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CASE REPORT

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Dysgerminoma in a 15 years old phenotypically female Swyer syndrome with 46, XY pure gonadal dysgenesis: A case report

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Abstract

Swyer syndrome is a 46, XY karyotype, with pure gonadal dysgenesis and primary amenorrhea. These females have primordial Mullerian structures and seek medical attention as they experience primary amenorrhea. Here, we report a 15-year-old girl, diagnosed as Swyer syndrome associated with left ovarian dysgerminoma.

KEYWORDS

dysgerminoma, pure gonadal dysgenesis, Swyer syndrome

1 | BACKGROUND

Sexual developmental disorders are a group of disorders that cause abnormalities in the gonad, internal organ, or external genitalia.[1] These disorders are categorized under three main subgroups according to karyotype (XX, XY, and sex chromosome for mosaic karyotypes).[2] Swyer syndrome or pure gonadal dysgenesis is a disorder of sex development with primary gonadal defect.[1] These patients with 46 XY chromosome are phenotypically female. Mutation of some genes such as SRY, Map3K1, DHH, DEAH37, SOX9, WT1, and NROB1 result in testicular formation failure.[1,3] These individuals present with a tall structure, female external genitalia, vagina and cervix, and primary amenorrhea.[4] Gonadal streaks in Swyer syndrome are at risk for developing cancer.[5] The most common tumor development in Swyer syndrome is bilateral gonadoblastoma, but both dysgerminoma and embryonal carcinoma are also reported.[6] These patients seek medical care in adolescence for primary amenorrhea or the absence of secondary sex characteristics, initially.[7] Here, report a 15-year-old case of dysgerminoma diagnosed as Swyer syndrome.

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2 | CASE REPORT

A 15-year-old patient with completed thelarche and pubarche was referred with a complaint of primary amenorrhea. On admission vital signs were normal. On examination, there was no excess hair on the face. Axillary hairs were seen. The external genitalia, labia majora and labia minora, clitoris, and mons pubis were normal, and the presence of normal hairs on the breast and pubis indicates complete thelarche and pubarche. The patient was 162 cm tall admission laboratory tests showed a beta-human chorionic gonadotropin (B-hCG) test of more than 1000 mIU/ml and a lactate dehydrogenase of 833 U/L and ultrasonography revealed an infantile uterus and a 6 cm free fluid echogenic solid mass containing fine ocular foci without vascularity in the left ovary. Magnetic resonance imaging (MRI) demonstrated a well-defined encapsulated mass lesion measuring about 66*62*50 mm in the pelvic cavity adjacent to the uterus that had high signal intensity on T2 and intermediate to low signal intensity on the T1 sequence. After contrast injection, heterogeneous enhancement was detected due to the small size of the uterus and hypoplasia of the ovaries, this lesion was suggestive of a sex cord tumor. Due to high FSH and LH, BHCG > 1000, LDH > 833, and the presence of a 6 cm mass in the left ovary in a 15-year-old girl with a complaint of primary amenorrhea, the patient underwent surgery under general anesthesia (GA). Exploration of abdominal cavity showed an apparently 6 cm in diameter malignant mass in left ovary indistinguishable of the ovary, which after by diagnosed as high-grade malignancy probably germ cell neoplasm. Left salpingo-oophorectomy was done. Also, 50 ml free fluid was sent for cryptologic evaluation. Gross pathologic findings revealed an encapsulated 11 × 10 × 7 cm smooth surface ovarian mass, which involved left ovary. The cut surface of the tumor showed a creamy brown heterogeneous appearance (Figure 1B). After tumor fixation in 10% formalin in six blocks, immunohistochemical staining was done. Also, a 9-cc bloody fluid was received. Two cytologic smears were prepared. Sections revealed a neoplastic of germ cells forming nests and sheets, which were outlined by fibrous seplates containing few lymphohistiocytic infiltrates. These cells were uniform with abundant clear to eosinophilic cytoplasm, sharply outlined cell membranes, a large centrally located nucleus and clumped chromatin pattern, and multiple elongated shapes and irregular contours

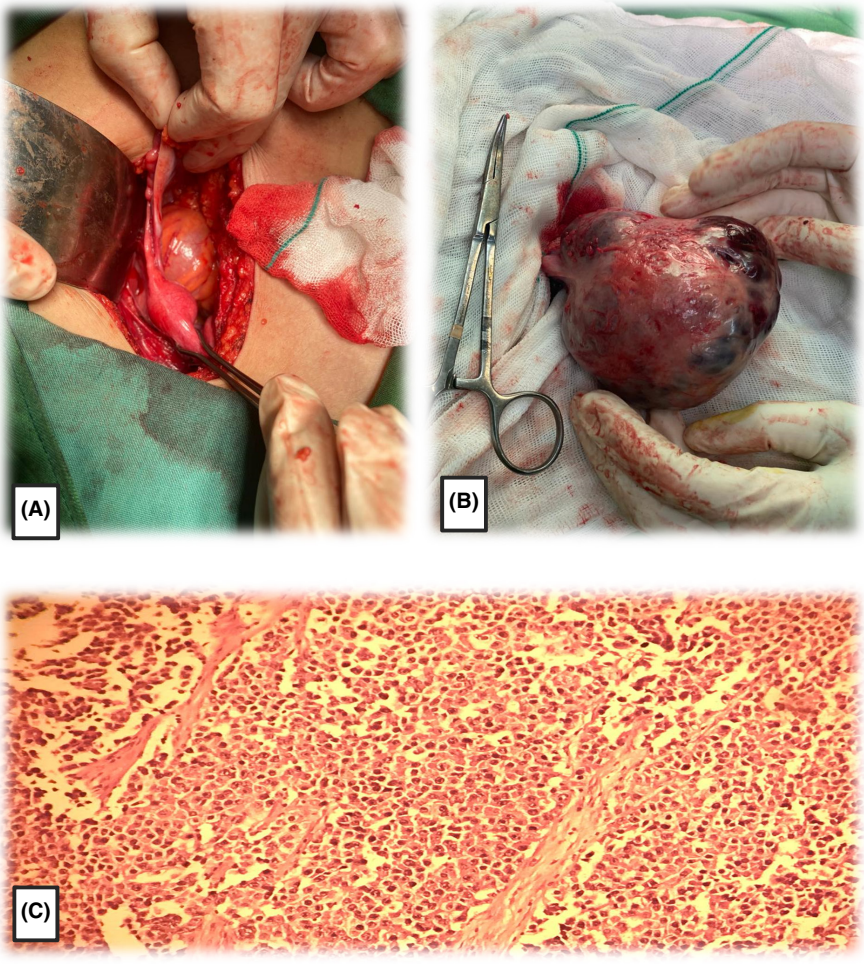

FIGURE 1 Gonadal dysgerminoma showing tumoral cells' nests that separated by fibrous septa (low power field, ×100, H and E staining).

(Figure 1C). Immunohistochemically, tumor cells were positive for PLAP. CD117 and positive in reactive lymphocytes in the background for LCA, but were negative for CD138, PanCK, Inhibin A, chromogranin, and CD99. Pathologic stage classification was PT1aNxMx. Abdominal fluid cytology was negative for malignancy. The uterus was infantile, and Omentum was apparently normal, no obvious pathologic lymph node was palpable. After the first operation when a laboratory test revealed a karyotype of 46, XY male pseudohermaphrodite, a second surgery was planned, and the patient underwent a laparoscopic right salpingo-oophorectomy. The gross feature of the right ovary was strip-shaped (Figure 1A). Two days after the second surgery patient was discharged with stable hemodynamic and a good general appearance.

3 | DISCUSSION

The Swyer syndrome is a disorder of sexual development (46 XY, DSD), in which patients exhibit female phenotypes and they have girls' appearance until they are generally diagnosed in adolescence.[7] Although thelarche as a secondary sexual characteristic is not usually seen in patients with Swyer syndrome, thelarche in our case was seen due to the existence of syncytiotrophoblastic giant cells in dysgerminoma.[8] Given her age, the patient's breasts were normal in terms of growth. Her vagina was normal, and her uterus was infantile. FSH and LH levels were elevated in this patient and as these individuals' findings are indicative of hypergonadotropic hypogonadism, they revealed low androgen levels and also low levels of androgen precursors. There are various differential diagnose of patients who are referred with primary amenorrhea, which should be considered; one of those is Mayer–Rokitansky–Kuster–Hauser syndrome (xx), the second most possible cause. Some conditions, but in that syndrome, we have varying degrees of Mullerian duct abnormalities and also an absent or rudimentary uterus and the karyotype is 46 XX.[9] One of the other differential diagnoses, which should be considered is complete androgen insensitivity syndrome which is formally known as Morris syndrome, 46, XY individuals with female external genitalia and breast development and complaint of primary amenorrhea, but with no uterus and the gonads are the testicles.[10] Another differential diagnosis is a 46, XY female with 17α-hydroxylase deficiency which is due to adrenal steroid synthesis disorder, these patients are hypertensive and hypokalemic, but there is no uterus.[11] Despite gonadoblastoma being the most common malignancy in Swyer syndrome, tumor development in our patient was dysgerminoma. All patients with gonadal dysgenesis, either pure (A 46, xx or 46, XY karyotype) or associated with physical features of Turner's syndrome (with a karyotype of 45, xo) gonads are exhibited as a streak of fibrous tissue which is almost similar to ovarian stroma.[12,13]

Although previously it was thought that these individuals are not at increased risk of gonadal tumors.[14] Recent Studies reported patients with 46, XY karyotype with pure gonadal dysgenesis are at higher incidence of gonadoblastoma and dysgerminoma, which even may be seen at young ages.[15] Considering the high risk of malignancy, these patients should undergo bilateral gonadectomy when the Swyer syndrome diagnosis is confirmed.[16,17] In these cases, hormone replacement therapy after surgery would induce second sexual characteristics and puberty.[18] In this report, the patient was immediately admitted due to ovarian mass noticed on ultrasound and MRI, high BHCG and LDH along with a history of primary amenorrhea and underwent laparotomy.

One of the most important goals of treatment in these patients is to prevent future osteopenia due to bone density reduction, so be started as soon as possible and continued until 50 years of age, when it may be discontinued.[4,19] In the reported case, hormonal replacement therapy started, to prevent developing osteopenia. Pregnancy is possible by oocyte donation in some countries if the uterus should not be removed due to malignancy, and the prognosis of those pregnancies is the same as those of 46, XX patients with ovarian failure.[20] Although many studies reported a 5-year survival of these patients in their follow-up, but rarely evaluated rates are better among patients with stage 1 tumors (96.9%, such as our case) in comparison with those with more advanced tumors (53.9%, stage 2–4).[21]

Reporting these cases is so valuable as it calls attention to the necessity of early evaluation of females with primary amenorrhea to exclude Swyer syndrome and other chromosomal anomalies which would expose patients to malignant transformation. Therefore, early and accurate diagnosis of these cases and prophylactic gonadectomy in patients with a high risk of malignancy would allow a better treatment plan in order to preserve patients' fertility, reduce emotional trauma, and improve their survival rates.[4,22]

4 | CONCLUSION

In patients with 46, XY gonadal dysgenesis, the presence of the Y chromosome may raise the incidence of gonadal malignancies. Those patients should be counseled to have a preventive bilateral salpingo-oophorectomy.

AUTHOR CONTRIBUTIONS

T.A.G is first operator in the case, planned and performed the procedure, and took decisions on hardware and technique used. ZP, AM, and MR assisted in procedure and drafted the manuscript. N.A.M and M.H assisted in procedure. All authors read and approved the final version of the manuscript.

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CONFLICT OF INTEREST

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

ETHICAL APPROVAL

Our institution does not require ethical approval for reporting individual cases or case series.

CONSENT

Written informed consent was obtained from the patient for the publication of this case report as well as accompanying images. A copy of the written consent is available for review by the editor-in-chief of this journal.

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