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Case Report

Incidental gonadoblastoma in swyer syndrome: a case report with brief review of literature

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ABSTRACT

Swyer syndrome is a disorder of sexual differentiation with an incidence of 1 in 80,000 population. Dysgenetic gonads have a propensity for malignant transformation particularly in the presence of Y chromosome and hence need prophylactic removal. We report a case of an adolescent girl who presented with primary amenorrhea who was identified as a case of 46 XY dysgenesis after karyotype studies. Extirpation of gonads were done laparoscopically and on histopathological assessment gonadoblastoma was detected. This case report aims to reiterate the importance of gonadectomy in patients with swyer syndrome as tumors could arise even in the absence of frank adnexal masses.

Keywords: Gonadoblastoma, Gonadal dysgenesis, Swyer syndrome

INTRODUCTION

Swyer syndrome is a rare disorder of sexual differentiation characterized by pure gonadal dysgenesis with an incidence of 1 in 80,000.[1,2] These patients typically present in adolescence with primary amenorrhea and lack of development of secondary sexual characters along with other characteristics of estrogen deficiency. Dysgenetic gonads form fertile ground for development of germ cell neoplasms. The probability of development of gonadoblastoma is as high as 30% in these cases with 50-60% risk of malignant transformation.[2] Management of pure gonadal dysgenesis is challenging and requires a multi-disciplinary approach. Early detection is vital with regards to risk of gonadal malignancy, need for pubertal induction and early hormonal replacement therapy.[2]

We report a case of 18-year-old patient with swyer syndrome who underwent prophylactic laparoscopic gonadectomy and post-operative histopathological evaluation revealed the gonadoblastoma that the dysgenetic gonads housed.

CASE REPORT

An 18-year-old girl presented to us with complains of not having attained menarche and absent development of breasts. There was no history of similar complains in any other family member. On examination Breasts were poorly developed (Tanner stage 1). Axillary hairs were sparse and pubic hair was Tanner stage 2. Examination of the external genitalia revealed no ambiguity. Labial folds, clitoris and vaginal canal were well developed. On digital rectal examination uterus was palpable. On further evaluation she found to have raised gonadotropins. Serum Follicular stimulating hormone level was 13.7 IU/L (normal range: 2-12 IU/L) and serum Luteinizing hormone level was 45.2 IU/L (normal range: 2-9 IU/L). Magnetic Resonance Imaging (MRI) revealed hypo plastic uterus and bilateral gonads were present. Further karyotype analysis detected 46XY genetic makeup. This picture of hyper gonadotropic

hypogonadism with a 46XY karyotype helped to pin the diagnosis of Swyer syndrome. The patient was then planned for laparoscopic bilateral gonadectomy due to risk of malignancy in future. Examination under anesthesia showed a well-developed cervix. On laparoscopy hypo plastic uterus was seen with bilateral streak gonads (Figure 1). Bilateral gonadectomy was done and gonads were retrieved in a glove bag. Post-operative period was uneventful, and patient was discharged after observation for 24 hours. On histopathological evaluation, presence of gonadoblastoma was detected in the gonads with no evidence of malignant transformation (Figure 2). Patient was started on hormonal therapy post-surgery. At 6 months of follow up patient is doing well.

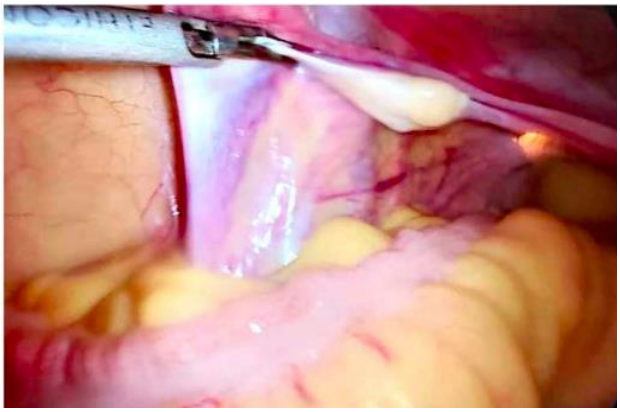

Figure 1: Laparoscopic view of the gonad.

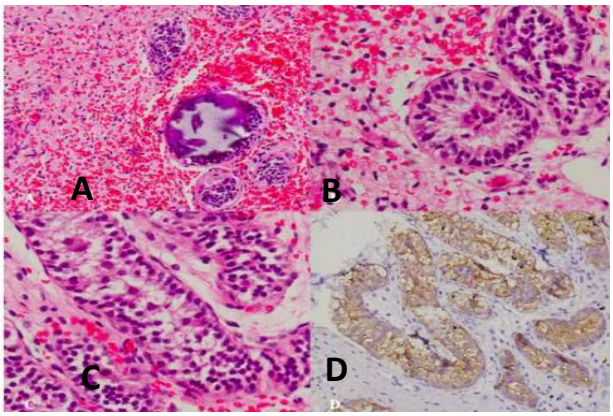

Figure 2: Hematoxylin and Eosin stained section of (A)-nest of germ cells with surrounding ovarian stroma (HE, 20X); (B,C)-showing gonadoblastoma (40X); (D)-immunohistochemistry showing CD117 positive germ cells encircled by cells positive for inhibin and calretinin (20X).

DISCUSSION

Swyer syndrome is a disorder characterized by 46XY pure gonadal dysgenesis. Ten to fifteen percent of cases carry mutation in SRY gene (sex determining region on Y chromosome).[1,2] Other genes implicated in gonadal dysgenesis include those involved in the sex differentiation pathway including SOX9, WT1, DHH, MAP3K1, NR5A1 located on autosomes, and DAX1 gene located on the X chromosome.[4] Inheritance may be sporadic or autosomal recessive or X-linked trait.

Dysgenetic gonads lead to under expression of the Anti-Mullerian hormone (AMH) and androgenic hormones thereby leading to development of the Mullerian structures in these patients despite the 46 XY genetic makeup.[3] These patients have completely female external genitalia with infantile uterus and streak gonads. Breasts are underdeveloped in most patients due to low circulating levels of sex hormones however axillary and pubic hair may be present but sparse.[3] Other features of hypoestrogenism like osteoporosis may also been seen in these patients.[4] Swyer syndrome patients usually present in adolescence with primary amenorrhea like in our case. Atypical presentation of the disease with breast development and menstruation have been reported in literature.[4] This may be spontaneous or secondary to hormone producing germ cell neoplasm in the dysgenetic gonads.[3,4] Menstruation can also be initiated in cases of swyer syndrome by pubertal induction with hormonal agents. Cases of virilization by androgen secreting gonadoblastomas have also been reported.

Evaluation of a patient presenting with primary amenorrhea begins with history and physical examination, hormonal analysis including serum levels of Follicle Stimulating Hormone, Luteinizing Hormone, Human Chorionic Gonadotropin, Thyroid Stimulating Hormone and Prolactin and a pelvic ultrasonography. Presence of uterus combined with high levels of follicle stimulating hormone and a female phenotype brings down the differential diagnosis to Turner syndrome, primary ovarian failure and 46XY gonadal dysgenesis. A karyotype at this juncture helps to confirm the diagnosis. Our patient who presented with primary amenorrhea was managed with the above algorithmic approach. Imaging detected the presence of uterus and hormonal analysis showed hyper gonadotropic hypogonadism. On proceeding with karyotype studies, male genotype was identified and a diagnosis of swyer syndrome made. As per current dictum, bilateral gonadectomy was planned at the outset in view of significant risk of development of germ cell tumors in the dysgenetic gonads.[3]

Dysgenetic gonads fail to perform normal physiological functions and act as a potential source of neoplasms. The risk of gonadoblastoma is found to be greater than 30%.[3] This risk is found to be directly proportional to the patients age with risk approaching 50-70% by third decade and around 80% by fifth decade of life.[1,3] Gonadoblastomas are gonadal tumors with germ cell and sex cord stromal cell derivatives. Although considered benign, they have potential for malignant transformation. Gonadoblastoma may give rise to Germ-cell malignancies like Dysgerminoma, Endodermal Sinus tumor, Teratoma, and Embryonal carcinoma. It hence becomes crucial to extirpate dysgenetic gonads at diagnosis. Gonadoblastoma under microscopy appears as nests of germ cells and sex

stromal cells surrounded by ovarian stroma. Hyalinization and calcification may also be seen like in our case (Figure 2). Immunohistochemistry highlighted presence of CD117 positive germ cells surrounded by a second cell line positive for inhibin and calretinin.

The diagnosis and management of 46XY gonadal dysgenesis involves a multidisciplinary approach.[2] Early diagnosis is vital in order to prevent occurrence of germ cell neoplasm. Prophylactic gonadectomy should be planned immediately after diagnosis and minimal invasive surgical technique is preferred over laparotomy. Advantages of minimal invasive gonadectomy include lower postoperative pain, lower incidence of wound infection, early recovery and early discharge from hospital. Another aspect to management of these patients includes pubertal induction and hormone replacement therapy. This helps in development of secondary sexual characters and restoration of bone mineral density.[2] Psychosocial development should be catered to in these patients by specialists in the field. Further, assisted reproductive technology offers prospects of childbearing in these patients. Successful pregnancies have been reported in cases of Swyer syndrome by in vitro fertilization with ovum donation.[1,4]

CONCLUSION

Successful management of cases of 46XY gonadal dysgenesis begins with early diagnosis and prophylactic gonadectomy preferably by minimally invasive techniques. This would prevent development of germ cell neoplasms, which are seen in high probability in dysgenetic gonads. Risk of gonadoblastoma in these cases is as high as 30%, which increases with age, and have potential for malignant transformation. Prognosis of patients with swyer syndrome thus depends on early detection and gonadectomy prior to onset of malignancies. With this case report, we aim to reiterate the importance of prophylactic gonadectomy in patients with swyer syndrome as tumors can arise even in the absence of frank adnexal masses.

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