PHENOTYPIC, CYTOGENETIC AND ENDOCRINAL STUDY OF GONADAL DYSGENESIS

by

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Introduction

Since the time of discovery by Ford *et al* in 1959 that individual of the Turner phenotype possesses a single X Chromosome, a spectrum of cytogenetic abnormalities has been described with rudimentary streak gonads (McDonough *et al*, 1977). The more recent availability of immuno-reactive Gonadotropin and the expanded use of laparoscopy/laparotomy have enabled the identification of increasing number of cytogenetically and phenotypically normal individual with rudimentary streak gonads.

The precise relationship between 46XX female with ovarian failure and those with abnormal sex chromosomes remains to be clarified. This entire group of patients with normal chromosomes or CCOF (Chromosomally competent ovarian failure) and those with abnormal chromosome or CIOF (Chromosomally incompetent ovarian failure), tend to be characterised as patient with gonadal dysgenesis or rudimentary streak gonads.

Material and Methods

Two hundred and five women attending the gynaecological Endocrine Clinic in the department of Obstetric & Gynaecology, Post Graduate Institute of Medical Education & Research, Chandigarh, India, during the period from January 1979 to December 1980 were selected for the study.

The clinical evaluation included detailed history and examination, routine blood studies, bone age determination, thyroid assessment with T_3,T_4 and TSH, Prolactin assay, plasma testosterone, plama estradiol, serum FSH and serum LH determinations by double antibody homologous radioimmunoassays. Cytogenetic sudies were made from buccal smear for sex chromatin and from lymphocyte culture for karyotyping from peripheral blood.

IVP was performed to rule out renal malformations associated with ovarian failure.

Results

There were 45 cases of gonadal dysgenesis with ovarian failure during the above mentioned period. Clinically and cytogenetically these 45 cases fell into 2 distinct groups. Group I consisted of patients with abnormal chromosomal constituents and ovarian failure (CIOF). The second group consisted of patients with normal chromosomal constituents and ovarian failure (CCOF).

Group-I CIOF: There were 10 patients in this group.

These patients had heights ranging between 133-155 cms. Only 1 of them had

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experienced some menstrual life. The cytogenetic findings in these patients with limited ovarian functions were as follows: 45X/46XX in 5 cases, 45X/46XY in 1 case, and 45X in 4 cases. The most frequent single cell-line abnormality was 45X. One patient from this group showed Grade-II hirsutism with mosacism (45X/46XY). In 5 of these patients, the secondary sex characters were underdeveloped, while in the rest had fairly well developed secondary sex character.

Group-II CCOF

There were 35 patients in this group. These patients had normal 46XX or 46XY chromosomal compliments. They had heights ranging from 152-172 cms and 23 of them had experienced some menstrual life. There were 6 patients who had had pregnancies prior to the inception of ovarian failures. Only 1 case had 46XY chromosome but without any evidence of masculinisation. There were 4 cases of Grade-II hirsutism (Garn, 1951) with chromosomal compliments of 46XX.

Serum FSH in all cases ranged from 40.9-91.5 miu/ml with a mean of 66.1 miu/ml. Serum LH values ranged from 14.8-70.0 miu/ml with a mean of 42.4 miu/ml.

Gonadal visualisation and biopsy by laparotomy was performed in 10 cases from both groups. Gonadal morphology was consistently rudimentary streak gonads without any histological evidence of primordial follicles.

Discussion

A spectrum of sex chromosome karyotype ranging from 45X to 45X/46XX and 45X/46XY have been described in patient with ovarian failure. These patients were termed as chromosomally incompetent ovarian failure (Mc Donough *et al* 1977). Short stature (less than 145 cm) is the principal findings in these individuals. To the contrary, the majority of patients with ovarian failure and 46 XX or 46 XY Karyotype tends to be referred as having pure gonadal dysgenesis or chromosomally competent ovarian failure. They are grouped under gonadal dysgenesis because their morphology of gonad is similar to Turner's or quasi-Turner's syndrome. These patients are normal or of tall stature and secondary amenorrhoea is the presenting symptoms in 40% of these patients (Mc Donough 1978).

In the present study, there were in all 45 cases of gonadal dysgenesis with elevated serum gonadotropin (FSH more than 40 miu/ml) and only 10 (22.2%) of them belonged to Group-I CIOF with abnormal chromosomes. Primary Amenorrhoea was the presenting symptoms in all these cases except I (10.0%) who had experienced some menstrual life. All but 2 cases from these groups were short statured (less than 145 cms). Chromosomal analysis showed mosaic pattern in 6 (60.0%) cases (45X/46XX—5 cases and 45X/46XY—1 case). While single cell-line abnormality (45X) found in 4 (40.0%) cases. Only 1 case had male distribution of hair with Karyotype of 45X/46XX but in this case inclusion of small fragment of Y chromosome could not be excluded.

In contrast to Group-I or CIOF, Group II or CCOF formed the major component of gonadal dysgenesis in the present study. Thirty-five (77.8%) cases belonged to this group. They had their height ranging from 152-172 cm and 23 (65.7%) of them had experienced some menstrual life prior to inception of ovarian failure. Moreover, there were 6 patients who had pregnancies. Most common Karyotype observed in these cases was 46XX (35

cases i.e. 97.1%) while 1 (2.9%) case had 46XY Karyotype but without any evidence of masculinization. Plasma testosterone value in this case was 1.6 ng/ml. There were 4 (1.4%) cases with grade-II (Garn 1951) abnormal distribution of hair but all had 46XX Karyotype and normal value of plasma testosterone (0.2-0.8 ng/ml).

Serum FSH and serum LH in the present study were ranging from 40.9 miu/ml to 91.5 miu/ml (Mean 66.1 miu/ml) and 14.8 miu/ml to 70.0 miu/ml (mean 42.4 miu/ml) respectively. Gonadal visualization and biopsy by laparotomy were performed in 10 cases from both the groups. Gonadal morphology was consistetntly rudimentary streak gonads without any histological evidence of primordial follicles.

Summary

Present study include 45 cases of gonadal dysgenesis with elevated serum gonadotropin. Ten (22.2%) cases belonged to CIOF (chromosomally incompetent ovarian failure) and 6 (60.0%) showed mosaic pattern. Primary amenorrhoea was the presenting symptoms in all but 2 cases.

CCOF (chromosomally competent ovarian failure) formed the major component of 35 cases, 77.8%. Twenty-three (65.7%) of them had experienced some menstrual life prior to inception of ovarian failure. There were 6 cases who had preghancies. Most common karyotype observed were 46XX while 1 case had XY chromosome.

Gonadal biopsies were performed in 10 cases from both the groups. Morphology were consistent with rudimentary streak gonads and without any evidence of primordial follicles.

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