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EVALUATION OF PRIMARY AMENORRHEA: A STUDY OF 46 CASES AT TERTIARY CENTRE

Obstetrics & Gynaecology

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ABSTRACT

BACKGROUND: About 2–5% of adolescent girls present with primary amenorrhea which is absence of menstruation .

Materials and methods: This retrospective single centred study was conducted in Department of obstetrics and Gyenocology, Nilratan Sircar Medical College . 46 cases of primary amenorrhoea from August 2017 to December2018 were included and cases were analysed according to history, physical examination, hormone profile, pelvic USG, MRI, and karyotype where necessary.

Results: The common causes of primary amenorrhoea were mullerian anomalies (23 cases, 50%), hypogonadotropic hypogonadism (10 cases, 21%) and Hypergonadotropic hypogonadism (7 cases, 13%) . Karyotype was performed in 20 patients and 8 cases showed abnormal karyotype. Definitive treatment was done accordingly.

Conclusion: Depending on its cause ,failure to attain menarche may lead to varying clinical sequalae. Timely evaluation of a broad differential diagnosis have important implications for emotional, physical and reproductive health in young women.

KEYWORDS

Primary amenorrhea, Mullerian anomalies, Hypogonadism

INTRODUCTION

Amenorrhea is the absence or abnormal cessation of the menses (1). Primary amenorrhoea is defined as absence of menses by 13 years of age in the absence of growth or development of secondary sexual characteristics or absence of menses by 15 years of age regardless of the presence of normal growth and development including secondary sexual characteristics (2). About 2–5% of adolescent girls present with primary amenorrhea [3]. Many broad differential conditions can lead to amenorrhea. Each of these conditions indicate varying clinical dysfunction of hypothalamic-pituitary-ovarian-uterine axis. There are different causes of primary amenorrhoea. It includes anomalies of mullerian development, gonadal dysgenesis, constitutional delayed puberty, tuberculosis, CNS tumors, idiopathic etc [4].Various studies indicate mullerian dysgenesis and gonadal failure are the leading causes.(5,6).

Materials and methods

This retrospective single centered study was conducted in Department of obstetrics and Gyenocology, Nilratan Sircar Medical College ,Kolkata. 46 cases of primary amenorrhoea who attended the Gynaecologic Clinic from August 2017 to December2018 were included in the study.All the patients in this study gave informed consent and fulfilled the eligibility criteria as per primary amenorrhoea definition.data was collected based on the medical records of the patients and evaluation of the patient was done by a proper sequential steps.

History-

Patients were about eating and exercise patterns,anosmia, headache, visual disturbances, changes in weight, previous menses (if any), medication use, chronic illness, presence of galactorrhea and symptoms of androgen excess, abnormal thyroid function, or vasomotor instability. Age of development of secondary sexual character/thelarche,presence of cyclical abdominal pain,abdominal lump,inguinal swelling should enquired. Family history including age at menarche was noted.

Physical examination

Detailed general survey including height,BMI, hirsutism,acne, stigma of turner syndrome such as webing of neck,shield chest,cubitus vulgus,short fourth metatarsal and tanner staging was done. Breast development is an excellent marker for ovarian estrogen production(7). Genital examination may reveal virilization, evidence of an outflow tract obstruction, or a missing or malformed organ.

Laboratory investigations:

The initial workup included serum luteinizing hormone, follicle-stimulating hormone, prolactin, and thyroid-stimulating hormone levels. If history or examination suggests a hyperandrogenic state, serum free and total testosterone and dehydroepiandrosterone sulfate concentrations were done. Pregnancy test and Karyotype analysis was performed wherever necessary.

Radiological imaging

Pelvic ultrasonography was done to confirm the presence or absence of a uterus, and to identify structural abnor- malities of reproductive tract organs. A suspected pituitary tumor or abnormal abdominal structure was evaluated by magnetic resonance imaging (MRI).

Results

The analysis of 46 patients with primary amenorrhoea was done and the diagnosis was made on. The etiological factor is given in Table 1 along with their clinical features.

Table 1. Causes of primary amenorrhoea according to etiology.

Hypergonadotropic hypogonadism	
• 45,XO	05
• 46,XY	02
Eugonadism	
• Mayer Rokitansky Kuster Hauser	13
• Androgen Insensitivity Syndrome	01
• Transverse vaginal septum	04
• Imperforate hymen	05
• Vaginal agenesis	01
• Polycystic ovarian Syndrome	05
Hypogonadotropic hypogonadism	
• Constitutional	08
• Idiopathic	02

The common causes of primary amenorrhoea were mullerian anomalies (23 cases, 50%), hypogonadotropic hypogonadism (10 cases, 21%) and Hypergonadotropic hypogonadism (7 cases, 13%) in the decreasing order of frequency. Mullerian anomalies contained 13 cases of Mayer Rokitansky Kuster Hauser and 5 cases of Imperforate hymen,4 cases of Transverse vaginal septum and 1 case of vaginal atresia.

Karyotype was performed in 20 patients and 8 cases showed abnormal karyotype. All patients with gonadal dysgenesis (7 cases) were subjected to karyotyping. There were 1 case of 46,XY gonadal dysgenesis, 5 cases were of Turner syndrome and 1 had Swyer syndrome (46XY). Amongst Turner syndrome cases, two cases with karyotype 45XO/del(x) and rest three 45XO/46XY. Androgen insensitivity syndrome (AIS, 46XY) was found in one cases.

The patients presented with various complains as per table 2.

Table 2. No of Cases according to Presenting feature.

Presenting feature	No of cases	percentage
Absence of menstruation	23	50
Absence of sexual characteristics	04	09
Abdominal cyclical pain	08	17
Urinary retention	02	04
Primary infertility	08	17
Ambiguous genitalia	01	02

In present study,some cases deserve brief discussion.Among gonadal dysgenesis, 5 alfa reductase 2 deficiency was an etiology. 14 years girl old with complaints of growth of penis like structure in last 6 months which was not present since birth, deepening of voice, started to grow upper lip line hair with no significant family/medical history with no menarche till now. On examination, BMI 19.4 kg/m2, Tanner staging-B1P2, Axillary hair-absent,3cm Penile shaft like structure present with distal urethral opening b/l small firm nodule (1*1)cm2 palpable at inguinal area,blind vaginal pouch. FSH-46miu/ml :LH-10miu/ml,Cortisol-10ug/dl,17-OH Progesterone-1.42 ng/ml ,DHT18.25ng/dl,Testosterone- 362 ng/dl,T/DHT ratio-19.8(raised),karyotype- 46, XY. USG showed genitalia shows penile shaft like structure with two corpora cavernosa and cavernosal artery.(2.2*.8) cm2 ellipsoid structure simulating with testis noted in rt inguinal ring with rt sided patent processus vaginalis.(2.1*.7)cm2 ellipsoid structure simulating testis at lt inguinal canal.No ovary detected. MRI detected Uterus ,adnexa not visualised., Hypertrophied labia/rudimentary penis is noted with focal marginated hyperintense lesion seen at inguinal canal could be undescended testis.

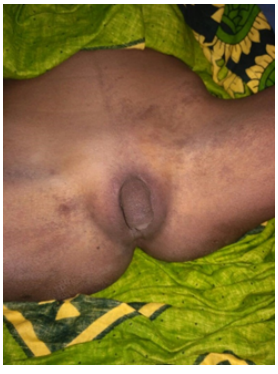

Fig no 1:. 14 years girl old with complaints of growth of 3cm Penile shaft like structure present with distal urethral opening in last 6 months which was not present since birth due to 5 alfa reductase2 deficiency.

Among mullerian anomalies, one transverse vaginal septum case was presented as 14 year old female who presented with primary amenorrhea with established normal secondary sexual characteristics with cyclical low abdominal pain and an abdominal suprapubic lump.On examination ,she had a female habitus with body weight 30 kg with height 132 cm.BMI is 17.2 kg/m^2. Midline deformity and gross scoliosis is noted .A 3*3 cm soft mass noted at inferior angle of right scapula.4 th metatarsal is normal and sexual maturation staging is A1 B3P2.Her TSH repot is 2.2 mcu/ml,prolactin is 6.8 ng/ml,FSH is 4.4 miu/ml and LH is .56 miu/ml. Ultrasonography shows hematocolpos with hematometra and left sided hematosalphinx with nonvisualisation of left kidney(fig 2). A cystic space with septations communicating with spinal canal suggestive of meningocele. MRI of pelvis shows the confirms the same diagnosis with location of upper vaginal septum.MRI study of dorsolumbar spine shows gross scoliosis of dorsolumbar spine with convexity to right side(fig 3),absence of left kidney,variable deformity ,rotation and partial fusion of several dorsal veterbrae and a large lobulated CSF intensity collection in left paraspinal region . Pulmonary function test shows moderate restriction as (FEV1/FVC)>95% and FVC <64 %.Echocardiography shows no gross cardiac anomaly. An excision of the upper vaginal septum was done and a vaginal stent were left in situ. Her post- operative recovery was uneventful.

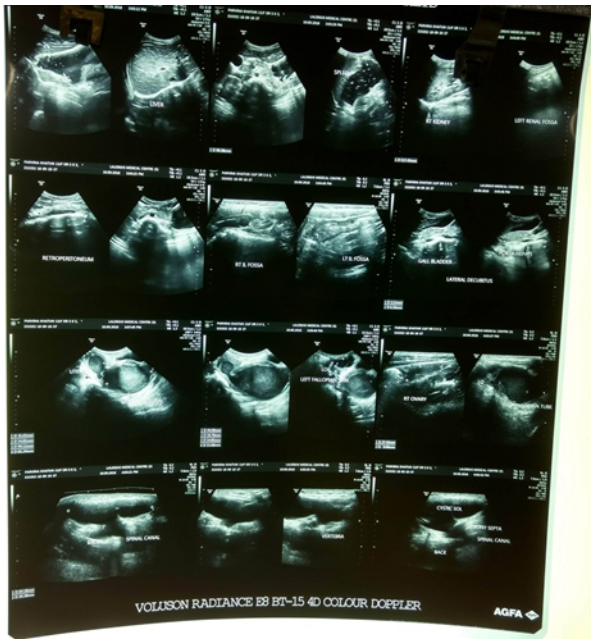

Fig no 2: Ultrasonography shows hematocolpos with hematometra and left sided hematosalphinx with nonvisualisation of left kidney

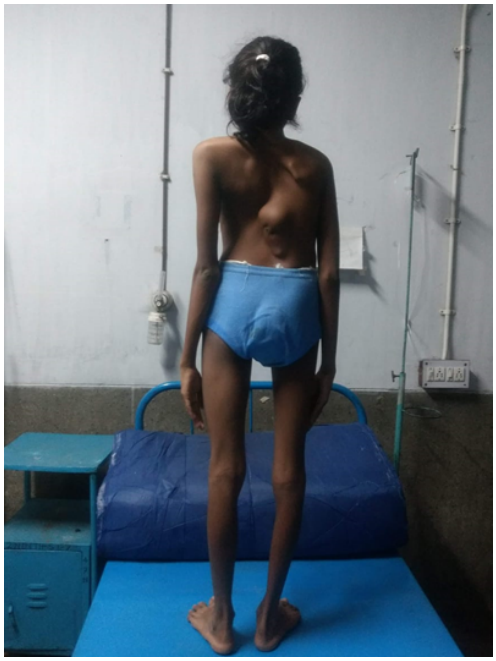

Fig no 3: Gross scoliosis of dorsolumbar spine

In Hypogonadotropic hypogonadism, one case polydactyly with constitutional primary amenorrhoea was diagnosed.Her karyotype shows 46 XX,9qh+ including large heterochromatin region in chromosome 9,which is considered to be polymorphic chromosomal variant.(Fig no 4 a ,b).

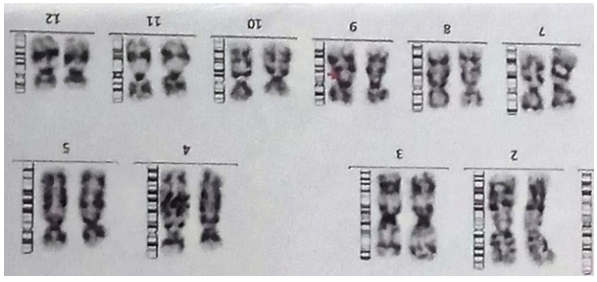

Fig no 4 a: polydactyly ;Fig 4 b: 46 XX,9qh+ including large heterochromatin region

Patients with gonadal failure were put on combined hormone therapy with estrogen for 21 days (conjugated equine estrogen 0.625 mg daily) and progesterone (medroxyprogesterone acetate 10 mg daily) in last 12 days of the month. They were also given calcium and vitamin D supplementation to prevent bone loss. Bilateral gonadectomy should be done in cases of Swyer syndrome, AIS (Androgen insensitivity syndrome) and Turner mosaic with Y line in karyotype. As far as fertility is concerned, these patients require donor-oocyte IVF (in-vitro fertilization).

Patients with MRKH (Mayer-Rokitansky-Kuster-Hauser syndrome) and Mullerian anomalies were treated with Mc Indoe's vaginoplasty . The patients with absent uterus were counselled regarding the future fertility option of surrogacy to have their own biological child or adoption.

We had 2 patients with hypogonadotropic hypogonadism were given ovulation induction with gonadotropins.

Discussions

Patients presented at different age groups. Adolescent girls with primary amenorrhoea are were brought to the physicians with major concern regarding their reproductive life and cyclical abdominal pain ,lump or retention of urine. Young married couple sometimes presented with infertility or coitus problems. The defects may lie within the uterus, ovaries, pituitary or hypothalamus. Genetic and chromosomal anomalies also contribute to a major portion of primary amenorrhoea especially in cases of gonadal failure. The workup of primary amenorrhoea should be very meticulous . The importance of karyotype cannot be overemphasized in establishing the diagnosis. It should be done in all cases of hypergonadotropic hypogonadism and patients with androgenic features. Karyotyping helps in establishing the diagnosis and also guides the treatment, especially for psychological counselling of the patient. It aids in decision for gonadectomy in the presence of Y line and future pregnancy option.

Various studies have been reported from all parts of the world and they are indicating the frequency of different etiologies. Gonadal dysfunction has been considered as the commonest factor for primary amenorrhoea worldwide followed by pituitary/hypothalamic disorder and outflow tract anomalies according to literature(5).Most of the studies show greater prevalence of gonadal dysfunction leading to primary amenorrhoea in western countries while outflow tract anomalies are commonest at Asian- African countries. A large study from Thailand of 295 cases has shown Mullerian anomaly as the commonest cause in Thai population (5,6). In our study, we also found Mullerian anomalies as the most common (50%)etiology for primary amenorrhoea followed by hypogonadotropic hypogonadism(21%). This difference might be the environmental and racial or genetic influence.

A study of 48 cases of primary amenorrhoea reported by kumar et al in 1998 from India where they have found mullerian anomalies in 54.2% cases followed by hypogonadotropic hypogonadism (22.9%), hypergonadotropic hypogonadism (16.6%) (8). Our study found similar result. Jyothi et al found abnormal karyotype is responsible for 21.5 % cases of primary amenorrhoea and Geckinli et al reported in 25% cases. (9,10) In our study it is 40%(8 cases).

Conclusions

Amenorrhea is a symptom, not a disease. Depending on its cause, failure to attain menarche may lead to varying clinical sequalae. Timely evaluation and consideration of a broad differential diagnosis have important implications for emotional, physical and reproductive health in young women. Team approach involving gynaecologist, geneticist, psychologist and paediatrician should be followed for individualising the management and counselling. Treatment and prognosis in terms of future fertility depends on the primary etiology of amenorrhoea.

Limitations

The major limitation of this study is the smaller sample size . This is a short term study and single centered study .

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