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Ovarian Gynandroblastoma – A Systematic Review

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Abstract **Review Article**

Gyandroblastomas are rare ovarian tumors, presenting in young aged women. They are benign tumors with malignant potential hardly reported. They have components of both granulosa cell tumor and sertoli leydig tumor and hence they present with the hormonal manifestation of both. Fertility preserving surgery is the preferred treatment for these tumours. The diagnosis of these tumours is mainly pathological, where the present of the above mentioned dual components in mandatory. Though benign, late recurrences are rarely reported and hence long term follow up may be necessary.

Keywords: Gynandroblastoma, Ovarian tumour.

INTRODUCTION

Gynandroblastoma, a rare ovarian tumor, manifest with a combination of two histological elements, granulosa cell tumor (GCT) and Sertoli-Leydig cell tumor (SLT) differentiation. First described by Robert Meyer in 1930, only less than 30 cases have been reported in the literature so far. Gynandroblastoma usually consists of adult-type granulosa cells. Gynandroblastoma with juvenile type of granulosa cell tumor is even rarer, with only 4 cases reported in the English literature [1]. Patients often present with symptoms caused by increased hormone, mainly androgen, production by these tumors. These tumors usually present with stage 1 disease and are usually considered to behave in a benign manner [2]. Recurrences have been rarely reported. Because the tumor is so rare, molecular pathways for development are completely uncharacterized [3]. Despite the advancement of diagnostic and therapeutic modalities, the imaging diagnostic features of gynandroblastoma have not yet been described [4]. Surgery is the most important therapeutic modality and must be conservative as possible to preserve reproductive function [5]. No large-scale studies available regarding the prognosis of this disease exists, and late-onset recurrence and subsequent death may occur in some cases [6].

CLINICAL PRESENTATION

Gynandroblastomas most commonly presents in less than 30 years of age and very few cases have been reported beyond 30 years of age. The most important clinical manifestation is hormonal dysfunction [1]. Symptoms of both hyperestrogenism (menometrorrhagia or postmenopausal bleeding) and masculinization (breast atrophy, clitoral hypertrophy, hirsutism, and voice change) may coexist in a patient with this type of tumor [6]. It is difficult to characterize the biological behavior of gynandroblastoma due to its extremely low incidence. Based on the reported cases, it appears to have a benign course. The majority of gynandroblastomas present as stage I tumors [1].

Pathology

Macroscopically, gynandroblastoma is a solid tumour with cystic formation, and the colour of the division surface is white or flavedo (Figure 1) [6]. Microscopically, gynandroblastomas usually demonstrate granulosa cells that grow in rounded islands arranged in a microfollicular pattern with typical Call Exner bodies and admixed Sertoli cells that grow in well- differentiated tubules (Figure 2) [3]. The diagnostic criteria for gynandroblastoma indicate that the minor tumor component (either Sertoli-Leydig cells in a GCT, or granulosa cells in an SLT) should account for at least 10% of the entire tumor. Therefore, sufficient tumor sampling is essential for an accurate

diagnosis. Although most reported GCT cases are of the adult-type, a juvenile-type has also been identified. The histology of adult-type and juvenile type cells is the same for GCT; therefore, it is not difficult to diagnose these tumors. Several immune histochemical markers exist to aid differential diagnosis, but these markers are used to diagnosis every type of ovarian sex cord-stromal tumor and they are not specific to gynandroblastoma. The representative sex cord-stromal cell markers include inhibin, calretinin, SF1, WT-1, and CD99. MART-1/melan-A is a marker specific to SLT and steroid cell tumors [Figure 3].[9] Additionally, the cell cycle regulatory protein 14-3-3 sigma was recently identified as a diagnostic marker for GCT and steroid cell tumors [1].

Fig-1: Gross findings showing solid tumour with cystic formation.

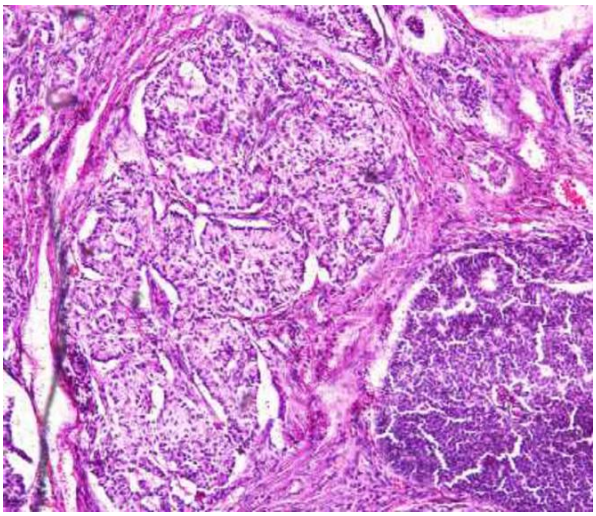

Fig-2: HPE showing granulosa cells that grow in rounded islands arranged in a microfollicular pattern.

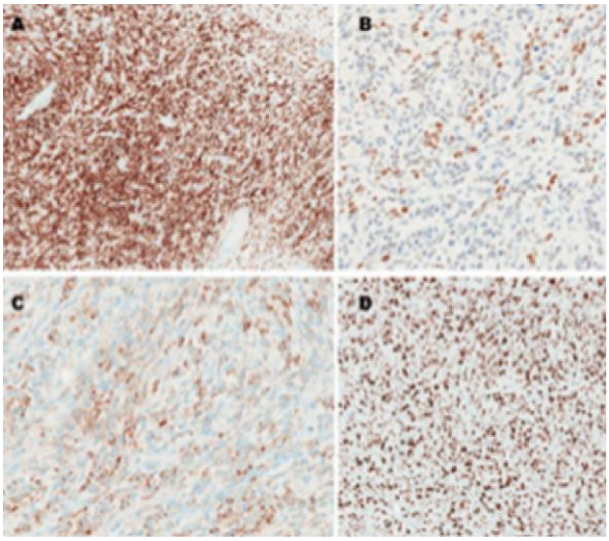

Fig-3: Immunohistochemical staining shows that tumor cells are diffusely positive for CD56 (A), SF1 (B), and inhibin (C). Tumor cells have a high Ki-67 labeling index (D).

Pathogenesis

The histogenesis of gynandroblastoma is unknown, but it is generally assumed that it originates from a single progenitor cell that can differentiate into both female and male elements. During embryogenesis, gonadal tissues develop from the mesoderm of the urogenital ridge and the ridge organizes the endocrinologically active tissues of the gonad, which includes granulosa cells, Sertoli cells, theca cells, ovarian stromal cells, and Leydig cells. Gynandroblastoma and other sex cord- stromal tumors are considered to have their origin in the cells of the urogenital ridge [1].

Recently, several genetic studies of ovarian sex cord-stromal tumors focusing on cytogenetic alterations have been published. The most widely studied genetic change is the FOXL2 mutation C134W (402 C > G) found in GCTs. FOXL2 is a transcription factor that is restrictedly expressed in granulosa cells during development and adulthood. This mutation is widely observed in adult type-GCT and can be a diagnostic or prognostic marker. Approximately 30% of JGCT tumors harbor the gsp oncogene and 60% contain the AKT1 gene mutation. These biological markers have the potential to be of therapeutic value. Regarding SLT, somatic or germline mutations of DICER1, which encodes an RNase III endonuclease, are well-known genetic alterations. Somatic hot spot mutations of DICER1 have been observed in approximately 60% of SLTs. These frequent genetic changes of sex-cord stromal tumors had been understudied with regard gynandroblastoma [1].

Treatment and prognosis

Most patients presents with stage I disease and hence were successfully treated by simple surgical resection with regular follow-up [1]. Surgery is the most important therapeutic modality and must be conservative as possible to preserve reproductive function.[5] Only one recurrence case has been reported, in which the tumor reportedly recurred 10 years after the original tumor was surgically removed [1].

CONCLUSION

Gynandroblastoma is very rare and it typically occurs in women of reproductive age. The pathogenesis and biologic behavior of gynandroblastoma are still not well known. However, based on the limited number of previous studies, this tumor shares many clinicopathologic characteristics with other sex-cord stromal tumors, including GCT and SLT. More comprehensive histologic and genetic studies are needed [1]. Being a very rare pathological entity, this is very challenging to a pathologist to diagnose gynandroblatoma and he must have a suspicious eye while passing through a histopathological specimen of an ovary. Correct diagnosis of this tumour is very useful for patients for hormonal balance and better quality life [5]. Because the granulosa cell tumors are known to recur 10 years after initial resection, some authors have suggested a similar follow-up in gynandroblastoma cases. On the other hand, Sertoli cell tumors are thought to be a benign tumor with some malignant potential. It remains unanswered whether gynandroblastoma should behave and be followed like one of the pure tumors (granulosa cell or Sertoli cell tumor) or as a unique entity [3].

REFERENCES

1. Jang N, Lee D, Jang E, Bae Y, Baek J, Jang M. (2018). Ovarian Gynandroblastoma with a Juvenile Granulosa Cell Tumor Component in a Postmenopausal Woman: A Case Report and Literature Review. J Pathol Transl Med, 52(5):344-348.
2. Wilberger A, Yang B. (2015). Gynandroblastoma With Juvenile Granulosa Cell Tumor and Concurrent Renal Cell Carcinoma. Int J Surg Pathol., 23(5):393-398.
3. Chivukula M, Hunt J, Carter G, Kelley J, Patel M, Kanbour-Shakir A. (2007). Recurrent Gynandroblastoma of Ovary-A Case Report. Int J Gynecol Pathol., 26(1):30-33.
4. Takeda A, Watanabe K, Hayashi S, Imoto S, Nakamura H. (2017). Gynandroblastoma with a Juvenile Granulosa Cell Component in an Adolescent: Case Report and Literature Review. J Pediatr Adolesc Gynecol., 30(2):251-255.
5. Fatima Q, Verma S, Bairwa N, Gauri L, BR A, Tyagi D. (2017). Gynandroblastoma: An extremely rare case. Int J Advanced Res Rev., 2(1):32-38.
6. Shichido S, Tashima L, Hori K, Kimura H, Nakatsuka S, Hoshida Y *et al*. (2016). Gynandroblastoma of postmenopausal women: a case report. Eur J Gynaecol Oncol., 37(4):581-83.