



**Solitary Lesser Sac Deposit of Recurrent Ovarian Cancer  
mimicking GIST: A Case Report from a tertiary care Centre  
with Review of Literature**

Dr. Supratim Bhattacharyya<sup>1</sup>, Dr. Suma S<sup>1</sup>, Dr. Jagannath Dixit<sup>1</sup>, Dr. Veena R<sup>2</sup>, Dr. Chitra Prabhu<sup>2</sup>, Dr. Srinivas BJ<sup>3</sup>, Dr. KG Kallur<sup>4</sup>, Dr. Shivkumar Swamy S<sup>5</sup>, Dr. Indusekhar Subbanna<sup>6</sup>

1. Department of Surgical Oncology, Health Care Global (HCG) Cancer Centre, Bengaluru, Karnataka, India.
2. Department of Pathology, Health Care Global (HCG) Cancer Centre, Bengaluru, Karnataka, India.
3. Department of Medical Oncology, Health Care Global (HCG) Cancer Centre, Bengaluru, Karnataka, India.
4. Department of Nuclear Medicine, Health Care Global (HCG) Cancer Centre, Bengaluru, Karnataka, India.
5. Department of Radiology, Health Care Global (HCG) Cancer Centre, Bengaluru, Karnataka, India.
6. Department of Interventional Radiology, Health Care Global (HCG) Cancer Centre, Bengaluru, Karnataka, India.

**Corresponding Author: Supratim Bhattacharyya**, Department of Surgical Oncology, Health Care Global (HCG) Cancer Centre, Bengaluru, Karnataka, India.

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**Abstract**

*Recurrence following completion of first line therapy is a common problem with advanced epithelial ovarian cancer. In most instances, the recurrence is along the peritoneal lining and multiple. The treatment options of recurrent ovarian cancer (ROC) include secondary cytoreduction in selective patients, systemic chemotherapy and biological therapy. The long term survival outcomes of ROC have improved over the last decade owing to introduction of anti VEGF agents, and PARP inhibitors to standard systemic chemotherapy. Herein, we report a case of recurrent epithelial ovarian cancer with a long platinum free interval presenting to us in HCG Cancer Hospital, Bangalore, with a lesser sac deposit mimicking gastrointestinal stromal tumor (GIST). To the best of our knowledge, this is the first reported case of a solitary lesser sac deposit of recurrent ovarian cancer. We reviewed the literature for incidence of solitary recurrence of ovarian cancer with special emphasis on those masquerading as GIST. We also looked into the etiology of pathological transformation from well differentiated to undifferentiated ovarian cancer on recurrent setting, the role of cancer stem cells in histological transformation, and explored the nuances of treatment options of recurrent ovarian cancer with uncommon presentation as in our case.*

**Keywords:** *Recurrent ovarian cancer, Solitary metastasis, GIST, Undifferentiated cancer, Case report*

## Introduction

Epithelial Ovarian Cancer (EOC) is the third most common gynaecological malignancy, affecting over 200,000 women per year (1,2). But the mortality rate of EOC is highest among all of the gynaecological malignancies, as over two thirds of the cases present as advanced disease (3, 4). Approximately 70- 80 percent patients with International Federation of Gynecology and Obstetrics (FIGO) stage III- IV disease present with recurrent disease within 5 years following completion of first line therapy (5, 6). Although the scope of secondary cytoreduction for these patients remains guarded, it seems those with a limited volume of disease with longer platinum free interval (PFI) and without ascites benefit the most from such extensive resection(7- 9). For the rest of patients who are unsuitable for secondary cytoreduction, systemic therapy in form of cytotoxic chemotherapy and targeted agents remain the treatment of choice, with an aim of improving disease related symptoms and quality of life, delay progression, and possibly to prolong survival, particularly in patients with platinum sensitive recurrence. Ovarian cancer typically spreads along the peritoneal lining and a solitary deposit of ovarian cancer in lesser sac is rather a very uncommon finding in recurrent setting. Hence, a MEDLINE search was conducted for all English language literature. To the best of our knowledge, this is the first reported case of a solitary lesser sac deposit of recurrent ovarian cancer.

## Case Report

The patient is a 60 years old lady diagnosed with stage IIIC ovarian cancer 7 years back and underwent primary chemotherapy with Carboplatin and Paclitaxel 3 weekly for 6 cycles, followed by interval cytoreductive surgery (CRS) which revealed left ovarian mass adherent to uterus, omental caking adherent to transverse colon, and multiple right hemidiaphragm deposits. The PCI score was 15. Complete cytoreduction to an extent of CC0 was obtained including hysterectomy and bilateral salpingo-oophorectomy, total parietal peritonectomy, greater and lesser omentectomy, bilateral pelvic lymphadenectomy, infra-renal para aortic lymphadenectomy followed by hyperthermic intra peritoneal chemotherapy (HIPEC) with Cisplatin 100 mg/m<sup>2</sup> and Paclitaxel 175 mg/ m<sup>2</sup> for 60 minutes at 42.5 C using open technique. Final histopathological report revealed high grade serous carcinoma, ypT3bN0. The patient received 3 cycles of adjuvant chemotherapy with Carboplatin and Paclitaxel 3 weekly, thereafter.

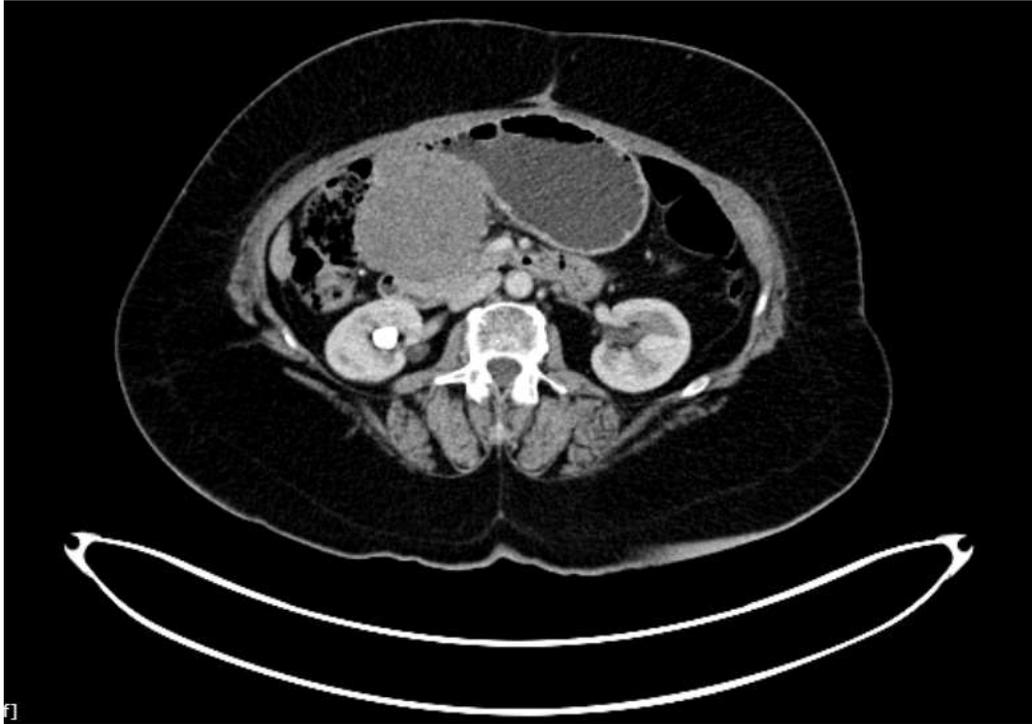
CA 125 at presentation was 117 U/ml which came down to normal value following completion of first line therapy. She was disease free and on follow up since then.

From September 2021 she started having upper abdominal discomfort and bloating sensation. PET CT revealed a metabolically active smooth walled encapsulated solid cystic lesion of size 8.1x 6.7 cm adherent to the posterior wall of antrum of stomach, extending to the first part of duodenum, abutting the head of pancreas, with signs of significant neo-vascularisation and SUVmax of 8.6. There was no disease elsewhere. Upper GI endoscopy showed thickened and edematous mucosa of pyloric antrum with features of extraluminal compression from posterior wall. Serum CA 125 was 25 U/ml. There was strong suspicion of the mass to be a Gastrointestinal Stromal Tumor (GIST) on PET/CT and UGI endoscopy. USG guided core needle biopsy of the mass revealed no evidence of malignancy. Considering the hypervascular nature of the mass, a decision was taken in favour of angio-embolisation, followed by diagnostic laparoscopy and guided biopsy within 24 hours of embolisation. There was a concern of bowel injury while creating pneumoperitoneum owing to the previous history of CRS and HIPEC using midline laparotomy incision. After reviewing the PET CT images and discussing with radiologists about the possible sites of adhesion, a plan was made for left upper quadrant entry using Veress needle with a higher than usual preset CO2 pressure of 15 mm of Hg. After creation of pneumoperitoneum, a 5mm port was placed 2 cm below the umbilicus in the midline after gently sweeping the adhesion away. This port was used for 30 degree telescope. Under vision two 5mm ports were placed in right and left flank respectively. Adhesiolysis was done. There was no evidence of disease in the greater sac. Lesser sac was entered. A mass of size approximately 8x7 cm was found to be arising from the posterior wall of pyloric antrum and first part of duodenum, adhered to the pancreatic head. The mass was encapsulated, seemingly solid cystic in nature, having prominent overlying blood vessels. The gross appearance of the mass was that of a GIST. Under vision, an 18 G trucut biopsy needle was advanced through an epigastric stab incision into the mass, multiple passes were made until retrieving adequate tissue for histology and immunohistochemistry (IHC).

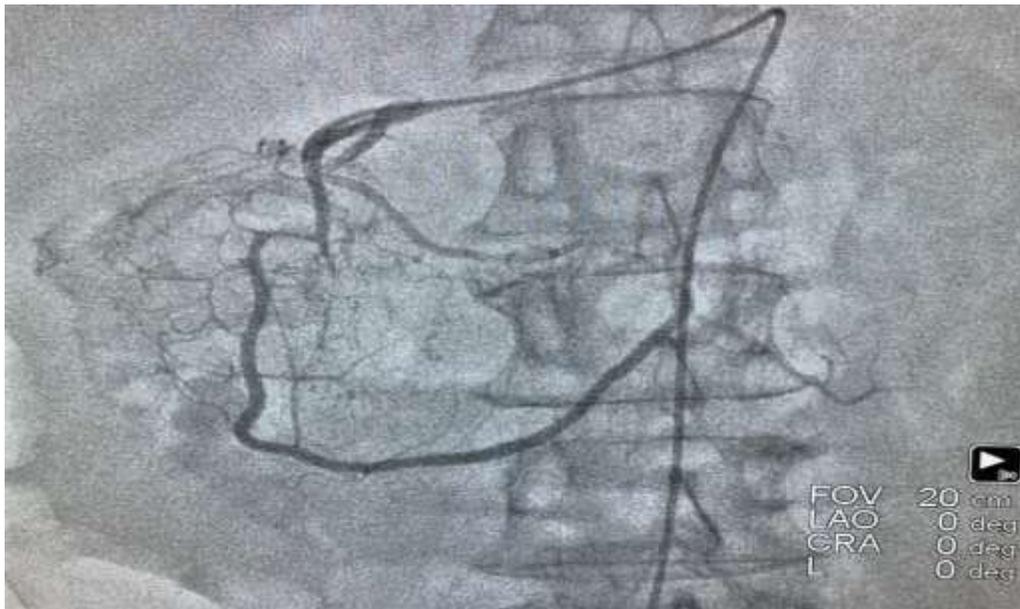
The biopsy report revealed an undifferentiated carcinoma of ovarian origin. IHC revealed tumor cells focally positive for PanCK, S100, and PAX8. They were negative for SMA, CD34, CD117, p16, WT1, CK7, CD10, and CA125. There was of low probability for MSI-H. PD-L1 was less than 1%. The treatment options, including secondary cytoreductive surgery, second line chemotherapy with platinum re-challenge, anti VEGF therapy, and hormonotherapy were discussed in multidisciplinary tumor board. The location of the tumor was such that secondary CRS would require a pancreaticoduodenectomy at the least. Considering the morbidity of such an extensive procedure in the recurrent setting of ovarian cancer,

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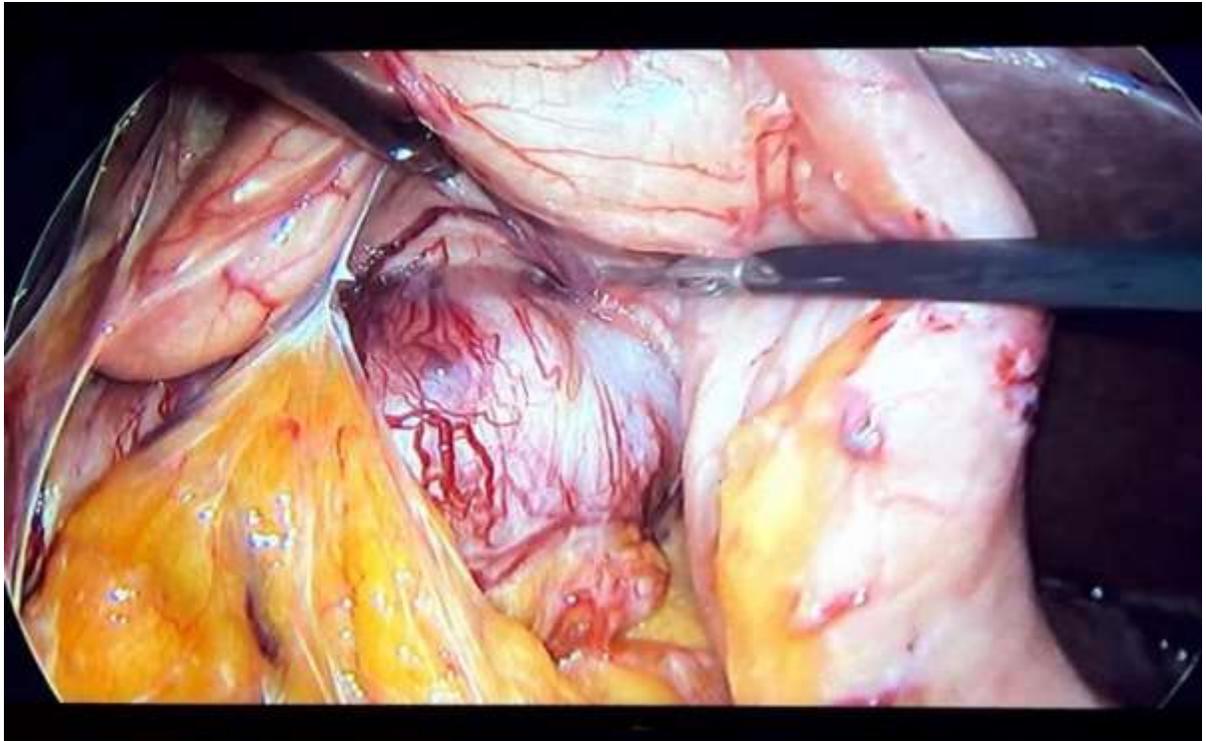
decision was made to continue with second line chemotherapy with or without stereotactic body radiation therapy (SBRT) and re-assessment of response after completion. She is still under treatment.



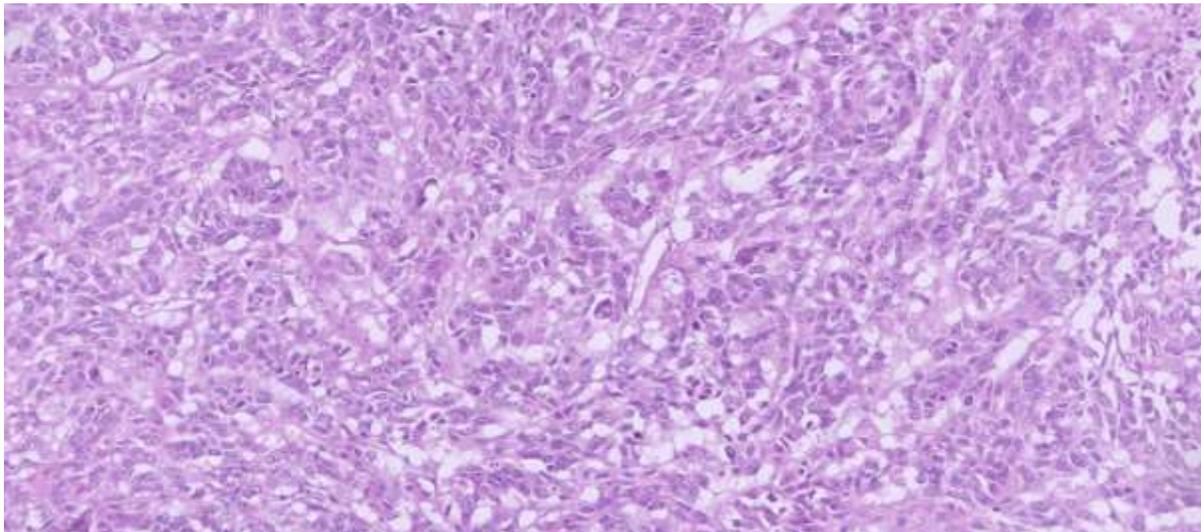
**Figure 1:** Cross sectional Contrast Enhanced CT showing an encapsulated mass of size 8.1x6.7 cm near gastric antrum, extending to second part of duodenum, abutting the head of pancreas.



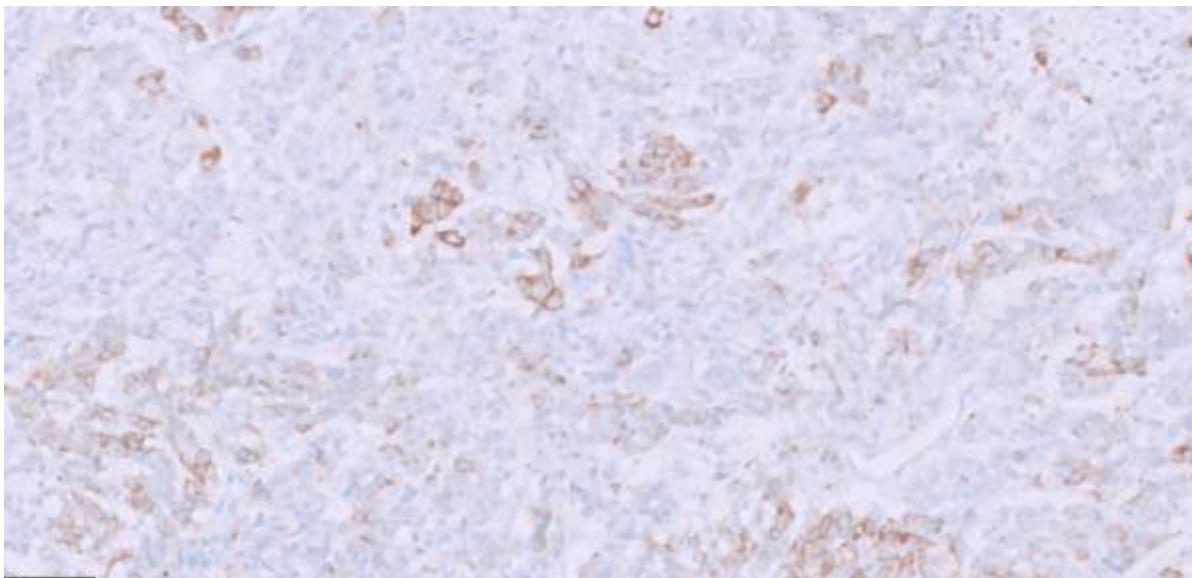
**Figure 2:** Pre operative angio-embolisation. The mass is mostly supplied by the branches of Gastroduodenal Artery (GDA).



**Figure 3:** Diagnostic Laparoscopy revealing a solitary mass of size 8x7cm, arising from lesser sac, posterior to gastric antrum, and adherent to second part of duodenum, the head of pancreas, with prominent overlying vasculature.



**Figure 4:** Intra operative Core Needle Biopsy revealing ovoid to spindle tumor cells with vesicular nucleus, prominent nucleoli and moderate amount of pink to clear cytoplasm. (Hematoxylin - Eosin, x10)



**Figure 5:** Immunohistochemistry - Pan CK highlights tumor cells focally.

## Discussion

This case is worth reporting as it challenges us with several atypical findings and makes us question ourselves about the management protocol of such a rare presentation of a relatively common disease. There are several aspects of this case that are worth discussing in depths, such as

1. How commonly does a recurrent ovarian cancer present as a solitary upper abdominal deposit?
2. What is the incidence of finding an undifferentiated histology in recurrent setting of a differentiated ovarian cancer and what are the implications of the same?
3. How commonly recurrent ovarian cancers mimic GIST clinically?
4. What are the treatment options of such a case of platinum sensitive recurrent ovarian cancer?

We tried to find out a correlation of our case, considering it's rarity, to the above mentioned broad headings in the following segment.

### **1. How commonly does a recurrent ovarian cancer present as a solitary upper abdominal deposit?**

Fifty-five percent of the first relapse of ovarian cancer are found at the pelvis or abdomen (10). Other recurrent sites include retroperitoneal nodes, liver or spleen, brain, and bone. Isolated solitary upper abdominal recurrence in the setting of recurrent ovarian cancer is rare and the literature support is sparse.

Minagawa et al. was the first to report isolated splenic metastasis in a case of recurrent ovarian cancer (11). Farias-Eisner et al. subsequently reported a series of four cases where all had solitary splenic parenchyma metastasis and were treated with secondary cytoreduction and splenectomy (12). Togami et al. reported a case of solitary recurrence of ovarian cancer in round ligament (13). We believe that lesser sac worked as a sanctuary site for recurrence in our patient, since it probably was not explored during interval CRS, iterating the importance of systematic exploration of all intra-abdominal sites (specially peripancreatic, retroduodenal, and the tail of pancreas) during any CRS procedure for advanced stage ovarian cancer.

## **2. What is the incidence of finding an undifferentiated histology in recurrent setting of a differentiated ovarian cancer and what are the implications of the same?**

The concept of histological transformation from differentiated to undifferentiated ovarian cancer following repeated chemotherapy challenge is believed to derive from the existence and contribution of cancer stem cells (CSC). CSCs possess tumorigenic and self renewal potential. It is also widely recognised that CSCs have the potential to differentiate into several different mature neoplastic cell lineages upon activation and deactivation of different signalling pathways. If a signalling pathway is terminated or weakened by external influence, such as chemotherapy and radiation, it's function is replaced by a different pathway, essentially leading to transformation of tumor histology (14). This concept was also supported by Bapat SA et al. who addressed the evolution of tumor genotype and phenotype under selective pressure of pre operative chemotherapy, radiation, and targeted therapy (15). The effect of CSCs has been documented in several malignancies, including head and neck squamous cell carcinoma, lung cancer, breast cancer, pancreatic cancer, stomach cancer, rectal cancer and others. CSCs have been identified in ovarian cancer by the expression of CD44, c-Kit, and CD133 (16). It is believed that epithelial tumors, germ cell tumors, sex cord stromal tumors, and other tumors may originate from ovarian CSCs and with repeated external insult to tumor by different therapeutic strategies, a differentiated tumor may turn into an undifferentiated one. Huang et al. reported a case of adenocarcinoma of ovary transformed into undifferentiated small cell carcinoma following eight cycles of chemotherapy and radiation (17). Besides, high grade serous carcinoma of ovary is known to display solid, pseudo- endometrioid, transitional cell- like (SET) patterns, and solid, transitional, endometrioid, and mucin-like (STEM) patterns (18). Hence extensive histological and immunohistochemical analyses is mandated for any known high grade serous ovarian cancer revealing discordant histology.

The prognosis and therapeutic implications of CSCs in ovarian cancer is an area of active research with an ever growing landscape. It is generally recognised that the presence of CSCs confers chemoresistance, and increase the likelihood of recurrence in ovarian cancer (19, 20). A meta-analysis by Liu et al. reported a negative association between the expression of aldehyde dehydrogenase (ALDH) by IHC in CSCs and the survival (21). In this meta-analysis of 1,258 patients from 7 studies, high ALDH expression was associated with poor overall survival (OS) and disease free survival (DFS). Similar results were also noted in another meta analysis by Ruscito et al. that showed high levels of ALDH1 expression to correlate with worse OS and progression free survival (PFS) in ovarian cancer (22). The therapeutic efficacy of Metformin has been explored lately in this subgroup of patients. A phase II study by Brown et al. concluded that tumors treated with Metformin had a 2.4 fold decrease in ALDH+ CD133+ CSCs and increased sensitivity to cisplatin ex vivo (23).

However, we should also give consideration to a second primary tumor in any patient of ovarian cancer displaying discordant histology and having a very prolonged platinum free interval, especially when the tumor is solitary and located at an uncommon site. This emphasises the importance of an adequate tissue biopsy and IHC before embarking upon a definitive treatment.

### **3. How commonly recurrent ovarian cancers mimic GIST clinically?**

Although GIST arising from pelvic cavity may simulate gynaecological malignancy, the opposite is not very common. Epithelial ovarian cancer typically spreads along the peritoneal surface, and it is rather rare to find an isolated visceral peritoneal deposit in absence of disease elsewhere in the peritoneal cavity. In our case, the solitary site, size, encapsulated nature of the deposit supported the clinical diagnosis of GIST. Similar case was reported by Kang et al. who found a transmural lesion along gastric antrum which was later found out to be a metastatic deposit from primary ovarian cancer following resection (24). Hence it is necessary to have an individualistic approach to each such patient with attention to the past history of malignancy, treatment received, biopsy and immunohistochemical report with the clinico- radiological findings before reaching a final diagnosis.

### **4. What are the treatment options of such a case of platinum sensitive recurrent ovarian cancers?**

Recurrent Ovarian Cancer (ROC) is a widely heterogeneous entity and the treatment options are also varied from surgical to medical management. Surgical option in platinum sensitive ROC in form of secondary CRS followed by chemotherapy has been prospectively compared with chemotherapy alone in three randomised trials, including DESKTOP III, SOC 1, and GOG 213. The prospective AGO-

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DESKTOP III trial recruited patients with platinum sensitive ROC and a positive AGO score to randomise between surgery followed by chemotherapy, or chemotherapy alone. In the final analysis, patients undergoing surgery showed a significant progression free survival (PFS), overall survival (OS), and median time to start of first subsequent therapy (TFST) benefit. This benefit was exclusively confined to patients having a complete resection (CR), emphasising the importance of optimised patient selection for surgery and of high volume centre to achieve CR (25). The PFS benefit of secondary CRS in platinum sensitive ROC was also shown in SOC 1 trial, the OS data, however, is not yet mature(26). The GOG 213 trial incorporated Bevacizumab along with chemotherapy, but the trial failed to demonstrate survival benefit of secondary CRS over chemotherapy alone arm (27).

For patients with platinum sensitive and yet unresectable ROC, treatment options include systemic chemotherapy with or without Bevacizumab. Platinum based combinations (Carboplatin/ PLD, Carboplatin/ Paclitaxel, Carboplatin/ Gemcitabine) is associated with better PFS, OS compared to non-platinum or platinum single agent treatments in this population (28, 29). Bevacizumab in combination with chemotherapy in platinum sensitive ROC has been approved on the basis of two randomised phase III studies, GOG-213 and OCEANS. While the GOG-213 study showed a non statistically significant OS advantage of 5 months on adding Bevacizumab to chemotherapy, in the OCEANS trial the Bevacizumab containing arm demonstrated a better objective response rate, a longer PFS, with no difference in OS (30, 31). Olaparib has been approved as maintenance therapy after platinum response in ROC patients harbouring a somatic or germline BRCA mutation after SOLO-2 phase III trial (32, 33). Similarly the results of phase III ENGOT-OV16/ NOVA study and ARIEL2 study led to approval of Niraparib and Rucaparib, respectively, as maintenance therapy in platinum sensitive BRCA mutated ROC (34, 35).

The role of SBRT has recently been evaluated in retrospective, multicentre MITO RT1 study. It concludes the safety and efficacy of SBRT in patients with metastatic persistent ROC and identifies the clinical and treatment parameters to predict local control and complete response (36).

The efficacy of hormonotherapy in form of Tamoxifen and Aromatase Inhibitors (e.g., Letrozole) in ROC is not very clear, and is probably independent of platinum sensitivity. The limited data from retrospective studies indicate a significantly longer duration of response with letrozole than tamoxifen in ER+ high grade ROC (37).

Our patient falls in an unusual clinical circumstance where the complete resection appears to be feasible as per radiological findings, but would require nothing less than a pancreaticoduodenectomy. The

selection of patient for such a morbid surgical procedure in the setting of ROC is however not well defined and probably best left to the decision of multidisciplinary tumor board. It was our decision to subject the patient to platinum re-challenge with/ without SBRT and re-evaluate to assess clinical response before taking up for complete resection. However the literature support for or against this policy is lacking.

## **Conclusion**

The treatment approach of ROC has evolved significantly in recent years. The indications of surgical cytoreduction as well as personalised therapy options including anti angiogenic agents, PARP inhibitors, and hormonotherapy have been standardised. However, in rare circumstances as reported in this case, the clinical decision making probably relies finally on the experience and judgment of the multidisciplinary team, in a tertiary care centre with modern facilities, tailored for the patient, and aimed at the best possible patient outcome.

## **Highlights**

1. Most of patients with advanced ovarian cancer recur at multiple sites within 5 years of completion of first line therapy.
2. To the best of our knowledge, this is the first reported case of solitary recurrent ovarian cancer at the lesser sac.
3. Histological transformation in recurrence maybe attributable to cancer stem cells causing chemoresistance, poor survival.
4. Encapsulated solitary recurrence at unusual sites may simulate GIST and needs extensive workup to confirm the diagnosis.
5. The best treatment of recurrence often relies upon the experience of the oncologist and the facilities available.

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