Case Report

Swyer Syndrome (46XY Pure Gonadal Dysgenesis) Presenting with Dysgerminoma

M. Banyameen Iqbal, Iqra Mushtaq, Tushar Kambale, Indranil Dey
Departments of Pathology and Ophthalmology, D.Y. Patil Medical College, Hospital and Research Centre, Pune, Maharashtra, India

Abstract

Dysgerminoma is the most common malignant germ cell tumor of the ovary. This malignancy can be associated with pure gonadal dysgenesis (Swyer syndrome), mixed gonadal dysgenesis, and partial gonadal dysgenesis. Dysgerminoma usually develops in phenotypic females with 46XY pure gonadal dysgenesis. This patient presented with an abdominopelvic mass. Laparotomy was done. 46XY karyotype was detected by lymphocyte culture. The patient underwent gonadectomy, and histopathological results were streak ovaries with dysgerminoma. Five percent of dysgerminomas are discovered in phenotypic female and 46XY karyotype; thus, in an adolescent with dysgerminomas and amenorrhea, karyotyping should be done.

Keywords: Dysgerminoma, gonadal dysgenesis, Swyer syndrome

Introduction

Swyer first described this entity in 1955.[1,2] He identified two phenotypic women with gonadal dysgenesis without Turner syndrome (46XY pure gonadal dysgenesis of Swyer syndrome). Since then, several authors have reported over 74 tumors of dysgenetic gonads.[3-6] The propensity of tumor development in Swyer syndrome is significant; an incidence of 20%–30% is reported. The most common tumors are the often-bilateral gonadoblastoma, but dysgerminoma and even embryonal carcinoma are also seen.[2] Approximately 5% of dysgerminomas are discovered in phenotypic females with abnormal gonads and 46XY karyotype.[1]

Case Report

A 20-year-old female was brought to the outpatient department by her parents, with complaints of primary amenorrhea. She did not give any history of cyclical abdominal pain, hormonal intake, radiation exposure, headache, or visual disturbances. She gave no history of significant trauma or any surgical procedure. There was no history of tuberculosis. She was the first issue of a nonconsanguineous marriage, and her mother’s age at the time of delivery was 27 years. On general examination, she was 148 cm tall and weighed 50 kg. There was no evidence of acanthosis nigricans, hirsutism, cushingoid features, or Turner syndrome. Examination of secondary sexual characteristics revealed that the breasts were small and poorly developed with hypopigmented areola. Pubic and axillary hairs were present but sparse. Examination of the external genitalia revealed that they were of female type, and there was no evidence of clitoromegaly. Examination under anesthesia showed that the vagina was poorly developed and the cervix was tiny and hypoplastic. Ultrasonography of the pelvis revealed a rudimentary uterus and a unilateral streak ovary while the other side showed a huge retroperitoneal mass in relation to the other ovary. The serum follicle-stimulating hormone level was raised at 45 IU/L. A karyotype repeated from two different laboratories showed a genotype of pure XY. The patient was taken up for an operative laparoscopic procedure under general anesthesia, and a bilateral gonadectomy was performed. The specimen was sent for histopathological examination. It measured 12 cm × 10 cm × 6 cm and weighed 500 g. The outer surface was grayish-white, capsulated, bosselated, and nodular. The cut-section was solid,
soft, and whitish with no evidence of hemorrhage or necrosis [Figure 1a and b]. On histopathological examination, the tumor showed sheets of fairly uniform round cells with large nuclei and clear cytoplasm. These cells were separated by fibrous trabeculae containing lymphocytes [Figure 2a and b]. These features were consistent with the diagnosis of dysgerminoma.

**Discussion**

Gonadal dysgenesis has characteristic histology in the gonads of the patient, and based on that, the 46XY gonadal dysgenesis may be divided into three histological categories.

**Complete or pure gonadal dysgenesis or Swyer syndrome**

These patients are phenotypic females with a karyotype of 46XY. They also possess hypoplastic gonads without germ cells. They most often present with primary amenorrhea but mostly normal stature. These patients have usually streak gonads, but there may be some development of secondary sexual characteristics. A few episodes of uterine bleeding can also be seen.[1,2]

**Mixed gonadal dysgenesis**

It is associated with primary amenorrhea and can be associated with various mosaic statuses like 45X/46XX. These patients when compared to pure 45X cell line are taller and have fewer abnormalities. Spontaneous menstruation occurs in approximately 20% of these patients.

**Partial gonadal dysgenesis**

These patients have a karyotype of 46XX with part of one of the X chromosomes missing. The phenotype is variable depending on the amount and location of the missing genetic material.

In these patients, there is some testicular development; therefore, they present as newborns with ambiguous genitalia. The etiology of 46XY gonadal dysgenesis is a short-arm Y chromosome deletion involving SRY, a mutation in other genes that leads to inhibition of SRY function or mutation of SRY function.[1] To date, 20% of 46XY pure gonadal dysgenesis is explained by a mutation or a deletion in SRY. In 80%, SRY is apparently normal.

Female patient having XY karyotype, palpable Mullerian system, normal female testosterone levels, and lack of sexual development is said to be suffering from Swyer syndrome.

Tumor transformation in the gonadal ridge is said to occur at any age.[1-3] In 50 reported cases, there were 11 malignancy, 15 adenoma, and 10 benign cases; a 22% incidence of malignancy and a 52% incidence of neoplasia. More recent series indicate a lower overall incidence of gonadal tumors of about 5%–10%, but in Swyer syndrome, the risk of gonadal neoplasia is high (20%–30%); hence, early prophylactic removal of these dysgenetic gonads is the key.[2] Słowikowska-Hilczer et al. reported that neoplasia may occur in 16.7%–23.1% of patients with gonadal dysgenesis.[7] The patients with 46XY gonadal dysgenesis are usually diagnosed in early adolescence and are suffering from delayed pubertal development. As expected, they have elevated gonadotropins, normal female levels of androgens, low levels of estrogen, female external genitalia, uterus and fallopian tubes, and minimal breast enlargement. Active menstrual function suggests tumor development in the streak gonad. These streak gonads often display ovarian stroma but no follicles.

Dysgerminoma is the most common malignant germ cell tumors of the ovary. It can be found either in a pure form or mixed with other germinal elements. Therefore, in premenarchal patients with a pelvic mass, karyotype should be determined. About 65% of dysgerminomas are Stage I at diagnosis. About 85%–90% of Stage I tumors are confined to one ovary; 10%–15% is bilateral. Dysgerminoma is the only germ cell malignancy that has this significant rate of bilaterality, other germ cell tumors being rarely bilateral.[1] The treatment of patient with early dysgerminoma is primarily surgical, which includes resection of the primary lesion and proper surgical staging. Chemotherapy/radiation is administered to patients with metastatic disease. In patients whose contralateral ovary has been preserved, they have a 5%–10% more chance of developing the disease over the next 2 years.[1]

**Conclusion**

Bilateral dysgenesis of the gonads (Swyer syndrome) affected individuals has XY karyotype and normal (infantile) female external and internal genitalia. These patients have a high risk of dysgerminoma; hence, gonadectomy is recommended.
Thus, in adolescent patients with dysgerminoma with primary amenorrhea and/or secondary amenorrhea, karyotyping should be done. Further, menstrual function in patients with 46XY karyotype may be associated with estrogen secretion of tumoral lesion, and investigation of gonads is recommended.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Berek JS, Hacker NF. Clinical Gynecology. 4th ed., Ch. 23. 2004. p. 514-8.
2. Speroff L, Feritza MA. Clinical Gynecologic Endocrinology and Infertility. 7th ed. 2005. p. 322-5, 348-9, 38-7.
3. Dimitri P, Cohen M, Wright N. Indications for familial screening and gonadectomy in patients with 46, XY gonadal dysgenesis. Int J Gynaecol Obstet 2006;95:167-8.
4. Cools M, Stoop H, Kersemaekers AM, Drop SL, Wolffenbuttel KP, Bourguignon JP, et al. Gonadoblastoma arising in undifferentiated gonadal tissue within dysgenetic gonads. J Clin Endocrinol Metab 2006;91:2404-13.
5. Jadhav MN, Yelikar BR, Karigoudar M. Gonadoblastoma with contralateral dysgerminoma in a young female – A case report. Indian J Pathol Microbiol 2006;49:274-6.
6. Nisolle M, Kridelka F, Fridman V, Claudot A, Lorquet S, Foidart JM. A bilateral dysgerminoma: A rare presentation of the Swyer syndrome. Rev Med Liege 2005;60:703-6.
7. Słowikowska-Hilczer J, Romer TE, Kula K. Neoplastic potential of germ cells in relation to disturbances of gonadal organogenesis and changes in karyotype. J Androl 2003;24:270-8.