



## Juvenile Granulosa Cell Tumor: A Case Report

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### Abstract

Granulosa cell tumours (GCT) are rare sex cord stromal tumour, encompassing only 2% of all the ovarian tumours<sup>1</sup>. Only 0.1% of all ovarian tumours and 4-5% of GCT occur in children. Juvenile GCT(JGCT), a sub-type of ovarian sex cord stromal tumour has a favorable prognosis if diagnosed at an early stage.<sup>2</sup> We present a case of a 19 year old female patient; presenting with symptoms of clitoromegaly, irregular menstrual cycles & hirsutism.

**Keywords:** Juvenile Granulosa Cell Tumor, ovarian neoplasm, reticulin, sex-cord stromal, rare.

### Introduction

Ovarian neoplasms are relatively rare in childhood and adolescence; & only 5% to 8% of the cases are of sex cord stromal origin. Granulosa cell tumors are a group of unique, estrogen producing sex cord stromal tumors of the ovary.<sup>3</sup>

They constitute 1 to 2% of all ovarian malignancies; with an overall incidence varying from 0.4 to 1.7 cases per 100,000 women. The juvenile form of granulosa cell tumours (5% of the cases) is even rarer as compared to its adult counterpart (remaining 95% of the cases); and usually presents as predominantly solid mass lesions.<sup>4</sup>

We present this rare neoplasm in a 19 year old girl with hirsutism, clitoromegaly & irregular menstrual cycles with a unilateral mass.

### Case History

A 19 year old female presented to our hospital with a history of excessive body hair growth & irregular

menstrual cycle; menstruation of 3-4 days duration occurring every 45-60 days.

**On Examination:** a non tender mass was palpable in the abdomen; appearing to arise from the pelvis. Clitoromegaly & hirsutism was also noted.

### Investigations

**CT & MRI:** revealed a cystic mass arising from the left ovary; with a thick walled multiloculated structure & minimal ascites.

**Hormonal Evaluation:** revealed elevated serum estradiol of 400 pg/ mL (reference: 63.9-356.7 pg/ml), FSH & LH at 0.40mIU/mL & 2.00 mIU/mL (reference range FSH: 1.40-18.10 mIU/mL & 1.50-9.30 mIU/ mL respectively) while AFP, hCG, CEA, CA 19-9 & Inhibin B levels were within normal limits.

She underwent a unilateral salpingo-oophorectomy.

### Gross Findings

We received an ovarian mass at the Pathology department measuring 22x15x6cm, with attached fal-

lopidian tube with fimbrial end measuring 8.5cm in length. The outer surface of the mass was grey white to grey brown; while the cut surface was solid grey white, with small cystic areas filled with mucinous material.

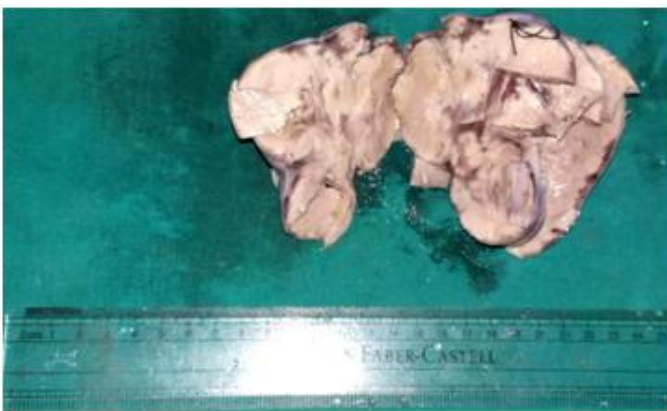
**Histopathological Examination:** Revealed variably sized follicles containing eosinophilic material, separated by sheets of round to polyhedral cells with hyper chromatic nuclei, occasional nuclear grooves & moderate amount of cytoplasm. Tumor cells in occasional tubules, trabeculae & nests were separated by fibromatous/thecomatous stroma, nests of luteinized cells with abundant vacuolated, eosinophilic cytoplasm & blood filled cysts.

Focal areas of poorly differentiated Sertoli Leydig cell tumor counterpart revealing spindle shaped cells with atypia admixed with Leydig cells showing bland nuclei & moderate amounts of dense eosinophilic cytoplasm were also seen.

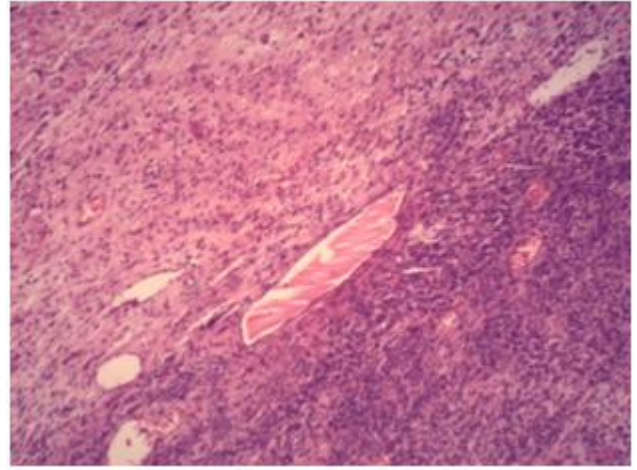
Mitotic activity revealed a mitotic index of 3 per high power field. Marked necrosis, haemorrhage & inflammatory cell infiltrate were also seen.

**Reticulin Staining:** showed that the thecomatous foci had a dearth of reticulin; indicating these to be of granulosa cell nature & the reticulin fibers were seen surrounding aggregates and nests of tumor cells.

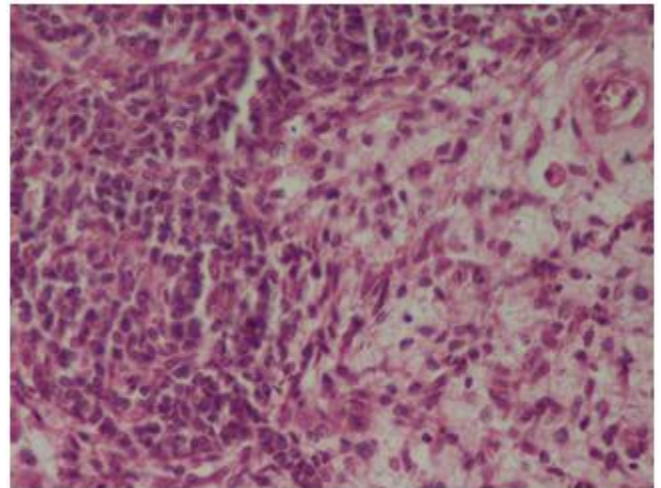
**Immunohistochemical Staining:** showed positivity for vimentin, CD99, CD56 & cytokeratin AE1/AE3, consistent with the diagnosis of Juvenile Granulosa Cell Tumor.



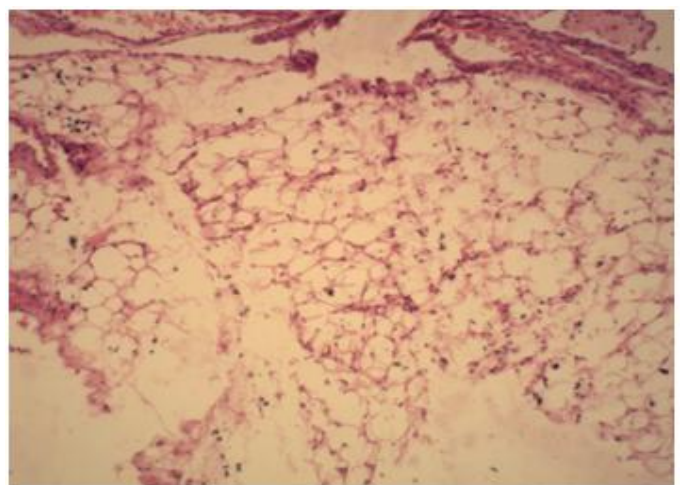
**Fig.1:** Cut surface of ovarian mass shows solid & focally cystic areas with mucinous material.



**Fig.2:** Photomicrograph shows sheets & follicles with eosinophilic material lined by hyperchromatic tumor cells with occasional nuclear grooves & moderate to abundant eosinophilic cytoplasm. (H&E, 100X)

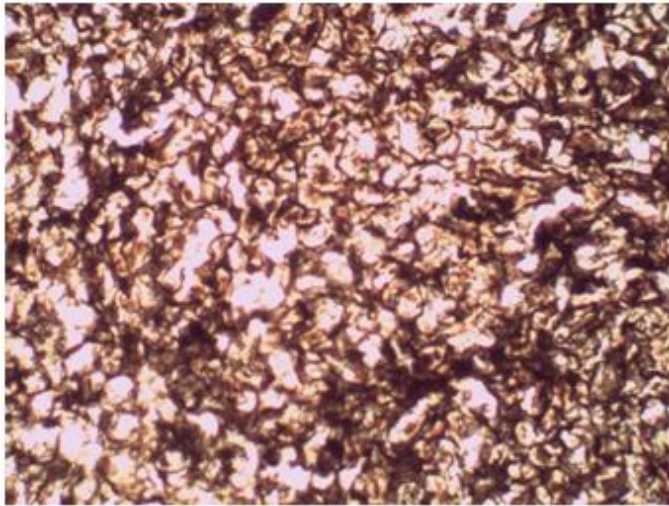


**Fig.3:** Photomicrograph shows tumor cells with adjacent thecomatous/fibromatous stroma. (H&E, 400X)



**Fig.4:** Photomicrograph shows omentum free from tumor (H&E, 100X)





**Fig.5:** Photomicrograph shows reticulin characteristically surrounding nests of tumor cells.(Reticulin stain, 400X)

### Discussion

Ovarian malignancies stand as a leading cause of gynaecological cancer death accounting for around 6% of all cancers diagnosed in females.<sup>5</sup>

Juvenile granulosa cell ovarian tumor (JGCOT) was first described by Scully in 1977.<sup>9</sup>

Less than 5% of GCTs are diagnosed before puberty.<sup>6</sup> The great majority of these tumors as well as many GCTs in young adults differ histologically from adult GCTs, the designation ‘juvenile’ being selected, as 97% occur in the first three decades.<sup>7</sup>

More than half of cases of the juvenile form have been reported in the “less than 10 years” age group<sup>8</sup>; hence our case differ by falling in the other group.

80% of JGCTs occurring in children result in isosexual precocity, accounting for 10% cases that syndrome in the female. The precocity is more specifically termed ‘pseudoprecocity’ as there is no associated ovulation or progesterone production, precluding the possibility of pregnancy, which exists in true precocity. Pseudoprecocity manifests as development of breasts, followed by pubic & axillary hair, stimulation & enlargement of external & internal secondary sex organs, irregular uterine bleeding, & a whitish vaginal discharge. Somatic & skeletal development is accelerated; clitoromegaly can occur.<sup>7</sup>

Post pubertal presentation occurs with abdominal pain or swelling, sometimes menstrual irregularities

or amenorrhoea, & 6% with acute abdomen due to rupture. This also contrasts with the index case presentation.

Only 2% are bilateral.<sup>7</sup> The single most common presentation is as a solid & cystic neoplasm.<sup>11</sup>

On microscopy, the two characteristic features that distinguish JGCT from AGCT are the rounded, hyper chromatic nuclei, mostly lacking grooves & frequent abundant content of eosinophilic luteinized cytoplasm. Nuclear atypicality varies from minimal to marked, with a variable mitotic rate; generally higher than AGCT.

The follicles of JGCT are more irregular in size & shape, with more luteinized cells, with round, more hyper chromatic nuclei, lacking grooves often. The mucicariminophilic, often basophilic follicular content differs from the eosinophilic fluid with degenerating nuclei or basement membrane material in micro follicles of AGCT.<sup>11</sup>

Reticulin stains are crucial in indicating the epithelial nature of thecomatous foci often noted in these tumors; ruling out other differentials such as thecoma, fibroma, sclerosing stromal tumor of the ovary and other stromal tumors. Reticulin is characteristically seen surrounding clusters of tumor cells.<sup>12,13</sup>

Unlike its adult counterpart, the juvenile form is considered to be relatively benign with excellent survival rates reaching as high as 97%.<sup>8</sup> Thus accurate diagnosis remains key.

Morphologically and radiologically it is not possible to differentiate between the two varieties of GCT, hence both clinical and histopathological guidelines are needed to correctly subcategorize granulosa cell tumours into the two types and age cannot be considered the definitive criterion.<sup>4</sup>

Although there are no prospective, controlled, and randomized studies, fertility sparing surgery is recommended because the disease is commonly unilateral. In addition, wedge biopsy from the contralateral ovary and chemotherapy are not recommended.<sup>10</sup>

### Conclusion

An uncommon malignancy particularly in pre pubertal girls, a high index of suspicion with timely removal with appropriate treatment warrants preservation of fertility & symptomatic cure for the range of complaints. A careful histopathological examination remains key to the diagnosis of this tumor.

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### Abbreviations

AGCT: Adult Granulosa Cell Tumor, JGCT: Juvenile Granulosa Cell Tumor, &: And, FSH: Follicle stimulating hormone, LH: Luteinizing hormone, AFP: Alpha fetoprotein, hCG: Human Chorionic Gonadotropin, CEA: Carcinoembryonic antigen, CA 19-9: Carbohydrate antigen 19-9.