesis. The hormonal profile of the patient revealed the lower levels of follicle-stimulating hormone (15.15 mIU/ml), but elevated levels of luteinizing hormone and prolactin 33.71 mIU/ml and 5.6 mIU/ml respectively. Later on estradiol of the patient was found to be <12.5 ng/ml, which is in the same range as in menopausal adult. Our genetic counselors diagnosed the patient with possible turner syndrome clinically and advised cytogenetic analysis.

We carried out the cytogenetic evaluation of the patient for the karyotyping to detect the possible chromosomal abnormality. Cytogenetic analysis was carried out for patient as well as parents using blood as the source of chromosomes. Whole blood was cultured in 5 ml of Roswell Park Memorial Institute 1640 medium with 10% fetal calf serum. Lymphocytes were stimulated by adding phytohemagglutinin. Cultures were incubated at 37°C for 48-72 h. The cell proliferation was arrested by

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colchine/colcemid, slides were prepared after hypotonic treatment and fixation with Carnoy's fixative. G-banding was done with trypsin and metaphase plates were scored and karyotyped using an image analysis system. The chromosomal evaluation revealed the female to possess only one X chromosome instead if two and the presence of one Y chromosome. Thus, genotype of the patient was a confirmed male one [Figures 3 and 4].

Discussion

PA has been defined as the clinical condition identified by the complete absence of menstrual cycles in women.[1] It is the 6th major cause of female infertility worldwide.[2] This disease manifests due to several different causes, which include endocrine imbalance, gonadal anomalies, genetic disorders coupled with the environmental factors.[3] Number of studies carried out to identify the cause of this disease have implicated chromosomal aberrations in about 50% of the cases.[3,4] However, in India Vijayalakshmi *et al.* reported the 27.8% of the PA patient to contain abnormal karyotype.[3] A similar study by Anupam *et al.* reported 25.6% of the patients of amenorrhea having abnormal chromosomal constituents.[5]

Consanguinity has been reported to be the primary reason resulting in the homozygous condition for recessive autosomal/deleterious genes.[6] The incidence of consanguinity reported in India is 5-60% and uncle-niece and first cousin are the more commonly occurring relationships in Indian population.[7] In a study by Amudha *et al.*, consanguinity was seen in 427 cases (29.14%) out of total 1465 patients with suspected genetic etiology, 305 cases were confirmed to have chromosomal abnormalities, among them 240 (78.7%) had numerical abnormality and 65 (21.3%) had a structural abnormality.[8]

Our case finding was in accordance with the reported ones from India[3] as well as from Singapore.[1] Both of these researchers have reported female with 46 XY karyotype.

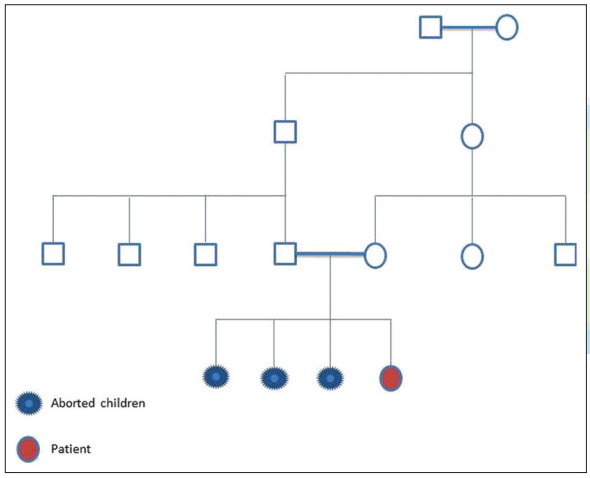

Figure 1: Pedigree chart of the patient showing single ancestor

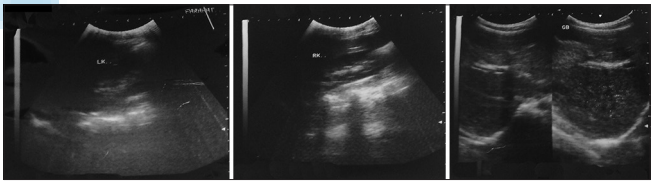

Figure 2: Ultrasonographic images of patients' abdomen. Uterus is not visible

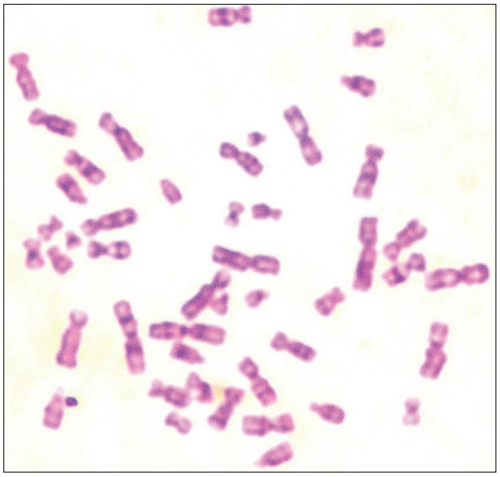

Figure 3: Proband stained and labeled metaphase spread of the patient

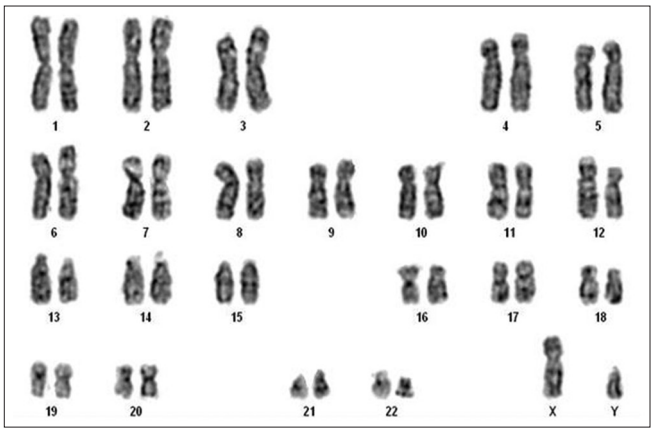

Figure 4: Karyogram of the patient showing 46, XY genotype

Hence, as suggested by Amudha *et al*., at the time of counseling a counselor should kept in mind, that consanguinity may have a higher risk than the general population risk on chromosomal abnormality. Keeping this thing in mind cytogenetic investigations should be made readily available for patients with genetic anomalies who have the history of consanguinity. These are essential in PA cases to detect sex chromosomal abnormalities, undetected mosaicism and multiple chromosome aberrations, which help in appropriate genetic counseling and management of the disease.

References

1. Ten SK, Chin YM, Noor PJ, Hassan K. Cytogenetic studies in women with primary amenorrhea. Singapore Med J 1990;31:355-9.
2. Meenakshi S, Balasubramanyam V, Rajangam S. Dermatoglyphics in amenorrhea – Qualitative analysis. J Obstet Gynecol India 2005;56:250-4.
3. Vijayalakshmi J, Koshy T, Kaur H, Mary FA, Selvi R, Parvathi VD, *et al.* Cytogenetic analysis of patients with primary amenorrhea. Int J Hum Genet 2010;10:71-6.
4. Franks S. Primary and secondary amenorrhoea. Br Med J (Clin Res Ed) 1987;294:815-9.
5. Anupam K, Surbhi M, Singh JR. Cytogenetic analysis in cases with sex anomalies. Int J Hum Genet 2004;4:167-71.
6. Master-Hunter T, Heiman DL. Amenorrhea: Evaluation and treatment. Am Fam Physician 2006;73:1374-82.
7. Mueller RF, Young ID. Elements of Medical Genetics. 11th ed. Edinburgh: Churchill Livingstone; 2001. p. 100-245.
8. Amudha S, Aruna N, Rajangam S. Consanguinity and chromosomal abnormality. Indian J Hum Genet 2005;11:108-10.

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