

Unusual and Late Recurrences in Ovarian Adult Granulosa Cell Tumours

Dear Editor,

Granulosa cell tumours (GCT) are rare functional sex cord stromal ovarian tumours constituting approximately 2% to 3% of all ovarian malignancies. They are characterised by low malignant potential, an indolent course, local spread, propensity for late recurrences and high survival rate.¹ We report 2 cases of adult type GCT with unusual and late recurrences.

Case 1

A 47-year-old woman presented 13 years after laparotomy for a malignant GCT. She had undergone total abdominal hysterectomy, bilateral salpingo-oophorectomy (TAH+BSO) and omentectomy for a stage I disease according to the classification by the Federation of International Society of Gynaecologists and Obstetricians (FIGO). Histology had confirmed the type and stage of the malignancy. Considering the early stage of the disease and apparent complete surgical clearance, she had not been offered adjuvant therapy.

She remained symptomless for 13 years after the initial surgery and developed abdominal pain associated with vague feeling of abdominal fullness. CA-125 level was 409 u/mL (reference range <35 u/mL). A contrast enhanced computed tomography (CT) scan of the abdomen and pelvis revealed a heterogeneous soft tissue density mass in the left para-aortic area at the level of the lower pole of the left kidney extending down to the aortic bifurcation (Fig. 1A). Laparotomy revealed a tumour mass involving para-aortic nodes below the level of the lower pole of right kidney with possible encroachment of the aorta and inferior vena cava (IVC). Biopsy and histology confirmed the recurrence of GCT. She was scheduled to undergo palliative chemotherapy. However she died 6 days after the surgery, possibly due to pulmonary thromboembolism.

Case 2

A 68-year-old patient presented 16 years after a laparotomy for a malignant GCT for a FIGO stage II disease. Initially she had undergone TAH+BSO and omentectomy. She has refused adjuvant therapy. This time she presented with backache, lower abdominal pain and loss of appetite 16 years after the initial surgical intervention. Ultrasound scan revealed a well-defined mixed echogenic lesion (150 x 144 mm) arising from the pelvis, filling the whole abdomen. CA-125 level was 22 u/mL. Laparotomy revealed a malignant pelvic mass filling the whole abdomen with multiple peritoneal, bowel and omental deposits amounting

to FIGO stage III disease. She had debulking surgery with the intention of maximum cytoreduction. Cisplatin and etoposide were used as adjuvant chemotherapeutic agents. Ten months after completion of chemotherapy, she developed rectal bleeding. Clinical examination and sigmoidoscopy was normal except for haemorrhoidal disease. However a CT scan of the abdomen and pelvis revealed a low density mass of 3 x 3 cm in the pelvic floor with evidence of compression of the anterior wall of the rectum. There was no pelvic or para-aortic lymphadenopathy.

Laparotomy revealed a solid tumour of 3 cm in the pelvic floor in between the bladder and the rectum. Complete enucleation was possible and histology revealed a recurrence of a malignant GCT (Fig. 1B). Considering the frequent recurrences, she underwent another cycle of adjuvant chemotherapy. At the time of writing this article, she was found to be symptomless 8 months after the third laparotomy.

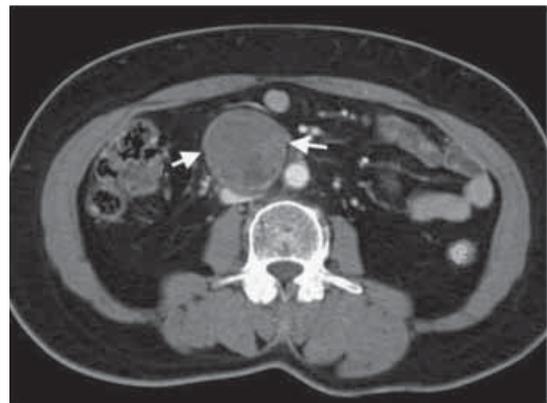


Fig 1 (A)

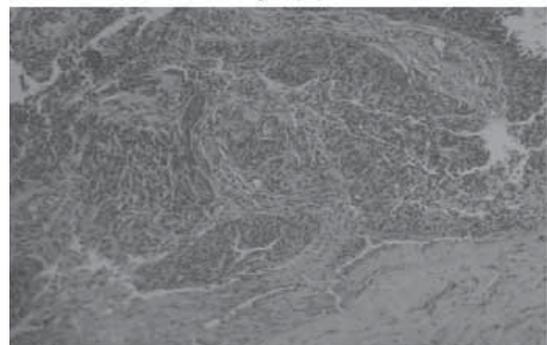


Fig 1 (B)

Fig. 1A. A non-enhanced CT showed a heterogeneous soft tissue density mass (arrows) in the left para-aortic area at the level of the lower pole of the left kidney.

Fig. 1B. A haematoxylin-eosin stained section (magnification x400) showing loose monolayers and individual cells with vacuolated cytoplasm and exuberant capillaries.

Discussion

GCT of the ovary is an uncommon ovarian sex cord stromal tumour. The mean age of the diagnosis is 52 years, but the age of presentation can span from the first to the tenth decade. Surgery represents the primary mode of treatment for early stage disease. Advanced or recurrent disease was found to be effectively treated with chemotherapy.¹ However, these recommendations have been made according to the findings of case series with level III evidence. Interval debulking can be considered in patients with gross residual disease and repeat cytoreduction was found to be useful for repeat recurrences.² It appears that the late stage of the disease and the presence of gross macroscopic residual disease after primary disease has the most unfavourable effect on prognosis.²

Recurrent disease of case 1 with enlarged para-aortic lymph nodes with high CA-125 levels warrants optimal cytoreduction to achieve good prognosis. However, she was found to have retroperitoneal recurrences with enlarged para-aortic lymph nodes encroaching the aorta and IVC, making the complete cytoreduction impossible. The second patient developed repeated recurrences, a phenomenon known to be associated with GCT. This could be due to the more virulent nature of some tumours. Repeat cytoreduction and chemotherapy are the current accepted treatment options.²

Our patients presented 13 and 16 years after the primary surgery, respectively. There had been few cases recorded with very late recurrences (Table 1).³⁻⁶ It is due to the indolent nature of the disease and it is found to have a median time of detection of recurrences of 6 years. Due to the potential for very late recurrences, some clinicians prefer surveillance for up to 10 years. However, the exact method of surveillance is still debatable, although regular follow-up with pelvi-rectal examination is advocated by most. Recurrences can easily be missed as in the second case unless a CT scan of the abdomen and pelvis is performed. Fortunately that patient developed rectal bleeding warranting a CT scan. Bleeding could well be due to the presence of haemorrhoids. Serial measurement of inhibin may be helpful in the follow-up of these women, particularly in the postmenopausal age group.⁷

The decision for chemotherapy and repeat surgery needs to be made by a multi-disciplinary gynaecological oncology team in patients with recurrent disease.⁷ Evidence to support clear decision-making in the management of GCT is lacking. Collaborative international multi-centre randomised controlled clinical trials are necessary to derive best evidence on the management. Given the propensity for very late recurrences, a prolonged follow-up is required. However, the cost-effectiveness of such a protocol is dubious. Selecting high-risk women for prolonged follow-up is a plausible solution and it may be worthwhile to produce clear guidelines and possibly a scoring system to identify

Table 1. Summary of Case Reports and Case Series of Ovarian Granulosa Cell Tumour with Late Recurrences

Author	Number of patients with recurrent disease	Duration between initial diagnosis and first recurrence	Special features of the recurrent disease
Hasiakos et al ³	1	25 years	Presented as a pelvic mass
Givalos et al ⁴	1	10 years	Sequential recurrences presented with as haemoperitoneum and as a hepatic mass respectively
Auranen et al ⁵	7	24 to 141 months	Presentation was variable. One of the patient had 7 recurrences
Rha et al ⁶	11	4 months to 18 years	Variable presentation with pelvic, extra-pelvic and para-aortic recurrences

such high-risk women who need prolonged care.

REFERENCES

- Schumer ST, Cannistra SA. Granulosa cell tumor of the ovary. *J Clin Oncol* 2003;21:1180-9.
- Lee YK, Park NH, Kim JW, Song YS, Kang SB, Lee HP. Characteristics of recurrence in adult-type granulosa cell tumor. *Int J Gynecol Cancer* 2008;18:642-7.
- Hasiakos D, Papakonstantinou K, Karvouni E, Fotiou S. Recurrence of granulosa cell tumor 25 years after initial diagnosis. Report of a case and review of the literature. *Eur J Gynaecol Oncol* 2008;29:86-8.
- Givalos N, Liakakos T, Machairas A, Gakiopoulou H, Karatzas G. Sequential recurrences of ovarian granulosa cell tumour 10 and 11 years after initial diagnosis as haemoperitoneum and subhepatic mass: a case report and review of the literature. *Eur J Gynaecol Oncol* 2005;26:572-6.
- Auranen A, Sundström J, Ijäs J, Grénman S. Prognostic factors of ovarian granulosa cell tumor: a study of 35 patients and review of the literature. *Int J Gynecol Cancer* 2007;17:1011-8.
- Rha SE, Oh SN, Jung SE, Lee YJ, Lee AW, Byun JY. Recurrent ovarian granulosa cell tumors: clinical and imaging features. *Abdom Imaging* 2008;33:119-25.
- Stuart GC, Dawson LM. Update on granulosa cell tumours of the ovary. *Curr Opin Obstet Gynecol* 2003;15:33-7.

Athula Kaluarachchi,¹MS, FRCOG, Jeevan Prasanga Marasinghe,²MBBS, MD

¹ Department of Obstetrics and Gynaecology, Faculty of Medicine, University of Colombo, Sri Lanka

² Professorial Obstetrics and Gynaecology unit, De Soyza Hospital for Women, Colombo, Sri Lanka

Address for Correspondence: Dr Jeevan Prasanga Marasinghe, Senior Registrar in Professorial Obstetrics and Gynaecology unit, De Soyza Hospital for Women, Colombo, Sri Lanka.

Email: jeevanmarasinghe@yahoo.com