Case Report

Swyer Syndrome With Gonadoblastoma: A Clinicoradiological Approach

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Abstract

Primary amenorrhea is a common diagnostic challenge in the gynecology department, wherein there are numerous causes that need to be approached in a systematic manner. However, when a case with a pelvic lump or a solid pelvic mass presents to a gynecologist or a radiologist, the approach becomes difficult to justify amenorrhea and pelvic mass as a single entity. We present the case of a 36-year-old female with the complaints of primary amenorrhea with a pelvic mass. The case was approached keeping in view the diagnostic possibilities and applying the role of clinical, radiological, and laboratory analyses. The final diagnosis of Swyer syndrome with gonadoblastoma was made, and she was further subjected to operative resection and hormonal therapy. This study stresses on the approach to a case, wherein the diagnosis was based only on the clinician's acumen and the radiologist's expertise, providing a way to simplify the protocol in the evaluation of such types of cases.

Keywords: *Amenorrhea, gonadal dysgenesis, gonadoblastoma, Swyer syndrome*

Introduction

Pure gonadal dysgenesis is a condition with a normal set of chromosomes, that is, 46XX or 46XY, and the latter is better known as Swyer syndrome, named after doctor Swyer, who first described the anomaly in 1955.[1] The condition is usually diagnosed in early adolescence during the workup for the chief complaint of primary amenorrhea. The incidence of Swyer syndrome is 1 in 100,000,[2] whereas its combination with gonadoblastoma is rarer and reported to be present in 5% of the cases.[3]

In this report, we present a rare case of Swyer syndrome with germ cell tumor, wherein the emphasis is on both the clinical and the radiological manifestations, which shall prove to be useful for a clinician and an imaging specialist. The case also describes the importance of the early management of such types of embryological abnormalities for evasion of the malignant differentiation of the streak gonads.

Case Report

A 36-year-old, married female presented with the complaints of primary amenorrhea, pelvic pain, and a feeling of lump on the right side of the lower abdomen for the last 2 months. The patient's height was 164 cm, weight was 60 kg, and no clinical stigmata of Turner syndrome were identified. The background knowledge of the patient revealed that she had no uterus (based on the previous workup by a local clinician). The clinical examination showed the female phenotype with relatively underdeveloped breasts (Tanner stage III), sparse pubic hair, and normal external female genitalia. The urine pregnancy test was negative. The per vaginal examination showed a red and dry vagina with a feeling of lump in the right adnexal region.

Pelvic ultrasound (US) was performed, wherein a solid mass was seen in the right adnexa [Figure 1] with the nonvisualized uterus and the ovaries. The patient was convinced for pelvic magnetic resonance imaging (MRI), which revealed a hypoplastic uterus with a solid right adnexal mass [Figure 1]. The bilateral gonads were not identified on imaging. Luteinizing hormone (LH) and follicle stimulating hormone (FSH) were high (300 and

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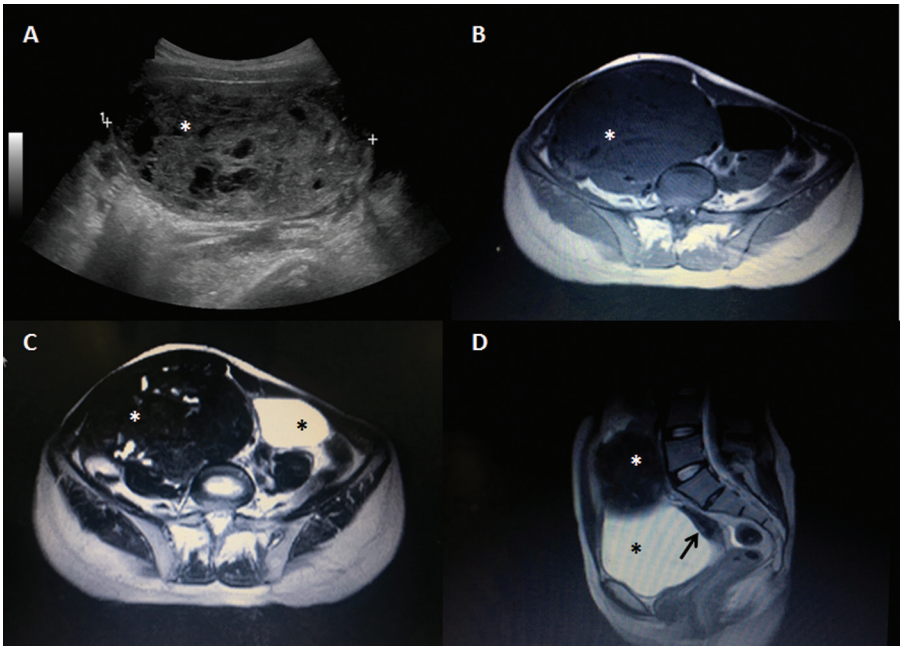

Figure 1: (a) Transabdominal US image showing a solid near-homogenous isoechoic mass. (b, c) Axial T1W and T2W MRI showing a large isointense-to-hypointense mass (white asterisk) in the right lower abdomen and the adnexal region compressing the urinary bladder (black asterisk). (d) Sagittal T2W MRI showing a small hypoplastic uterine tissue/Mullerian remnant (black arrow) behind the urinary bladder (black asterisk)

150 mIU/ml, respectively) with low levels of serum estradiol (10 pg/ml). Prolactin and thyroid-stimulating hormone (TSH) levels were within normal limits. Further evaluation was performed with karyotyping and serum testosterone levels, which revealed 46XY pattern genotype [Figure 2] and low serum testosterone levels (0.45 ng/dl).

Hypergonadotropic hypogonadism with 46XY karyotype associated with the hypoplastic uterus confirmed the diagnosis of Swyer syndrome with pelvic mass likely to be germ cell tumor. Tumor markers such as serum beta human chorionic gonadotropin, lactate dehydrogenase, alpha feto-protein, and CA-125 were within normal limits. Exploratory laparotomy was performed, and the right-sided tumor and the left-sided streak gonad were extirpated with peritoneal wash cytology. The tumor margins were free from the adjacent structures. Post-operative combination of estrogen and progesterone was prescribed with regular follow-up. Histopathological analysis showed the right-sided gonadoblastoma and the left-sided streak gonad of ovarian origin [Figure 3].

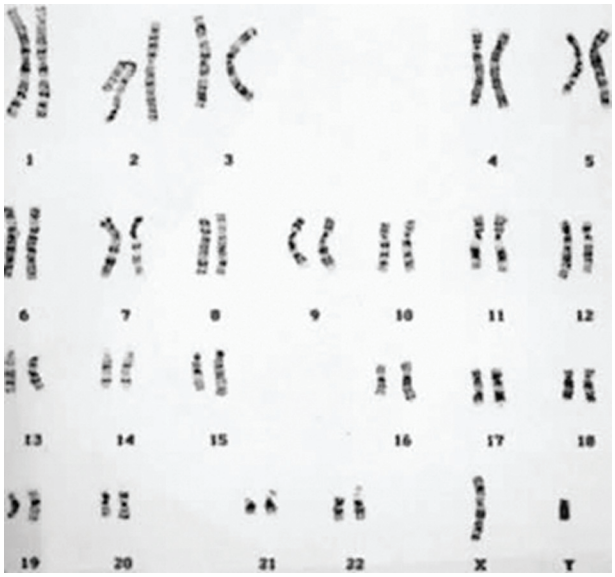

Figure 2: Karyotyping of the patient shows normal male genotype (46XY)

Discussion

Swyer syndrome is 46XY type of the pure gonadal dysgenesis manifesting as primary amenorrhea with female phenotype. Mutation in the SRY gene (the sex-determining region of the Y chromosome) is noted in 10–15% of the cases, whereas the rest are unexplained.[4,5] Despite the presence of the Y chromosome, there is underexpression of the antimullerian hormone (AMH) and the androgenic hormones due to the dysgenetic gonads, leading to female type of internal and external genitalia.[6] The syndrome also manifests with poorly developed secondary sexual characteristics in the form of sparse pubic hair and underdeveloped breasts. The hormonal parameters are indicative of hypergonadotropism (increased LH and FSH) with normal or low testosterone levels as present in our report.

Primary amenorrhea with female phenotype can be approached in a systematic manner with a clinical- and imaging-based algorithm [Figure 4]. After

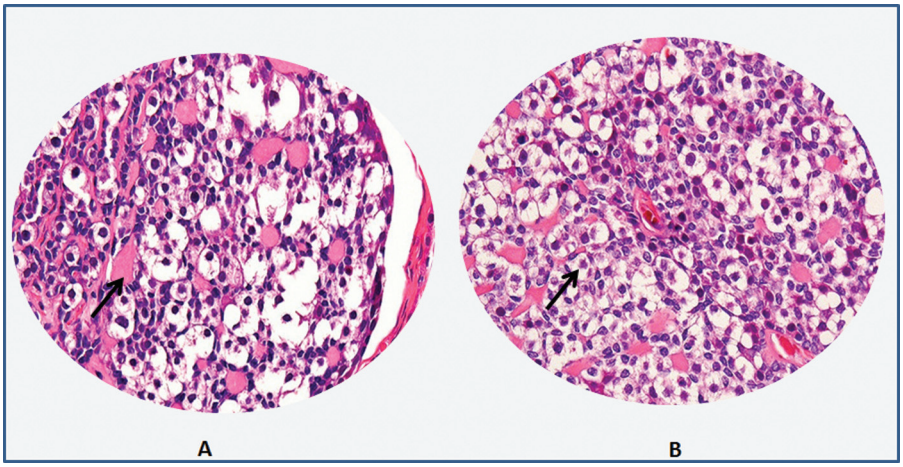

Figure 3: Histopathological analysis of the mass (a) on H&E staining. Complex neoplasm composed of a mixture of large primordial germ cells, immature sertoli cells, and gonadal stroma (black arrow). (b) The streak gonad showing the loss of gonadal stroma (black arrow) with paucity of the germ cells

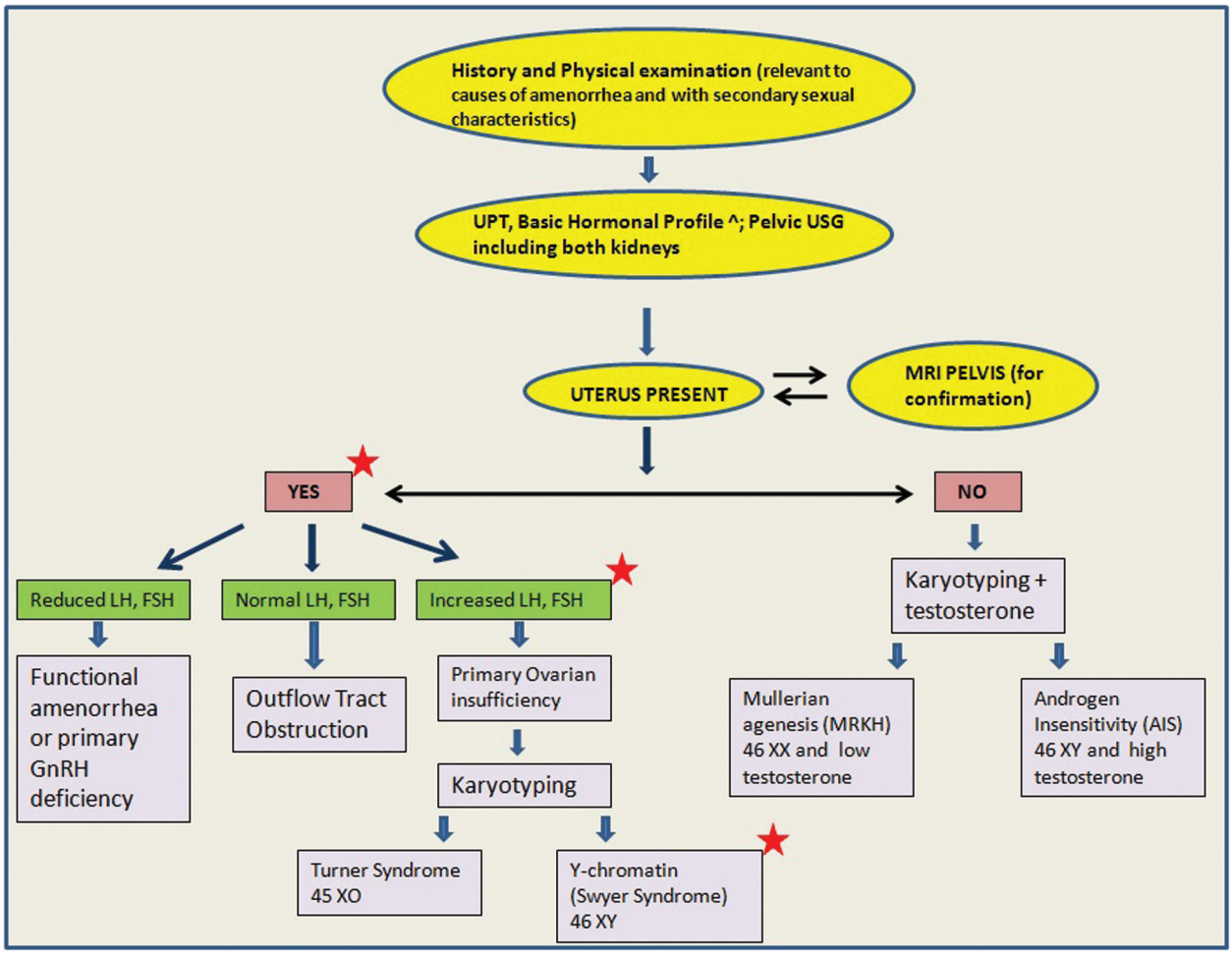

Figure 4: Algorithm-based approach to primary amenorrhea. ^Serum levels of luteinizing hormone (LH), follicle stimulating hormone (FSH), thyroid stimulating hormone (TSH), and prolactin. GnRH = gonadotropin releasing hormone. Red stars denote the case under study

excluding pregnancy stage and other hormonal causes of primary amenorrhea such as hyperprolactinemia and hyperthyroidism, the diagnostic possibilities should be narrowed down to the congenital causes of the outflow tract obstruction (the imperforate hymen and the transvaginal septum) and primary ovarian insufficiency. Ultrasonography plays a central role in excluding the outflow tract obstruction.

The major causes of primary amenorrhea due to congenital or structural causes of ovarian insufficiency with female phenotype can be enumerated as Turner syndrome, Mayer Rokitansky Kuster Hauser (MRKH) syndrome, and androgen insensitivity syndrome (AIS), with the rarest being the Swyer syndrome.[7] The most common among them is the Turner syndrome, which also shows elevated FSH and LH; however, the clinical features of short stature, webbed neck, and 45XO karyotype are diagnostic features and thus excluded in this patient's profile. The other two major causes, that is, MRKH syndrome and AIS, can be excluded based on the US and MRI findings of the hypoplastic uterus, which is not present in both the syndromes. Individuals with MRKH syndrome exhibit normal, symmetrical breast and pubic hair development, with no visible vagina and sometimes rudimentary uteri with nonfunctional endometrium. The majority of the patients have normal ovaries and a karyotype of 46XX contrary to our case.

AIS shows the male karyotype similar to the Swyer syndrome, that is, 46XY; however, the levels of AMH and testosterone are modestly elevated, whereas they are reduced in the Swyer syndrome. They also show female phenotype with blind-ended short vaginal pouch.

Gonadal dysgenesis with the Y chromosome is found to be associated with the occurrence of the germ cell tumors with a reported incidence of 10–30%.[8] The most prevalent tumors associated with Swyer syndrome are the gonadoblastoma, dysgerminoma, and sometimes seminoma. A total of 5–10% of the cases of Turner syndrome are also associated with gonadoblastoma. The risk of the tumor development increases with age; it is reported that the risk is 50–70% in the third decade of life while being as high as 80% in the fourth decade of life.[9] Hence, the laparoscopic extirpation of the gonads at an early stage in the cases of primary amenorrhea and Y chromosome is of prime consideration. The early cases of gonadoblastoma are surgically removed as was performed in the present case; however, chemotherapy/radiotherapy is required for the metastatic tumors, which are reported in 10% of the cases.

In this case report, a rare combination of a case with its complication is evaluated, highlighting the importance of early removal of the gonads. The role of clinical assessment and imaging (US and MRI) is of utmost importance in narrowing down the diagnosis, to delineate the internal genital anatomy, and to correlate the biochemical as well as the genetic markers. Algorithm-based assessment of a case of primary amenorrhea should be performed to reach a confident diagnosis.

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Conflicts of interest
There are no conflicts of interest.

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