Journal of Gynecology Obstetrics and Human Reproduction 48 (2019) 283–286

Available online at
ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com/en

Case Report

‘Size does matter’: Prophylactic gonadectomy in a case of Swyer syndrome

Parkhi Mayur[a], Gupta Parikshaa[b,*], Bhansali Anil[c], Gainder Shalini[d], Rajwanshi Arvind[b]

[a] Department of Histopathology, Postgraduate Institute of Medical Education and Research, Chandigarh, India
[b] Department of Cytology and Gynecological Pathology, Postgraduate Institute of Medical Education and Research, Chandigarh, India
[c] Department of Endocrinology, Postgraduate Institute of Medical Education and Research, Chandigarh, India
[d] Department of Obstetrics and Gynecology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

ARTICLE INFO

Article history:
Received 8 November 2018
Received in revised form 22 January 2019
Accepted 23 January 2019
Available online 25 January 2019

Keywords:
Swyer syndrome
Dysgenetic gonads
Complete gonadal dygenesis
Dysgerminoma
Gonadoblastoma
Immature teratoma

ABSTRACT

Swyer syndrome also known as pure or complete gonadal dysgenesis is a very rare disorder of sex development wherein the individuals are phenotypically females with 46, XY genotype and preserved mullerian structures. These individuals characteristically have dysgenetic streak gonads which carry an increased risk of malignant transformation. Prophylactic gonadectomy is highly recommended as soon as a clinical diagnosis is established to diminish the chances of tumor development. We present a case of complete gonadal dysgenesis with bilateral small gonads with a dysgerminoma arising in a background of gonadoblastoma in one gonad and immature teratoma in the other. The present case, besides adding a rare case to the literature, highlights the importance of detailed pre-operative assessment of gonadal size and prompt prophylactic gonadectomy in cases with gonadal dysgenesis.

Introduction

Disorders of sex development (DSD), also referred to as differences of sex development, are congenital conditions characterized by atypical development of chromosomal, gonadal or the anatomical sex, with a frequency of approximately 1 in 4500–5000 births [1]. These are classified on the basis of genetic composition and the state of the gonads [2]. In 1955, Swyer reported two cases of sex reversal that differed from the known forms of what was then referred to as ‘male pseudo-hermaphroditism’ [3]. The condition, named after Swyer, was later linked to dysgenetic gonads and is also known as pure or complete gonadal dysgenesis (CGD), affecting approximately 1 in 50,000 to 80,000 women. This condition is thought to be caused by a mutation in the DNA-binding region of the SRY (sex determining region Y) gene in 10%–20% of cases, however, few other genes involved in sex determination have also been implicated over the past years [4].

Individuals with Swyer syndrome or CGD are phenotypical females, with female genitalia at birth. Owing to complete gonadal dysgenesis, there is lack of secretion of anti-mullerian hormone (AMH) that leads to the normal development of mullerian structures. These women usually present during adolescence with delayed puberty and primary amenorrhea, often accompanied by tall stature [5,6]. Additionally, the dysgenetic, characteristically “streak” gonads have a 30% risk of development of gonadoblastoma, with a 50%–60% risk of subsequent malignant transformation, typically to dysgerminoma [7–9]. Therefore, bilateral prophylactic gonadectomy should be performed as soon as the diagnosis is ascertained. In the current report, we present a case of CGD with apparently normal sized gonads, however, histopathological examination revealed presence of germ cell neoplasms.

Case report

A 24 years old female, married for the past 5 years, presented with history of primary amenorrhoea and infertility. Her past developmental history revealed delayed and poor development of secondary sexual characters. She was prescribed cyclical combined estrogen-progesterone pills, following which she experienced development of breasts and had cyclical withdrawal bleeding. On clinical examination, she was a moderately built female with a height of 171 cm and weight of 70 kg. Her secondary sexual characters were under-developed. She had no features suggestive of Turner’s syndrome. Hormonal evaluation revealed thyroid function tests to be within normal limits with elevated leutinizing

* Corresponding author at: Department of Cytology and Gynecological Pathology, Research ‘A’ Block, PGIMER, Sector 12, Chandigarh, 160012, India.
E-mail address: parikshaa@gmail.com (G. Parikshaa).

http://dx.doi.org/10.1016/j.jogoh.2019.01.009
2468-7847/

hormone and follicle stimulating hormone levels and low estrogen (E_2) levels. Karyotyping done using the peripheral blood lymphocytes revealed a 46, XY karyotype (International System for Human Cytogenetic Nomenclature-2016). Ultrasonographic examination of the abdominal and pelvic organs revealed a uterine size of $5.4 \times 1.4 \times 3.8$ cm with endometrial thickness of 4 mm. In addition, both the gonads were noted to be small in size, left measuring 2.2×1.5 cm and the right measuring 1.7×1.2 cm. Based on these features, a clinical diagnosis of 46, XY pure/ complete gonadal dysgenesis (Swyer syndrome) was made and she was planned for prophylactic gonadectomy. Subsequently, she opted to undergo a laparoscopic gonadectomy. On laparoscopy, the uterus and both the fallopian tubes were seen to be of normal size and both the gonads were smaller in size as compared to normal but were definitely larger than the 'streak' gonads and measured around 2.5 and 2 cm in diameter, respectively (Fig. 1).

The gross specimen comprised of bilateral fallopian tubes and gonads. The fallopian tubes measured 7 cm in length each and were grossly unremarkable. One of the gonad was larger than the other and measured $2.5 \times 2 \times 1$ cm. The outer surface was yellowish-white and lobulated and the cut surface was solid and firm in consistency. The smaller gonad measured $2 \times 2 \times 0.6$ cm. The outer surface was smooth and the cut surface was solid and firm. On histopathological examination, the larger gonad showed a tumor with tumor cells arranged predominantly in the form of nests surrounded and separated by fibrous septae showing dense lymphocytic infiltration. The individual tumor cells were large with mild to moderate nuclear pleomorphism, well defined cell borders, round nuclei with vesicular chromatin, prominent nucleoli and abundant amount of clear cytoplasm. In addition, large areas of calcification were seen along with few scattered clusters of leydig cells. On immunohistochemistry, the tumor cells were found to show nuclear positivity for Oct-4 and the scattered sex-cord stromal cells were highlighted by the inhibin immunostain (Fig. 2). Based on these histological and immunohistochemical features a diagnosis of dysgerminoma arising in a background of gonadoblastoma was rendered for this gonad. The smaller gonad showed a tumor composed of a variety of tissues derived from ectoderm, endoderm and mesoderm, including keratinized stratified squamous epithelium, smooth muscle bundles, fibrous tissue and glial tissue. In addition, large areas showing immature mesenchyme, multiple foci showing immature neuroepithelium and immature endodermal derivatives in the form of irregular gland-like structures were also seen (Fig. 3). Based on these histological features, a diagnosis of Immature teratoma, Grade III was given for this gonad. Both the fallopian tubes were microscopically within normal limits. She was followed up every 3 monthly. Her serum β-human chorionic gonadotropin levels and alpha-feto protein levels were observed to be within reference range. FDG positron emission computerized tomography (PET-CT) did not reveal any significant abnormality.

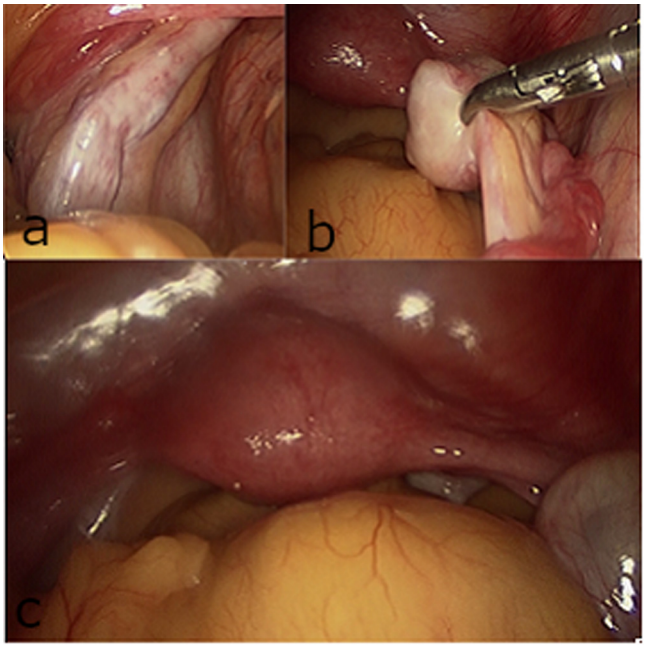

Fig. 1. Laparoscopic images showing grossly normal sized left ovary (1a), right ovary (1b) and uterus (1c).

Discussion

Patients with complete/pure gonadal dysgenesis show hypergonadotropic hypogonadism with low levels of estrogens and normal female levels of androgens. Their minimal breast development is a result of peripheral aromatization of androgens. They have scanty pubic and axillary hair and are taller than their peers. On histological examination, their streak gonads (ovaries) display fibrous tissue but no follicles [5,10]. The psychosocial and reproductive implications of the condition require multidisciplinary management involving pubertal induction, psychosocial support and assisted reproductive technologies [11]. As the müllerian structures are preserved in CGD, the uterus may show an increase in size with the initiation of estrogen replacement and in some cases successful pregnancies have been reportedly achieved following egg donation [12].

Some individuals with CGD may be identified in late adulthood with gonadal tumors, typically gonadoblastoma and/or dysgerminoma [13–15]. Other reported tumors include teratoma and embryonic carcinoma. The lifetime risk of development of gonadal tumors is these individuals is in the range of 15–35% [16]. In a comprehensive clinicopathologic review of 140 cases of neoplasms arising in dysgenetic gonads, 103 (53.1%) were gonadoblastomas, 38 (19.6%) dysgerminomas, 34 (17.5%), gonadoblastoma with areas of dysgerminoma, and 19 (9.8%) were of other histologic types [17]. Surgery is performed for staging as well as initial treatment of these neoplasms. Some cases of CGD demonstrate the development of dysgerminomas within a pre-existing gonadoblastoma, which is a benign or an in situ germ cell ovarian neoplasm composed of germ cells and sex cord stroma, in phenotypic females who have a Y chromosome [18,19]. This was also evident in the present case in one of the gonads, and she had an immature teratoma in the other gonad. To the best of our knowledge, such a combination of tumors, although theoretically possible, has not been reported till date in literature.

The importance of early diagnosis of gonadal dysgenesis (GD) and prophylactic bilateral gonadectomy, especially in 46, XY individuals is undeniable. This helps in substantially eliminating the risk of development of subsequent malignant germ cell neoplasms in them. In cases where the diagnosis of neoplasm precedes the diagnosis of CGD, appropriate multimodality oncological management should be introduced with simultaneous gonadectomy. Using prompt surgical treatment, either alone or with appropriate chemotherapeutic regimens, favorable clinical response can be attained even in cases with metastases or recurrence [20].

The present case, besides adding a rare case to the literature, highlights the importance of detailed pre-operative assessment of gonadal size and prompt prophylactic gonadectomy in cases with gonadal dysgenesis.

Funding

None.

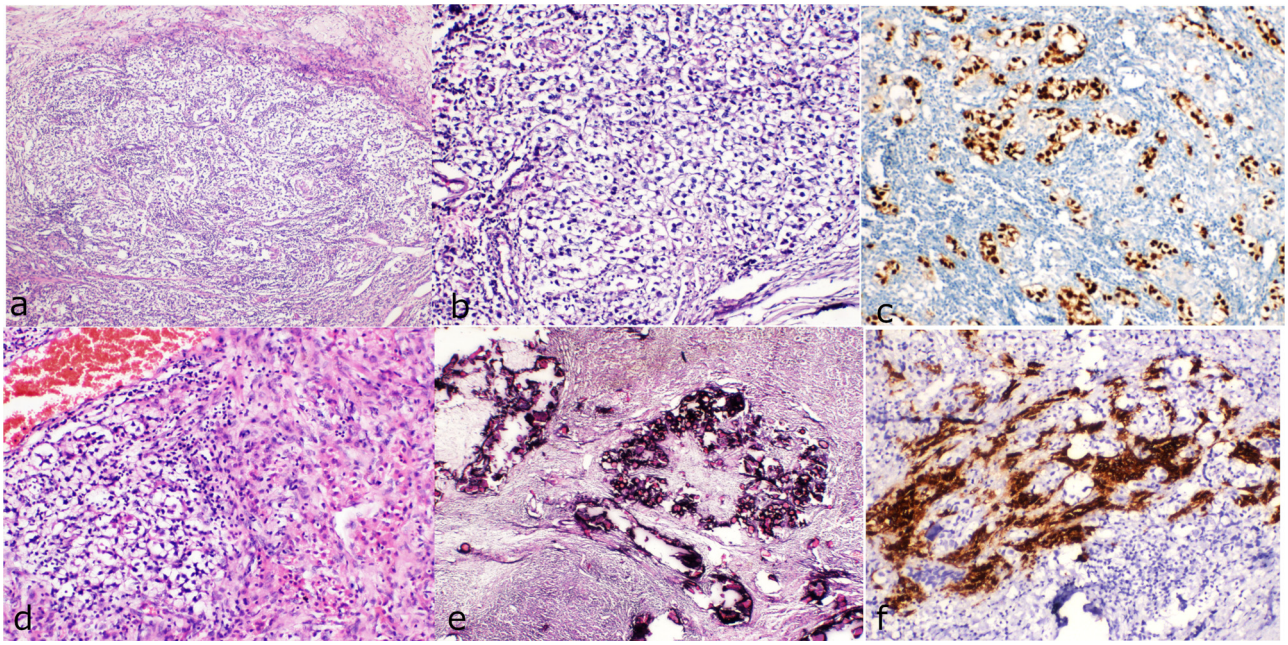

Fig. 2. 2a: Section from the larger ovary showing tumor arranged in nests separated by fibrous septae with lymphocytes (H&E; 4×); 2b: Higher magnification showing nests of moderately pleomorphic tumor cells with well defined cell borders and abundant clear cytoplasm representing dysgerminoma (H&E; 20×); 2c: Immunohistochemical staining for Oct-4 showing nuclear positivity in the tumor cells (20×); 2d: Section showing clusters of Leydig cells adjacent to the dysgerminoma (H&E; 10×); 2e: Section showing large areas of calcification surrounded by fibrous tissue (H&E; 2×); 2f: Immunohistochemical staining for inhibin highlighting the scattered leydig cells (20×).

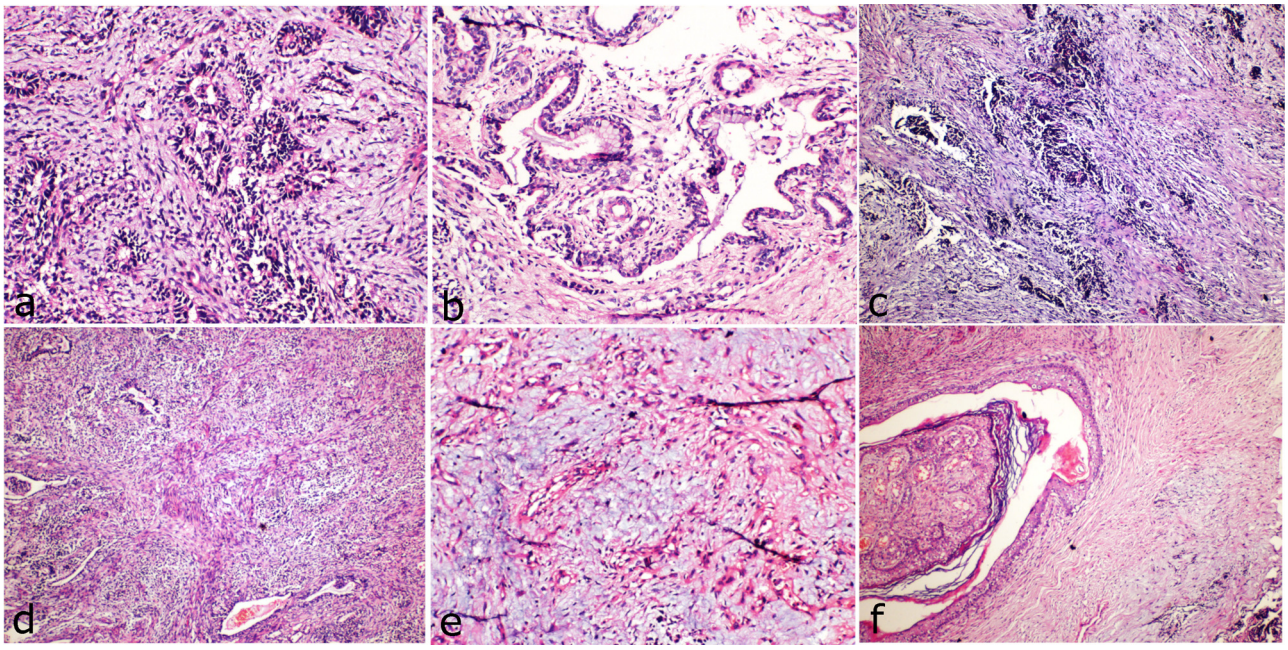

Fig. 3. Sections from the smaller ovary showing an immature teratoma with varied morphology, 3a, c: Section showing immature neuroepithelium (H&E; a:10×; c:4×); 3b: Section showing mucinous glands (H&E; 10×); 3d: Section showing irregular gland surrounded by fibrous tissue and smooth muscle bundles (H&E; 4×); 3e: Section showing immature mesenchyme (H&E; 10×); 3f: Section showing tissue lined by keratinized stratified squamous epithelium (H&E; 4×).

Conflicts of interest

None.

References

[1] Hughes IA, Houk C, Ahmed SF, Lee PA, LWPES Consensus Group, ESPE Consensus Group. Consensus statement on management of intersex disorders. Arch Dis Child 2006;91:554–63.

[2] Lee PA, Honk CP, Ahmed SF, Hughes IA. Consensus statement on management of intersex disorders. Pediatrics 2006;118:e488–500.

[3] Swyer GI. Male pseudohermaphroditism: a hitherto undescribed form. Br Med J 1955;2:709–12.

[4] King TFJ, Conway GS. Swyer syndrome. Curr Opin Endocrinol Diabetes Obes 2014;21:504–10.

[5] Michala L, Goswami D, Creighton SM, Conway GS. Swyer syndrome: presentation and outcomes. BJOG 2008;115:737.

[6] King TF, Conway GS. Swyer syndrome: a review. Reprod Endocrinol 2014;21:504–10.

[7] McCann-Crosby B, Mansouri R, Dietrich JE, McCullough LB, Sutton VR, Austin EG, et al. State of the art review in gonadal dysgenesis: challenges in diagnosis and management. Int J Pediatr Endocrinol 2014;2014:4.
[8] Krasna IH, Lee ML, Smilow P, Sciorra L, Eierman L. Risk of malignancy in bilateral streak gonads: the role of the Y chromosome. J Pediatr Surg 1992;27:1376–80.
[9] Pleskacova J, Hersmus R, Oosterhuis JW, Setyawati BA, Faradz SM, Cools M, et al. Tumor risk in disorders of sex development. Sex Dev 2010;4:259–69.
[10] Han Y, Wang Y, Li Q, Dai S, He A, Wang E. Dysgerminoma in a case of 46, XY pure gonadal dysgenesis (Swyer syndrome): a case report. Diagn Pathol 2011;6:84.
[11] Jorgensen PB, Kjartansdóttir KR, Fedder J. Care of women with XY karyotype: a clinical practice guideline. Fertil Steril 2010;94:105.
[12] Plante BJ, Fritz MA. A case report of successful pregnancy in a patient with pure 46, XY gonadal dysgenesis. Fertil Steril 2008;90(2015):e1–2.
[13] Yao Y, He HJ, Han JS, Guo HY. Dysgerminoma and gonadoblastoma with para-aortic lymph node metastasis in a patient with swyer syndrome. Chin Med J (Engl) 2017;130:1882–3.
[14] Agarwal A, Agarwal S. Swyer syndrome with gonadoblastoma: a clinicoradiological approach. J Hum Reprod Sci 2017;10:65–8.
[15] Yada-Hashimoto N, Komura H, Nagata S, Kubo C, Fujita M, Kamiura S. Unexpected diagnosis of stage IIA dysgerminoma in streak gonad in a patient with Swyer syndrome: a case report. Gynecol Endocrinol 2018;34:464–6.
[16] Hughes IA. Normal and abnormal sexual differentiation. In: Warrell David A, Cox Timothy M, Firth John D, editors. Oxford textbook of medicine. Oxford: Oxford University Press; 2010. p. 1963–74.
[17] Troche V, Hernandez E. Neoplasia arising in dysgenetic gonads. Obstet Gynecol Surv 1986;41:74–9.
[18] Ben Temime R, Chachial A, Attial L, Ghodbanel I, Makhloufl T, Koubaal A, et al. 46 XY pure gonadal dysgenesis with gonadoblastoma and dysgerminoma. Tunis Med 2008;86:710–3.
[19] Xue DU, Zhang X, Li Y, Han Y. 46, XY female sex reversal syndrome with bilateral gonadoblastoma and dysgerminoma. Exp Ther Med 2014;8:1102–4.
[20] Kumar NP, V M, Mathews A, James FV. Mixed germ cell tumour in a case of pure gonadal dysgenesis (Swyer syndrome)-a case report. Cureus 2016;8:e459.