Primary Amenorrhoea – A Review of 26 Cases

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This is a study of twenty six subjects who presented to Sir Ganga Ram Hospital, Lahore 1999-2001 and were cases of primary amenorrhoea 20(76.9%) of patient presented between 15-25 years of age. Five (19.2%) had lower abdominal pain. Secondary sex characters were developed in 69.2%. Uterus was absent in 4(15.5%) and ovaries were present in 17(65.5%). FSH was high >40mIu in 12(46.5%) and low <3mIU in 2(7%), 14(53.5%) were put on HRT 1(3.8%) had gonadectomy. 5(19.3%) patients had imperforate hymen, where excision was done. It was concluded that detailed history, through clinical examination and minimal investigations are required to diagnose cases of primary amenorrhoea.

Key words: Primary amenorrhoea age, secondary sex characters, pelvic ultrasound, FSH level, HRT.

Failure to have menstruation by the age of 16 years is called as primary amenorrhoea, as the normal upper age limit for menarche's 15 years. The most important initial distinction is whether the patient is sexually infantile or it there is any evidence of secondary sex characteristics.

Individuals with sexual infantilism can be further divided into those where there is idiopathic delay of sexual development and those who have a pathological sexual infantilism, the cause of which may lie in the hypothalamic – pituitary – ovarian axis.

The diagnosis of amenorrhoea may be perplexing because of the sheer number of possible causes and the complexity of the structures involved (CNS-pituitary – ovarian axis)[1]. The incidence of hypothalamic – primary amenorrhoea is higher than previously appreciated comprising 26% of the total amenorrhoea[21].

Primary amenorrhoea may be manifested by primary ovarian failure. Abnormal choromosomal number like in turner syndrome is one of the important causes. Thirty one percent cases showed numerical or structural abnormalities of the sex chromosomes[9].

Turner syndrome should be suggested in individuals with delayed onset of puberty, primary amenorrhoea and short stature in whom pelvic ultrasonography fails to reveal ovaries[18]. Chromosome studies when puberty is delayed and a thorough pelvic examination when menarche fails to appear at proper time leads to an early definite diagnosis of primary amoenorrhoea[4].

Majority of the patients have normal chromosomal number, in whom the cause of primary amenorrhoea is true gonadal dysgenesis. Gonadal dysgenesis is the commonest cause of primary amenorrhoea[20].

Ovarian failure is associated with autoantibodies to adrenal gland, testes, theca cells of graffian follicles and corpus lutteum[7,11]. In above-mentioned patients, the FSH, LH levels are higher.

Other categories of patients develop amenorrhoea due to suppression of hypothalamusand low FSH level. Exercise and weight loss are associated with hypothalamic amenorrhoea. The prevalence of primary amenorrhoea was substantially higher in atheletes than in control group[7,3].

Isolated gonadotrophin deficiency can easily be diagnosed[10]. Kalman syndrome commonly presents with delayed onset of puberty and decrease or absent sense of smell[24].

Majority of the patients shows development defect in reproductive organs in whom hormonal assays are normal. Mullerian agenesis, a congenital malformation of genital tract is the second most common cause of primary amenorrhoea[5]. Mullerian agenesis is characterized by the absence of fallopian tubes, uterus and internal part of vagina[22]. Congenital absence of the vagina is the second leading cause of primary amenorrhoea[14].

Imperforate hymen is an uncommon anomaly of the reproductive tract occurring in 1% of new born females[19].

Primary amenorrhoea combined with abdominal colics should always suggest the possible existence of a genital malformation[2]. Congenital atresia of the uterine cervix is a rare mullerian anomaly[15].

A few patients present with the features of androgen insensitivity. Complete androgen in sensitivity is the most common cause of male pseudohermaphriditism[10].

Small number of patients presents with features of congenital adrenal hyperplasia, which include hirsuitism, primary amenorrhoea, premature pubarche and clitomegaly[12]. Congenital adrenal hyperplasia is generally considered to be a rare disease, incidence of severe disease being in 10,000.

Subjects and methods

This study was carried out in Sir Ganga Ram Hospital, Lahore over a period of two years from 1999-2001. All the subjects of primary amenorrhoea who visited the Gynae OPD filled the predesigned proforma. After taking history & clinical examination, necessary investigation were carried out like pelvic ultrasound & hormone profile of FSH prolactin & serum E_2. Expensive test of karryotyping was carried out in 5 cases. Surgical treatment was given in 5 cases. Subjects with high & low FSH were put on HRT.

Results

Twenty six patients were included in study. Age of presentation is mentioned in Table 1.

Table 1. Age of presentation

Age	No.	%age
15-26 years	20	76.9
26-35 years	06	23.1

Secondary sex characters were well developed in 18(69.2%). Partially developed and scanty pubic and auxiliary hairs in 8(30.8%). Chief complaint of all 26(100%) was absence of menstruation 5(19.2%) had cyclical lower abdominal pain and 5(19.2%) presented with primary infertility, 1(3%) had retention of urine. Uterus was normal in 16(61.5%), infantile in 6(23%) cases and absent in 4(15.5%). Ultrasonographic findings of ovaries are mentioned in Table 2.

Table 2. Ultrasound finding of ovaries

Ovaries	No.	%age
Present	17	65.5
Streak	04	15.5
Absent	05	19.0

Vagina was well developed in 20(76.9%), small blind in 5(19.3%) and absent in 1(3.8%). 5(19.3%) had imperforate hymen. Serum FSH profile in Table 3.

Table 3. Serum FSH level

FSH	No.	%age
High>50mIU	12	46.5
Normal <20mIU	12	46.5
Low <3mIU	02	7.0

LH, prolactin and TSH were carried out in all and were normal. E2 was normal in 12(46.5%), low in 14(53.5%). Bar bodies were present in 23(88.3%) patient and absent in 3(11.5%).

Progesterone challenge test was negative in 20(76.9%) and positive in (33.8%) and in 5(19.3%), challenge was not carried out.

Karyotype was carried out in 5(19.3%) cases. 3(11.4%) were 46XX, 1(3.8%) was 45 XY, gonadectomy done. One (3.8%) patient was 46 X and was mentally retarded. Height/weight in all were average.

Fourteen patients (53.5%) were put on HRT One (3.8%) had gonadectomy done. Five (19.3%) had imperforate hymen and excision was done.

Discussion

The diagnosis of amenorrhoea may be perplexing because of the sheer number of possible causes and complexity of the structures involved (CNS, pituitary, ovarian axis)[2]. In this study 26 patients were enrolled. Secondary sex characters were well developed in 18(69.2%) and partially developed in 8(30.8%). It is important to understand normal developmental landmarks and of detecting aberrant physiology associated amenorrhoea earlier in lfie[22].

All patients presented with complaints of absent menstruation. Cyclical or abdominal pain was present in 5(19.2%). The primary amenorrhoea combined with abdominal colics should always suggest possibility of genital malformations[2].

In our study uterus was present 16(61.5%), infantile in 6(23%) and absent in 4(15.5%) cases. Vagina was present in 20(76.9%), small in 5(19.3%) and absent in 1(3.8%).

Mullerian agenesis is characterized by the absence of fallopian tube, uterus and internal portion of vagina[22].

Mullerians agenesis is the second most common cause of primary amenorrhoea[5]. Congenital atresia of the cervix is a rare mullerian anomally[5].

In our study, imperforate hymen was present in 5(19%) cases imperforate hymen is an un common anomaly of the reproductive tract occurs in 1% of the new born females[19].

In our study ovaries were present in 17(65.5%). Partial, streak in 4(15.5%) and absent in 5(19%) cases. The patients who were chromosomal mosaic showed a range of findings from absent to infantile to normal adult size ovaries[18].

FSH was below 3 IU in 2(7%) cases, <20 I.U. in 12(46.5%) and >40 i.u. in 12(46.5%).

Primary amenorrhoea with gonadotrophins low or normal has been considered to be relatively rare[21].

Isolated gonadotrophin deficiency can be easily diagnosed[10]. Estradial was low in 12(46.5%) while normal in 14(67.7%). The experiment had shown that the average E_2 level in amenorrhoea patients to be <150 P mol/L[23].

Bar bodies were present in 23(88.5%) and absent in 3(11.5%). Investigations using bar body study are unsatisfactory and inaccurate in the diagnosis of primary amenorrhoda[20].

Progesterone challenge test carried out in 21 patients and was positive in 1(3.8%) and negative in 20(76.9%). Patients who did not bleed were diagnosed a having hypothalamic failure or primary ovarian failure[25]. Karyotyping was required in 12, but was carried out in only 5(19.3%) because of cost.

Among those 3(11.4%) were 46XX, 1(3.8%) was 45X and mentally retarded. Thirty six cases (31%) showed numerical or structural abnormalities of the sex chromosomes[9]. Gonadal dysgenesis was the commonest cause of the primary amenorrhoea[20].

Turners syndrome should be suggested in individual with delayed onset of puberty, primary amenorrhoea, short stature in whom pelvic ultrasonography fails to reveal ovaries[18].

Gonadectomy was carried out in 46XY patient. Gonadectomy should performed in all cases of XY gonadal dysgenesis. Height and weight of all patients were average. Twenty one (80.7%) were put on HRT. There is

association between hypo-oestrogenemia, reduced bone density and stress fractures so increased calcium intake and oestrogen/progesterone supplement should be prescribed[7].

In 5 patients with imperforate hymen, excision of hymen was carried out.

Conclusion

It was concluded that detailed history through clinical examination and minimal investigations are required to diagnose the cause of primary amenorrhoea.

The clinical approach to the patients with primary amenorrhoea will be systems approach. The detailed history and physical examination will point to most of disorders. Limited laboratory and selected imaging studies will be necessary to confirm a selected diagnosis. The most common cause of primary amenorrhoea. In our study was in hypothalamic-pituitary-ovarian axis. All patients with high FSH that 40mIU/l and very low FSH <3mIU need hormone replacement therapy to prevent osteoprosis.

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