

CASE REPORT

GONADOBLASTOMA: A CLINICOPATHOLOGIC STUDY

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Gonadoblastoma is a rare tumor found almost exclusively in patients with an underlying gonadal disorder, and accounts for two-thirds of gonadal tumors in women with abnormal gonadal development. Three cases of gonadoblastoma are reported here. One had Swyer syndrome (pure gonadal dysgenesis) with a 46-XY karyotype, the second patient had a mixed 46-XY and 46-XO karyotype, and the third patient had male pseudohermaphroditism and a 46-XY karyotype. Patients with pure gonadoblastoma have an excellent prognosis, when bilateral excision is performed. Gonadoblastoma may be overgrown by dysgerminoma, however, there is a good prognosis. Gonadoblastoma has never been detected with metastatic lesions. The prognosis for gonadoblastoma, including cases of Swyer syndrome, is good, provided early excision is performed bilaterally.

Keywords • dysgerminoma • gonadal dysgenesis • gonadoblastoma • Swyer syndrome

Introduction

Gonadoblastoma is an uncommon tumor. The neoplastic nature of gonadoblastoma has been questioned because some lesions are small and may undergo complete regression by hyalinization and calcification. In 1953, gonadoblastoma was described in detail by Scully¹ as a gonadal tumor composed of germ cells and sex-cord derivatives resembling immature granulosa and Sertoli cells. Gonadoblastoma occurs almost entirely in patients with pure or mixed gonadal dysgenesis or in male pseudohermaphroditism.² The association with dysgerminoma is seen in 50% of cases and with other, more malignant germ cell neoplasms, in an additional 10% of cases as reported in Iran by Kariminejad et al in 1972.³

Case Report

Case 1

A 24-year-old patient with complete female phenotype presented with primary amenorrhea and

infertility of 5 years' duration.

Laparoscopic findings showed a normal uterus and fallopian tubes with small sized fibrotic ovaries. Karyotyping revealed a 46-XY pattern, which is compatible with the diagnosis of Swyer syndrome. The patient underwent bilateral

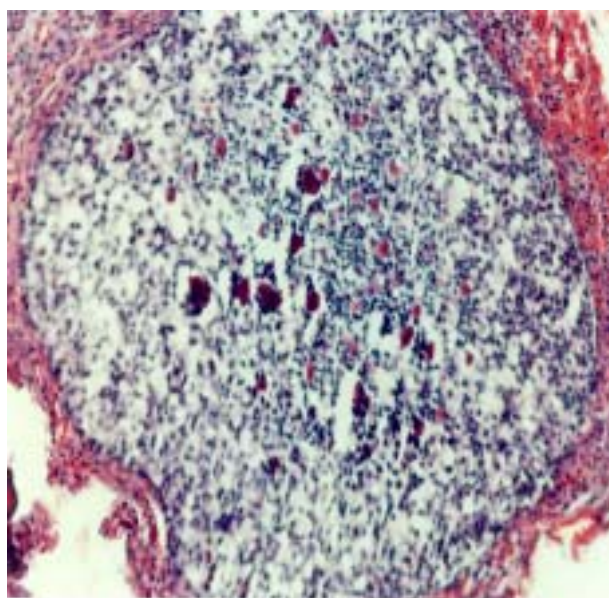


Figure 1. Well-circumscribed nests of gonadoblastoma contain an intimate mixture of germ cells and granulosa cells (Hematoxylin and eosin X 400).

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Gonadoblastoma: a Clinicopathologic Study

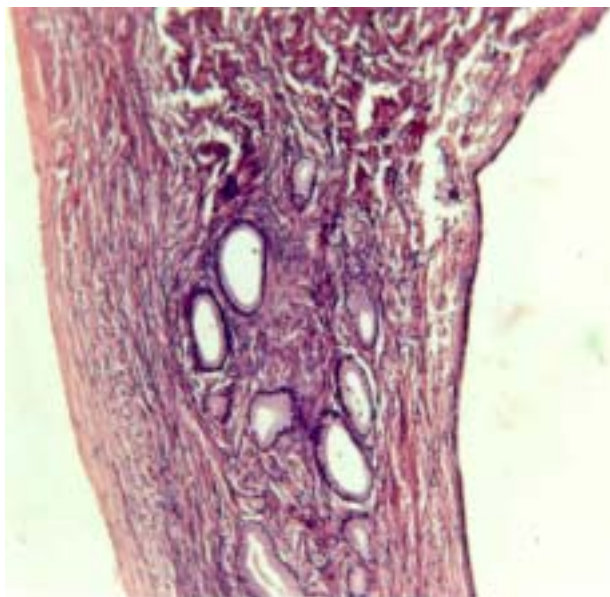


Figure 2. Benign mucinous cystadenoma with a typical endocervical – type epithelium was associated with gonadoblastoma (Hematoxylin and eosin X 100).

gonadectomy. Histopathology of the right gonad revealed discrete cells of sex-cord type along with laminated spheres of calcification. These are the characteristic features of gonadoblastoma (Figure 1). Within the left gonad, cortical gonadal tissue was seen.

Case 2

A 19-year-old patient with female phenotype presented with primary amenorrhea. Ultrasonography indicated uterine agenesis, and showed a 12 mm simple cyst on the right gonad. The left gonad was very small (approximately 8 mm in maximal diameter) on ultrasonography. Karyotyping showed 85% 46-XY and 15% 46-XO patterns. Sex chromatin was negative. Bilateral gonadectomy was performed. Gonadoblastoma in both gonads was documented. A simple mucinous cystadenoma

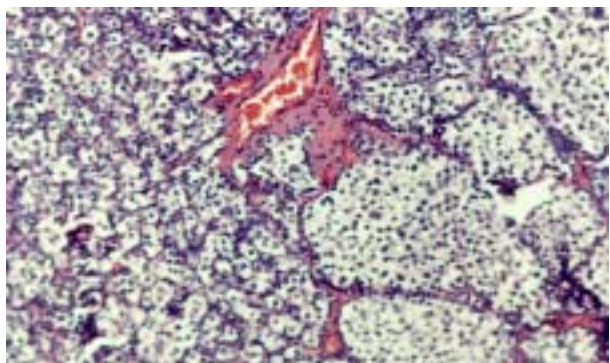


Figure 3. Gonadoblastomas are overgrown by dysgerminoma (Hematoxylin and eosin X 400).

was also detected in the right gonad (Figure 2).

Case 3

A 19-year-old patient with female phenotype presented with primary amenorrhea. A very small infantile uterus (3 × 2 cm) was detected on ultrasonography. Chromosomal analysis revealed a 46-XY pattern. After bilateral gonadectomy, both gonads showed gonadoblastoma overgrown by dysgerminoma (Figure 3).

Discussion

The most distinctive member of the group of tumors composed of a combination of germ cells and sex-cord stromal cells is gonadoblastoma.^{1,4,5} This tumor occurs in sexually abnormal individuals, most commonly affected by gonadal dysgenesis and carrying the Y chromosome^{3, 6 - 9} (i.e., XY gonadal dysgenesis and XO-XY mosaicism).^{10 - 13} However, gonadoblastoma has also been documented in both phenotypically and chromosomally normal females, even those with successful pregnancies.¹⁴

All patients in this study showed abnormal karyotyping. Gonadoblastomas are bilateral in over one-third of cases.¹⁵ In this study, two-thirds of the cases were bilateral. The nature of the gonad in which a gonadoblastoma originates is frequently not determined because there is often a mixed pattern of growth by the gonadoblastoma or a neoplastic germ cell element, most frequently a dysgerminoma.^{5,16} One case in this study had bilateral gonadoblastomas and was overgrown by dysgerminoma. Patients with a pure gonadoblastoma have an excellent prognosis provided both gonads are excised. The prognosis of patients with gonadoblastoma associated with dysgerminoma is also good.^{5,16,17} Gonadoblastoma has never been detected with metastatic lesions and has never been encountered outside the gonads.⁵ A unique combination of an ovarian gonadoblastoma, dysgerminoma, and mucinous cystadenoma in a patient with Turner's syndrome was reported by van del Bijl et al.² In our study, the association of a gonadoblastoma with a simple mucinous cystadenoma (tumor of epithelial origin) was observed with interest.

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References

- 1 Scully RE. Gonadoblastoma. A review of 74 cases. *Cancer*. 1970; **25**: 1340 – 56.
- 2 Van del Bijl AE, Fleuren GJ, Kenter GG, et al. Unique combination of an ovarian gonadoblastoma, dysgerminoma and mucinous cystadenoma in a patient with Turner's syndrome: a cytogenetic and molecular analysis. *Int J Gynecol Pathol*. 1994; **13**: 267 – 72.
- 3 Kariminejad MH, Movlavi MA, Nasserghossi MA, et al. Gonadoblastoma associated with mixed gonadal dysgenesis. *Am J Obstet Gynecol*. 1972; **113**: 410 – 4.
- 4 Rosai J. *Ackerman's Surgical Pathology*. 8th ed. St. Louis: Mosby; 1996: 1521.
- 5 Fox H. *Obstetrical and Gynecological Pathology*. 4th ed. New York: Churchill Livingstone; 1995: 897 – 907.
- 6 Sternberg SS. *Diagnostic Surgical Pathology*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 1999: 2371.
- 7 Gibbons B, Tan SY, Yo CC, et al. Risk of gonadoblastoma in female patients with Y chromosome abnormalities and dysgenetic gonads. *J Paediatr Child Health*. 1999; **35**: 210 – 3.
- 8 Uehara S, Funato T, Yaegashi N, et al. SRY mutation and tumor formation on the gonads of XP pure gonadal dysgenesis patients. *Cancer Genet Cytogenet*. 1999; **113**: 78 – 84.
- 9 Gitlay JC, Ausems MG, Van Seumeren L, et al. Short stature as the only presenting feature in a patient with an isodicentric (Y) (q 11.23) and gonadoblastoma. A clinical and molecular cytogenetic study. *Eur J Pediatr*. 2001; **160**: 154 – 8.
- 10 Medina LRA, Merchan FI, Conde MAF, et al. Gonadoblastoma in Swyer syndrome [in Spanish]. *Acta Urol Esp*. 1997; **21**: 708 – 10.
- 11 Joki-Erkkila MM, Karikoski R, Rantala I, et al. Gonadoblastoma and dysgerminoma associated with XY gonadal dysgenesis in an adolescent with chronic renal failure: a case of Frasier syndrome. *J Pediatr Adolesc Gynecol*. 2002; **15**: 145 – 9.
- 12 Simko J, Horvathova L, Mezenska R, et al. Y-chromosome mosaicism as markers of increased risk for development of gonadoblastoma in patients with Turner's syndrome [in Slovak]. *Ceska Gynekol*. 1997; **62**: 89 – 91.
- 13 Gravholt CH, Fedder J, Naeraa RW, et al. Occurrence of gonadoblastoma in females with Turner syndrome and Y-chromosome material: a population study. *J Clin Endocrinol Metab*. 2000; **85**: 3199 – 202.
- 14 Zhao S, Kato N, Endoh Y, et al. Ovarian gonadoblastoma with mixed germ cell tumor in a woman with 46-XX karyotype and successful pregnancies. *Pathol Int*. 2000; **50**: 332 – 5.
- 15 Russell P, Farnsworth A. *Surgical Pathology of the Ovaries*. 2nd ed. New York: Churchill Livingstone; 1997: 576.
- 16 Teter J, Boczkowski K. Occurrence of tumors in dysgenetic gonads. *Cancer*. 1967; **20**: 1301 – 10.
- 17 Scully RE. Gonadoblastoma. A gonadal tumor related to the dysgerminoma (seminoma) and capable of sex hormone production. *Cancer*. 1955: 455 – 63.