CLINICAL AND LABORATORY EVALUATION IN PRIMARY AMENORRHOEA

BHARUCHA K.E. ● BIIOSALE R.A. ● SUTARIA U.D.

SUMMARY

Correct diagnosis and treatment of primary amenorrhoea is a challenging problem to clinicians. Seventy four patients of primary amenorrhoea attending endocrine clinic were followed. Along with detailed history, physical examination, investigations like ultrasonography, laparoscopy and karyotyping were carried out. Patients could be grouped into Mullerian tract anomalies 39.19%, primary gonadal failure 31.08%, pituitary failure 9.46%, hypothalamic pituitary ovarian dysfunction 14.86% and genital tuberculosis 5.41%. Somatic anomalies and mosaic karyotype were noted in patients with primary gonadal failure. Surgical or medical treatment was instituted in 50% of patients.

INTRODUCTION

The initiation of spontaneous menstrual cycles represents the onset of reproductive maturity. Normal menstruation is the end result of co-ordinated activity of central cortex, hypothalamus, pituitary, ovarian and uterine axis. Primary amenorrhoea is defined as the failure of menses to begin by the age of 16 and can be caused by a variety of disorders. It makes the young girl, her parents and treating physician, aware about the underlying serious condition which in future may deny her vital role in reproduction, or produce poor development of body and secondary sexual characters and give lot of anxiety and depression in her teenage or prove fatal at times.

Department of Obst. and Gyn. B.J. Medical College, Poona - 411 001.

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This study pertains to patients of primary amenorrhoea collected over a period of time who have been analysed with a view to identify etiological categories of primary amenorrhoea and determine the scope of establishing menstruation in such patients.

MATERIAL AND METHODS

74 patients with primary amenorrhoea attending Sassoon General Hospital between January 1986 and July 1990 were evaluated. A detailed history was taken and clinical profiles with emphasis on sexual development, stature, skeletal deformities were used. Diagnostic endoscopies and ultrasonography, intravenous pyelography, serum hormones and genetic make up studies were done whenever possible.

OBSERVATIONS AND RESULTS

Age and marital status : (Table 1). The youngest patient was 14 years of age and the oldest was 27 years of age. 10.81% of patients were under 16 years of age. 73% patients reported between the age of 16 and 21 years.

55 of 74 girls were unmarried and 2 of the 19 married were divorced on grounds of inability to conceive. 44.59% remaining unmarried till the age of 18 and 71.62% upto age of 21 is high specially in our country where age at marriage is much lower.

Etiology : (Table 2) : A large majority of patients i.e. 70.27% had either mullerian tract anomalies with normal gonads and normal karyotype or gonadal failure (31.08%). Hypothalamic pituitary dysfunction diagnosed on gonadotrophic status was the next in order of frequency though associated in only 14.86% cases. Of the 11 patients 3 were diagnosed as having polycystic ovarian disease. Pituitary failure was responsible for 9.46% and a small group of 5.41% had end organ failure as diagnosed on negative estrogenprogesterone challange. In 2 of these 4 patients histological diagnosis of endometrium was established as tuberculosis.

TABLE - I

Age and Marital Status

Age (years)	No.	%	Unmarried	Married	Separated
13 - 15	8	10.81	8	-	-
16 - 18	28	37.84	25	3	-
19 - 21	26	35.14	20	5	1
22 - 24	10	13.51	2	8	-
25 - 27	2	2.70	-	1	1
Total	74	100	55	17	2

TABLE - II

Etiological Groups

Etiological group	No. of patients	Percentage
Mullerian tract anomalies (MTA)	29	39.19
Gonadal failure (GF)	23	31.08
Pituitary failure (PF)	7	9.46
Hypothalamic - pituitary - ovarian dysfunction (HPOD)	11	14.86
End Organ Failure (EOF)	4	5.41

Associated symptoms : Eight patients had cyclical abdominal pain associated with amenorrhoea.

5 patients out of these had hematometra aspirated or drained. One of them who had presented as an emergency underwent emergency laparotomy where the hematometra was drained per abdomen. She had ended up with an abdominal sinus and scar endometriosis. 7 patients presented with infertility and 4 complained of dyspareunia.

8 patients had presented to their family physician, paediatrician and finally in the genetic clinic for their stunted growth. Other associated symptoms were absence of development of secondary sexual characters in 6 patients, headache in 2, blurring of vision in 2,frequency of micturation in 1, fever in 1, and galactorrhoea in 1.

Chromosomal complements : (Table 3)

Analysis of karyotype showed majority of patients to have normal karyotype where as only 17.57% patients had abnormal karyotype. Except gonadal failure all patients in each group had karyotype.

Secondary sex characters : (Tables 4)

Breast and pubic hair development were poor,

TABLE - III

Karyotype

Karyotype	No.	Percentage
46, XY	5	
45, X	4	
45, X/46, XX	1	
45, X/46, XX, inv (X q1)	1	17.57
46, X, I (Xq)	1	
46, XXq22	1	
46, XX	61	82.43

TABLE - IV

Secondary Sexual Characters

Etiological group	Breast		Pubic hair	
	Tanner II above	Tanner I below	Tanner II above	Tanner I below
Mullerian tract anomalies	29	Nil	29	Nil
Gonadal failure	2	21	1	22
Pituitary failure	5	2	5	2
Hypothelamic pituitary dysfunction	11	Nil	11	Nil
End organ failure	4	Nil	4	Nil

Tanner I in 91.3% of patients with gonadal failure. Almost 63.5% patients with pituitary failure and all patients with mullerian tract anomalies, hypothalamic pituitary dysfunction and end organ failure had Tanner stage corresponding to their chronological age.

Renal anomalies : Intravenous pyelography or ultrasonography was done in 32 cases. Renal anomalies were found in 21.4% cases with mullerian tract anomalies and 13.04% of cases with gonadal failure. Various renal anomalies were found i.e. renal agenesis in 2 patients, pelvic kidney in 3, horse shoe shaped kidney in 2, hypoplastic kidney in 1 and hydronephrotic kidney in 1 patient.

Dysmorphic features : Abnormal features were almost always seen in the category of gonodal failure. However, 1 more patient from category of pituitary failure had coarse features due to a chromophobe adenoma. Various dysmorphic features were webbing of neck in 3 patients, short neck in 2, cubitus valgus in 3, pectus excavatum in 1, finger toe anomaly in 4, masculine features in 1, wide spaced nipples in 1, abnormal facies in 1, clitoromegaly in 1 and nystagmus in 1 patient.

Height : (Table 5) - The height of 18 patients was below 147 cms and only 44.4% of them belonged to gonadal failure group. Patients with 46 XY were above 160 cms.

TABLE - V

Height of Patients

Height (cms)	No.
121 - 130	6
131 - 140	8
141 - 150	37
151 - 160	21
161 -	2

Mullerian anomalies : Amongst various mullerian tract anomalies encountered during work up (Table 6), complete or partial absence of vagina leaving behind only short blind pouch was the commonest. Next common were the absence of uterus though in some cases upper part of mullerian duct was developed in the form of fallopian tubes. In 3 patients absent uterus was associated with chromosomally incompetent gonadal failure.

There were 3 patients who had functioning uterus above with no canalised cervix and vagina lower down.

Treatment : Four patients were relieved by simple procedure of hymenectomy. Vaginoplasty using skin and lately amnion were done in 16 patients. Excision of vaginal transverse septum was done in 2 patients.

Of the 5 patients of pituitary failure due to pituitary adenoma 3 were advised surgery. However, only 2 underwent surgery. One of them died on third post operative day.

Three of the 5 patients with 46 XY underwent gonadectomy while the others are lost to follow up.

Antitubercular treatment was started on histologically proved tuberculosis and emperically in one case of end organ failure. Hormone replacement therapy was started in 7 patients with 10-30 ug ethinyl estradiol per day orally for 21 days with medroxy progesterone 10 mg/day from day 12 to 21 for secondary sexual development and prevention of osteoporosis.

DISCUSSION :

Obviously chief role of physician in primary amenorrhoea is to identify the etiology, type and extent of structural defect and hormonal milieu and plan the treatment accordingly.

In this study, after history taking, physical examination and diagnostic procedures patients could be grouped according to localisation of cause, into definite etiological groups (Table 2).

TABLE - VI

Mullerian Anomalies

Etiological group	Uterus		Tubes		Vagina		
	Absent	Hypopl-astic	Absent	Hypo-plastic	Complete agenesis	Partial agenesis	
Mullerian tract anomalies	14	5	7	9	16	6	
						2	Transverse septum
						4	Imperforate hymen
Gonadal failure	5	18	3	15	3	4	
Pituitary failure	-	6	-	5	-	-	
H.P.O. dysfunction	-	2	-	1	-	-	
End organ failure	-	-	-	-	-	-	

The presence or absence of breast development provides valuable information about the patient's previous estrogen exposure. The degree of breast development may provide more useful clinical information than the measurement of baseline serum E2 levels (Mashchak et al, 1981). Poor breast development and pubic hair growth, short stature and dysmorphic features strongly classified patients under gonadal failure group. Associated symptoms, when they were present, pointed to the probable cause.

Mullerian tract evaluation and gonadal morphology helps in localisation of the problem. Rajan and Girija (1990) have strongly suggested the use of pelvic sonography in etiological diagnosis and also renal anomalies. Pelvic ultrasonography and/or laparoscopy revealed etiology in more than 70% of patients (MTA 39.19% and GF 31.08%). Patients with normal gonad and mullerian defects are considered in MTA group and patients with streak gonads are considered in GF group. Uterovaginal agenesis is one of the most frequent cause of primary amenorrhoea. Shearman and Roberts (1982) have reported 17.14% incidence while Mashchak et al (1981) presented 17.74% incidence of uterovaginal agenesis. In this study it constitutes the major group.

Findings of polycystic ovarian disease of normal gonad with normal mullerian tract grouped patients under PF, HPOD or EOF which is further worked out by hormonal studies, radiological investigations of sell a turcica, endometrial histology etc. All patients in MTA had normal karyotype while all of them with abnormal karyotypes belonged to the group of gonadal failure.

IVP is a necessary procedure, as in this series renal anomalies were found in 21.4% of MTA and 13.04% in GF. Ojha and Sarin (1987) have reported excretory system anomalies in 16.66% patients of vaginal agenesis. Serious possibilities of pituitary adenomas and tuberculosis in these young girls are to be always remembered at the beginning of work up. In this study, one patient of pituitary adenoma has died on third post operative day.

At least 50% patients could be treated with corrective surgery, antitubercular therapy, hor-

mone replacement, gonadectomy etc. As most of the patients can be helped, dysmorphic features, associated symptoms and finally failure to menstruate by the age of 14 should include earlier approach to the case and save time.

Patients reported to the clinic till 14 years after the common age of menarche. It is necessary to attend this problem earlier, because many girls either have to remain unmarried (71.62%) till age of 21 or live unhappy married life. For this early diagnosis and treatment can be done by creating awareness by proper education and premarital counselling.

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