CLINICAL PROFILE OF 32 CASES OF PRIMARY AMENORRHOEA

by

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SUMMARY

Thirty-two cases of primary amenorrhoea admitted in Queen Mary's Hospital, Lucknow were evaluated by clinical examination, diagnostic laparoscopy and chromosomal and hormonal studies. Mullerian duct atresia was present in 62.5%, gonadal dysgenesis in 9.4%, and uterine hypoplasia in 12.5% patients. One patient had hypogonadotrophic hypogonadism, 1 premature ovarian failure, 1 Turner Syndrome, and 1 Polycystic ovarian disease. Two patients had genital tuberculosis. The study indicates that if the uterus is absent on clinical examination, further investigations are not required. But if the uterus is present, extensive investigations should be done to reach at a definitive diagnosis, as in some patients menstruation and even fertility may be obtained by proper treatment.

Introduction

Normal menstruation is the end result of coordinated activity of hypothalmo-pituitary-ovario-uterine axis. Menstruation is also influenced by other endocrine glands like thyroid, adrenal cortex and pancreatic islets. It is also dependent on normal genetic chromosomal pattern and well balanced metabolic state of the body. Amenorrhoea is not a disease but a symptom indicating organic or functional derangement at any level of these mechanism. Carefully planned investigations pertaining to all above factors are essential in pinpointing the exact etiological factor causing primary amenorrhoea. The present study was undertaken to study the etiology of patients of primary amenorrhoea coming to the Queen Mary's Hospital, Lucknow.

Material and Methods

A total of 32 patients of primary amenorrhoea admitted to the Queen Mary's Hospital, Lucknow between Oct. 1983 to Sept. 1984 were studied. Patients having true primary amenorrhoea after the age of 16 years were included. Twenty four patients were below 20 years, 6 between 21-25 years and 2 more than 26 years. Patients suffering from cryptomenorrhoea were not included.

The patients were evaluated clinically and particular emphasis was given to stature, development of secondary sex characters (according to Tanner's classification, Tanner 1962), and presence or

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absence of uterus. Diagnostic laproscopy was done to see the morphology and development of gonads. Hormonal profile was carried out (by standard methods using RIA) to assess the blood levels of FSH, LH, oestradiol and prolactin. Lastly the genetic make up of the patients was studied by examining the buccal smear for the presence of sex chromatin (Barr and Bertnam, 1949) and by culturing the peripheral blood lymphocytes for chromosomal analysis by modified method of Moorhead *et al*, 1960). To establish norms for Tanner's classification, 50 normal healthy girls at the age of 16 years were studied for secondary sex characters.

Results

Twenty three (71.9%) patients were married and majority of them were uneducated and had been left by their husbands resulting in a major social problem. Secondary sex characters of patients of primary amenorrhoea as compared to controls are shown in Table I.

Twenty eight (87.5%) had normal external genitalia. The secondary sex characteristics showed Tanner's stage III in 24 patients and stage II in 4 patients. Four patients had infantile external genitalia. Secondary sex characters of 3 of them could be classified as Tanner's stage I and 1 as Tanner's stage II.

TABLE I
Tanner's Classification in Two Groups Regarding Sexual Development

Tanner's Stage	Control (50)	Primary Amenorrhoea (32)
Stage I	1 (2%)	3 (9.38%)
Stage II	Nil	5 (15.62%)
Stage III	Nil	24 (75%)
Stage IV	49	Nil

Twenty patients of primary amenorrhoea had absent uterus. All of these patients had normal external genitalia. Amongst these laparoscopy revealed normal ovaries in 13 patients. In 1 patient only 1 ovary was visualised and in 2 patients both the ovaries were absent alongwith the absence of uterus. These 3 cases had normal sex chromatin and 46, XX chromosomal make up. Hormonal profile showed normal levels of all the hormones. These cases most probably had ectopic ovarian tissue. Two patients

TABLE II
Laparoscopic Appearance of Gonads in Primary Amenorrhoea

Gross Appearance of gonads	Absent Uterus (n=20) with normal ext. genitalia	Small Uterus	
		With normal ext. genitalia (n=8)	With Infantile ext. genitalia (n=4)
	No. of cases	No. of cases	No. of cases
Normal	13	4	—
Under developed	—	1	2
Polycystic Ovary	—	1	—
Tubo-ovarian mass	—	2	—
Cystic enlargement	2	—	—
Streak like	1	—	1
Only one Ovary present	1	—	—
Both ovaries absent	2	—	—
Laparoscopy not done	1	—	1

of mullerian aplasia had cystic enlargement of ovaries, 1 had high serum oestradiol suggesting the ovarian enlargement due to hyperoestrogenic state, the other had normal hormonal levels. One patient of mullerian aplasia had streak gonads, normal 46XX chromosomal make-up, and normal gonadotrophin levels but low oestradiol (Table II).

In 4 patients hypoplasia of uterus was present without any other abnormality. Gonadotrophins and prolactin levels were normal. Three of them also had normal oestradiol but 1 had low serum oestradial. Chromosomal make-up was 46XX in all these patients. These cases were treated by cyclical oestrogen therapy and regular menstruation resumed in one case.

Genital tuberculosis was the cause of primary amenorrhoea in 2 patients. In both the patients the uterus was small with bilateral tubo-ovarian masses and adhesions with the surrounding structures. Serum oestradiol was low in one case and normal in the other. The low oestradiol could have been due to supression of ovarian function by tuberculous pathology.

One patient had polycystic ovarian disease. The external genitalia was normal and the uterus was small in size. There were no signs of virilism but the vagina was not canalised. At laparoscopy, the uterus was 60% of normal size, both ovaries were enlarged 2" in diameter and covered by a thick white sheath. Her gonadotrophins were within normal range but oestradiol was low. Karyotype was 46XX. She was treated by vaginoplasty and subsequent clomiphene therapy.

One patient had underdeveloped ovaries and a small uterus; the karyotype was 46XX. Circulating gonadotrophins were high and oestradiol was low. She could have been a case of premature ovarian failure or resistant ovarian syndrome.

Of the 4 patients with infantile external genitalia, 1 had Turner's syndrome, 2 had pure gonadal dysgenesis and 1 had hypogonadotrophic hypogonadism. The patient of Turner's syndrome was short statured with Tanner's stage I development of secondary sex characters. She also had slight webbing of neck and cubitus valgus. Her uterus was hypoplastic and both the ovaries were very small and underdeveloped. Sex chromatin was 2-5% and chromosomal analysis could not be done.

The patient of hypogonadotrophic hypogonadism was short statured and her secondary sex characters belonged to Tanner's stage II. The vagina was canalised. At laparoscopy her uterus was small and both the ovaries were underdeveloped. Hormonal profile revealed low levels of FSH and oestradiol. Sex chromatin was 28%.

In both the cases of pure gonadal dysgenesis, the gonads were streak like. Secondary sex characters were Tanner's stage I. Hormonal status was hypergonadotrophic and hypo-oestrogenic. Prolactin levels were normal. Chromosomal analysis could not be done.

Discussion

In this study of 32 cases of primary amenorrhoea, 62.5% were due to mullerian duct atresia, 12.5% due to hypoplasia of uterus, 9.4% due to gonadal dysgenesis, 6.25% due to genital tuberculosis, besides 1 patient (3.1%) each of premature ovarian failure, hypogonadotrophic hypogonadism and polycystic ovarian disease.

We did not encounter a high incidence of chromosomal anamolies as noted by Jacobs *et al* (1961) (46.9%). Gun *et al* (1978) and Chakravarty *et al* (1979) have carried out larger studies in India on 217 and 262 cases of primary amenorrhoea respectively. While Gun *et al* (1978) found gonadal dysgenesis in 33% and Mullerian duct anomalies in 25% patients only. Chakravarty *et al* (1979) found that 77% patients were due to developmental defect of genital tract and only 13% patients due to chromosomal anomalies. Our study also favours a higher incidence of Mullerian duct anomalies as a cause of primary amenorrhoea in India. However, this high incidence could be due to the study being a hospital based one.

We have noted that patients with Mullerian aplasia may have associated anomalies like ectopic ovarian tissue and streak gonads. Chakravarty *et al* (1979) reported an incidence of 40% of such anomalies in patients with Mullerian duct anomalies. Whether such patients form a distinct syndrome or are just variations of Mullerian duct anomalies is not known.

The above study shows that only a very small group of patients with primary amenorrhoea are treatable. The cases of Mullerian duct anomalies are not curable in terms of menstruation and fertility but they can be helped by vaginoplasty for establishment of marital relationship if the vagina is not canalised.

The patients of gonadal dysgenesis, hypogonadotrophic hypogonadism and premature ovarian failure can only get the psychological satisfaction of menstruation by having withdrawal bleeding after cyclic hormone therapy.

Cases of genital tuberculosis with primary amenorrhoea carry a poor prognosis as ovaries and endometrium are grossly damaged. The outlook for menstruation and reproduction is good in women with polycystic ovarian syndrome where ovulation can be induced medically or surgically.

The study indicates that on clinical examination if the uterus is absent, further investigations are not required except for academic interest as these will not benefit the patient. But if the uterus is present, extensive investigations should be done to reach at a definitive diagnosis and to know whether the patient can be cured or not. In the cases where cure is not possible in terms of menstruation and reproduction, counselling of patients is required.

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