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Case Report

Juvenile Granulosa Cell Tumour with Precocious Puberty

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Abstract

Ovarian Granulosa cell tumour is a rare ovarian neoplasm, which typically occurs in children and young women. More than ninety percent of the patients are diagnosed in stage IA, who can be cured by unilateral oophorectomy. Meanwhile, the remaining is diagnosed in more advanced stages, wherein tumors may exhibit aggressive behavior. In this stage, surgery and adjuvant chemotherapy may be required. The study report a 5 year old girl with granulosa cell tumour with precocious puberty. She underwent laparotomy followed by unilateral salphingo ophorectomy. As histopathology report showed juvenile granulosa cell tumour with capsular invasion (stage IC), she was scheduled for 3 cycles of adjuvant chemotherapy with Bleomycin, Etoposide and Cisplatin (BEC) regimen. She has been disease free since for more than six months.

Keywords: Granulosa cell tumour, Juvenile, Precocious puberty, Salphingo-Ophorectomy, Surgery, Chemotherapy.

INTRODUCTION

Approximately 90% of the Granulosa cell tumour cases diagnosed in prepubertal girls and most women less than 30 years of age are of juvenile type (JGCT) (Young et al., 1984).The majority of prepubertal patients present with clinical evidence of isosexual precocious pseudopuberty, which may include breast enlargement, development of pubic hair, increased vaginal secretion, advanced somatic development and other secondary sex characteristics(Young et al., 1984; Lack et al., 1981; Plantaz et al., 1992; Vasal et al., 1988; Zaloudek and Norris, 1982). They arise from sex cord tumours and stroma. Juvenile form of Granulosa Cell Tumour has more pronounced signs of malignancy and increased risk of recurrence. We are here reporting a case of 5 years old village girl of Juvenile Ovarian Granulosa cell tumour, presenting at Gynecology OPD with frequent pain lower abdomen, enlargement of bilateral breast and abnormal vaginal discharge for 3 months. Clinical examination was suggestive of precocious puberty, (Figure 1).Patient was diagnosed as Juvenile Granulosa cell tumour (Stage IC) following surgery .Adjuvant chemotherapy was given.

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Case

We report a case of a 5 years old Female child presented to Gynecology OPD with symptoms of frequent pain in the lower abdomen, enlargement of bilateral breast and abnormal vaginal discharge for 3 months (Figure 1). Clinical examination was suggestive of precocious puberty. Preliminary work-up with ultrasonography (USG) abdomen and routine blood test revealed 15x10 cm solid, cystic mass with moderate vascularity and minimal ascites, marginally high estradiol (59 pg/ml) with mildly suppressed FSH (1 mIU/ml) and LH(1.2 mIU/ml) levels, and high level of inhibin A (612 pg/ml). She underwent laparotomy followed by unilateral salphingo-oophorectomy with omentectomy and peritoneal wash. Per-operatively no separate ovarian tissue was observed, whole ovary was replaced by

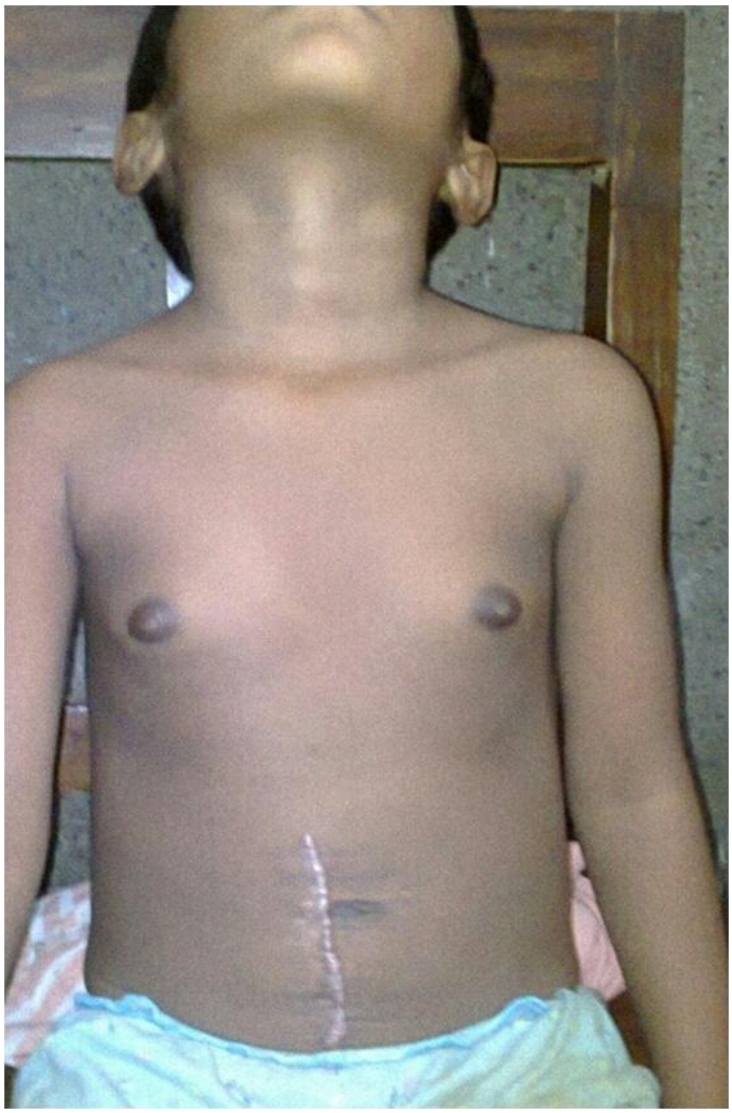

Figure 1. Case of Juvenile Granulosa cell tumour ovary with precofilename precocious puberty

solidcystic mass, slightly adherent to peritubal fat. Enlarged lymph-node or peritoneal fluid was not observed. Cyst contained hemorrhagic fluid and the solid part was yellow with hemorrhage and necrosis. Microscopic examination revealed cellular tumour with trabecular and micro follicular pattern. Neoplastic juvenile granulosa cells were diffuse with rounded, hyper chromatic nuclei, lacking grooves, abundant eosinophilic cytoplasm and moderate nuclear atypia (vide microscopic picture, figure 2-4). Remnant portion of ovary, omentum and peritoneal fluid were free from tumour cell invasion. Hence, the diagnosis was juvenile granulosa cell tumour - stage IC. Post-operative period was uneventful. Two weeks after surgery, patient was scheduled for 3 cycles of BEP regimen chemotherapy at 21 days interval. Patient is now tolerating chemotherapy well.

DISCUSSION

Ovarian neoplasm is relatively rare in childhood and adolescence, when encountered the majority are of germ cell origin while only 5%-7% account for sex cord stromal tumour. Granulosa cell tumors, which belong to the sex cord-stromal category, were described for the first time in 1855 by Rokitansky (Gittleman et al., 2003). In younger age group, majority are of granulosa cell tumour type which has a distinct cellular biology from typical granulosa cell (Young et al., 1984). In a clinicopathological study composed of 125 cases of JGCT 44% occurred in less than 10 years age group and only 3% after the third decade of life (Young et al., 1984). The majority of prepubertal patients presented with clinical evidence of isosexual precocious pseudopuberty, which may include breast enlargement,

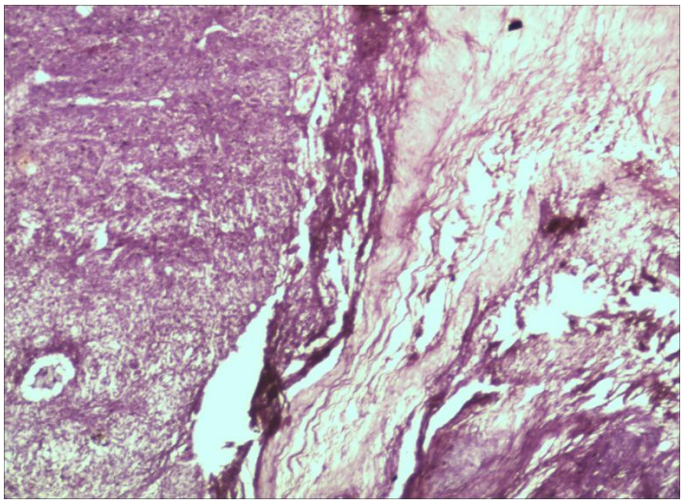

Figure 2. Microscopic picture of Ovarian SO-L Cellular tumour with-trabecular,follicular pattern

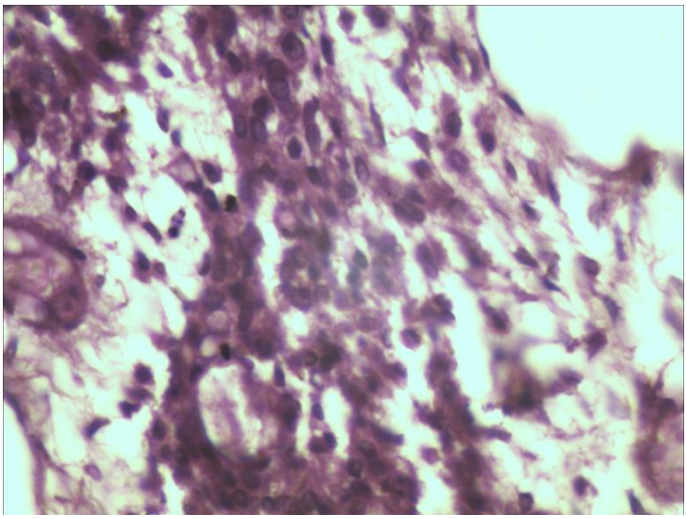

Figure 3. Microscopic picture-Ovarian tumour with hyper-chromatic nuclei and cellular atypia and eosinophillic cytoplasm

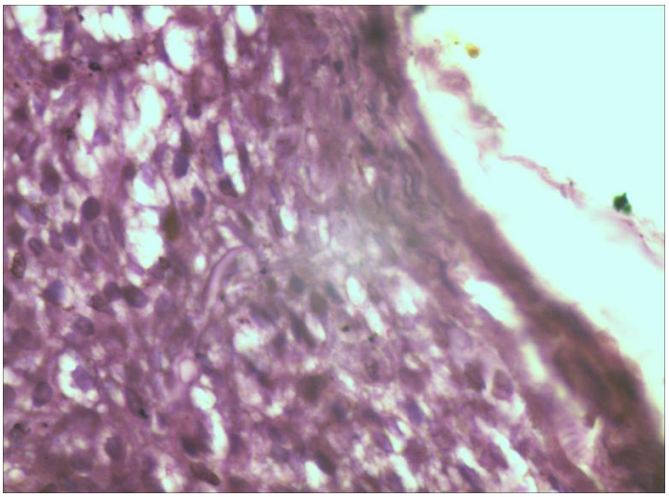

Figure 4. Microscopic picture- Ovarian tumour with rupture of capsule.

development of pubic hair, increased vaginal secretion, advanced somatic development and other secondary sex characteristics (Young et al., 1984; Lack et al., 1981; Plantaz et al., 1992; Vasal et al., 1988; Zaloudek and Norris, 1982).Serum estradiol level was reported to elevated in 17/17 cases of JGCT with pseudo puberty (Plantaz et al., 1992). Elevated levels of serum progesterone and testosterone, as well as suppressed level of luteinizing hormone and follicle stimulating hormone, were likewise observed. The occasional patient would harbor an androgen secreting JGCT. Accompanied by virilization (Lack et al., 1981; Plantaz et al., 1992; Vasal et al., 1988).When stage was assigned based on surgical and histopathological parameters, 88% were stage IA,2% stage IB,8% stage IC, and 3% stage II. Extra-ovarian spread was infrequently encountered, whereas rupture was noted in 10% of cases. Ascitis contributed to abdominal distention in 10% to 36% cases (Young et al., 1984; Lack et al., 1981; Plantaz et al., 1992; Vasal et al., 1988; Zaloudek and Norris, 1982)

Kalfa et al. (2009) identified a mutation in FOXL2 gene (transcription factor gene) which could be the next target for use in treatment . Yoo et al. (2012) also identified mutations of genes Fas, Flip and Bcl-2 related to alteration of apoptosis. Various factors determine the prognosis. With stages as the most important prognostic variable. With regard to survival results, overall survival was approximately 90% at 5 years during the early stage (Malmstrom et al., 1994; Wu et al., 2000; Uygan et al., 2003) .The results of Ahyan's study of 80 cases with Granulosa cell tumour revealed recurrence rate of 54%, 21%, and 40% for stage I, stage II and stage III respectively. In most studies larger tumour size was found to be associated with poor prognosis particularly that measured more than 10 cm (12). Moreover, residual disease after surgery and tumour rupture, expression of p53 mutation, number of mitosis or ploidy were all associated with poor prognosis (Sehouli et al., 2004; Schumer and Cannistra, 2004; King et al., 1996; Costa et al., 1996; Al-Fosi et al., 1997). Schneider et al. (2003) addressed in their study the outcome of JGCT patients in accidental stage IC due to violation of tumour capsule during surgery versus natural stage IC with pre-operative rupture or ascitis. Concerning Inhibin, its value is correlated to the tumour mass and clinical relapse (Boggess et al., 1997; Lappohn et al., 1989).

The mainstay of treatment in JGCT is complete surgery. Fertility preserving surgery with unilateral salphingo-ophorectomy appears appropriate for patients with stage IA disease who wish to preserve their reproductive potential. There is little benefit in performing routine lymphadenectomy in the absence of grossly suspicious lymph node. Adjuvant therapy is required in stage IC –IV diseases as evident by German study (1985 -2000) BEP (Bleomycin, Cisplatin, Etoposide) or PEI(Cisplatin, Etoposide, Ifosfamide) were the most commonly used regimen. Recurrence rate is higher in comparison to adult GCT. Powell and Otis 1997; Powel et al. 2001 reported a patient with long term disease free survival following salvage chemotherapy for recurrent JGCT, who delivered a normal baby following caesarian section after 4 years.

CONCLUSION

JGCT of ovary is a rare neoplasm. Stage at presentation is an important prognostic factor. Surgery is the mainstay of treatment, while, adjuvant therapy is required in advanced stages. Due to rarity of tumour prospective studies are needed to establish a consensus regarding better modality of treatment.

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