

Primary Amenorrhea in a Teenage Girl with Polycystic Ovarian Syndrome

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Abstract: Polycystic ovarian syndrome (PCOS) usually present after the establishment of menstruation but rarely may present as primary amenorrhea. Here we present a case of a 18-year-old teenage student presenting with the non-establishment of menstruation despite the development of secondary sexual characteristics along with excessive facial hair growth, blackish discoloration of the neck skin, and obesity. Clinical assessment and bio-chemical and imaging study confirmed her as a case of PCOS with primary amenorrhea. Anatomical and hormonal and genetic causes were excluded. After taking several courses of hormonal management she noticed no withdrawal bleeding and remained amenorrhoeic. Despite following lifestyle modifications, she gained a weight of about 20 kg in two years. Non-establishment of menstruation even after getting treatment results in a disquieting state for the patient and her parents.

Managing primary amenorrhea due to PCOS might be sometimes difficult. Working up to rule out causes of primary amenorrhea is exhaustive, expensive, and time-consuming in a low resource country. That might put the girl in a difficult and challenging situation which could be overcome by an arrangement of diagnostic facilities in government/public health care facilities.

Keyword: Primary Amenorrhea, Polycystic ovarian syndrome, life style modification.

Introduction:

The absence of any menstrual vaginal bleeding is known as amenorrhea¹. Primary amenorrhea is one when there is no menstrual bleeding by the age of 16 years or older or also non-establishment of menstruation at least 4 years after initiation of secondary sexual characteristics in a young girl².

Polycystic ovarian syndrome (PCOS) is a spectrum of disorder where there is a combination of clinical and biochemical features, which includes symptoms of anovulation, hyperandrogenism, and polycystic ovaries. In 35% to 50% of cases, obesity is a common feature^{3,4,5}.

In adolescent PCOS many of the girls present with secondary amenorrhea (SA) or oligomenorrhea (OM) and as symptoms of androgen excess like acne and

hirsutism^{3,6-8}. Girls with PCOS very rarely present with primary amenorrhea. Data on primary amenorrhea and PCOS is scarce^{9,10}. Among the reported cases the percentage of primary amenorrhea as a presenting feature of PCOS girls has varied between 1.4%¹¹ and 14%^{9,12}.

The presentation as primary amenorrhea in PCOS girl indicate the severe spectrum of the PCOS and indicate a high level of circulating androgen and metabolic disturbances at early stages of adolescent life.

Case Presentation:

A 18-year-old higher secondary student presented with non-establishment of menstruation, excessive weight gain (20 kg in 2 years) and excessive hair growth, blackish discoloration of the skin of the

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back of the neck within the last two years. She was apparently healthy since her birth and grown-up normally like other girls of similar age. Her secondary sexual characteristics developed around 13 years of age. But these physical changes are not followed by onset of menstruation. At 15 years of age, her parents consulted with the local doctor and was advised her to wait for the spontaneous onset of menstruation for one more year. At 18 years of age, she consulted with several physicians and was prescribed different hormonal medications of different duration. But her menstruation was not established following those medications. She also noticed excessive hair in the lower abdomen, chest, and face – which was gradually increasing in the distribution. She did not give any history of cyclical lower abdominal pain or feeling of a lump in the abdomen or urinary retention. She had no history of chronic illness like Tuberculosis, galactorrhea, deepening of the voice, severe headache, anosmia, excessive stress, exercise, anorexia nervosa. Her mother was diabetic. There was no family history of primary amenorrhea with her other cousins and aunt and other diseases like Tuberculosis or Diabetes Mellitus.

On Examination:

She was found to be anxious, BMI- 32, waist circumference-97cm, waist-hip ratio- 0 .95; and there was no buffalo hump, moon face, webbing of neck, cubitus valgus. Breast nipple, areola, glandular structures are well developed (Tanner stage 5). Galactorrhea is absent. Axillary and Pubic hair shows a normal feminine pattern of distribution. But hirsutism present in the face. She also has acanthosis nigricans. There were excess hairs on the lower abdomen. No palpable swelling was found in the abdomen and inguinal region. Vaginal Examination: vulva and perineum look normal without any clitoromegaly but labia minora hypertrophied. Hymen intact and there was no evidence of hematocolpos. The uterus was palpable during per-rectal examination in the dorsal position.

Investigations:

She was advised to do an ultrasound(USG) and other hematological tests. USG shows uterus normal in size and anteverted, with normal myometrial and endometrial echoes, both ovaries enlarged, the volume of right and left ovary 13ml and 18 ml respectively (Figure 1). TSH -6.758 μ IU/ml; initially after two months of thyroxine replacement which turns later to TSH .999 μ IU/ml. Prolactin-21.08 ng/ml, S.FSH -4.9 mIU/ml, LH -2.68 mIU/ml, Testosterone -0.85 ng/ml and DHEA-SO₄ -302 μ gm/ml, 17 α -OH Progesterone -2.01 ng/ml, ACTH-23.52 pg/ml, Morning cortisol-11.1 μ gm/ml, Fasting blood glucose-4.30 mmol/l, Blood glucose 2 hours after 75 gm glucose-12.8 mmol/l, Fasting plasma insulin-72.60 μ u/ml, Fasting plasma glucose-insulin ratio-1.08, S. Cholesterol-201 mg /dl. HDL Cholesterol-33 mg/dl-Triglyceride-197 mg/dl, CXR skull lateral view reveals nothing abnormality. Chromosome Analysis (karyotype) reveals 46XX.

Figure1: USG showing polycystic ovaries



Management:

She was counseled for lifestyle modification including diet control and exercise just before the COVID pandemic in Bangladesh. But because of lockdown, social distancing, and the spread of COVID infection she failed to reduce weight by dieting and exercise.

For withdrawal bleeding, she took norethisterone acetate 5mg thrice daily for seven days and gradually increasing it to 10mg thrice daily for 7 days. But no measure could bring out the desired menstrual bleeding. She also took a high dose of combined oral contraceptive pill for more than three months followed by estrogen-progesterone sequentially for consecutive three cycles. Metformin was added as an adjunct for a period of six months. She was treated with different modalities of medication for long two years. Anatomical and hormonal abnormalities were excluded and diagnosis as adolescent PCOS was made. Management of primary amenorrhea by hormonal treatment couldn't solve her problem. COVID pandemic made forced restriction of facilities for weight reduction and lifestyle modification as expected resulting in suffering and anxiety of an obese teenage girl as well as her family.

Discussion:

Obese teenage with PCOS with obesity may present with primary amenorrhea.

Nduwayo et al described 9 patients with PCOS and primary amenorrhea and the entire girl presented with a raised level of circulating androgen. Dramatic et al^{9,13} noted that most PCOS girls who were obese presented with either primary amenorrhea or prolonged secondary amenorrhea, and girls of normal body mass index presented with oligomenorrhea^{13,14,15}.

Girl, who presented with primary amenorrhoea exhibit with acanthosis nigricans, raised diastolic blood pressure, elevated fasting insulin levels, higher body mass index, and lower high-density lipoprotein cholesterol levels. This reflects the fact Resulting in continuum suffering and anxiety of an obese teenage girl as well as her family. that adolescents with PCOS and primary amenorrhea have a high risk of development of metabolic syndrome than those with PCOS and secondary amenorrhoea or oligomenorrhoea. The PA group had higher androstenedione levels compared

with the OM/SA group. Adolescents who are primary amenorrhoeic had higher serum androstenedione levels. They seem to be non-responsive to progesterone withdrawal bleeding¹⁶. Because hyperandrogenism causes persistently decidualized endometrium as a result of prolonged anovulatory state in PCOS¹⁷.

Wang et al explored that hypothalamic amenorrhea and PCOS might coexist and these patients may fluctuate between symptoms of hypothalamic amenorrhea and polycystic ovarian syndrome, depending on the status of their hypothalamic activity¹⁸.

PCOS in teenage girls with primary amenorrhea may represent a severe spectrum of PCOS disorder. Hyperandrogenism in teenage PCOS might be the main cause of primary amenorrhea. Most of the primary amenorrhoeic teenagers seem to be obese, which might lead to such presentation. Teenage PCOS with primary amenorrhea may have a higher risk for features of metabolic syndrome. Hyperandrogenism has been suggested as a rare cause of negative withdrawal response to progesterone treatment.

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