

Low Grade Serous Ovarian Cancer: A case Report

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Objective

Approximately 10 percent of serous ovarian carcinomas are low-grade. Low-grade serous carcinoma of the ovary (LGSOC) has a distinct pathology, clinical behaviour, and prognosis compared with high-grade serous carcinoma. Presenting symptoms can be very vague which will delay in getting the diagnosis and the definitive treatment. Hence, understanding of the nature of the disease is crucial in early detection and management of the patient.

Case report

In July 2021, 51-year-old healthy lady presented to the gynaecological clinic with vague abdominal discomfort and pelvic pain off and on for three moth duration. Apart from slight tenderness at the umbilicus and the right lower abdomen, no abnormality was detected.

She had two vaginal deliveries, was on minipills and still has regular period. There was no family history of ovarian or gynaecological cancer. Ultrasound abdomen and pelvis showed 5cm complex suspicious looking left adnexal cyst with solid elements with no other abnormal findings. CA 125 was 70. Subsequent MRI pelvis did not show pelvic mass nor cyst but encysted fluid around the left ovary. The findings reassured to continue conservative management with repeat CA 125 in three-month time, which was 77. Repeat ultrasound pelvis showed tiny cysts in both ovaries with 4.5cm free fluid collection in pelvis.

She developed soft stool with pain which increased with opening of her bowels but never had rectal bleeding. She was treated with medications for irritable bowel by the gastroenterology team. There was no history of loss of weight or loss of appetite and she was not keen for colonoscopy.

She remained stable apart from the dull ache suprapubic pain and repeat CA 125 in four months later reduced to 49. Pelvic ultrasound showed increased fluid collection in pelvis, 9cm with some internal septation and the same small cysts in both ovaries. Repeat MRPG and

CT TAP showed moderate free fluid in abdomen and pelvis with thick peritoneum and no lymphadenopathy. CA 125 was 50 and other tumour markers such as CEA, CA 19.9 were normal.

The case was discussed at the gynae-oncology MDT meeting and decided for diagnostic laparoscopy, peritoneal washing and proceed. The operation was done fourteen months after her first presentation. On laparoscopy, there were strange looking extensive flimsy adhesions in the abdomen, pelvis and between all the bowel loops with mildly inflamed uterus, fallopian tubes, ovaries and appendix. There was no significant ascites but few small tumour deposits were present at the anterior abdominal wall. Peritoneal washing, bilateral salpingo-oophrectomy, appendisectomy, omental and peritoneal biopsy, biopsies from the small bowel serosa and deposits at the anterior abdominal wall were done.

Histology confirmed LGSOC, FIGO stage IIIA2 with 5 mm focus of serous carcinoma was buried within the superficial cortex of one ovary. There were multiple disseminations and tumour deposits of serous carcinoma and scattered psammoma bodies at the small bowel serosa, omentum, anterior abdominal wall, ovaries and the fallopian tubes. Immunohistochemical staining shows nuclear positivity for both PAX-8 and WT-1 and positive cytoplasmic staining for CK7. She was managed by the multidisciplinary team at the tertiary centre. After thorough counselling, instead of further extensive debulking surgery or chemotherapy, she decided to continue with endocrine monotherapy which was Letrozole. It has been nearly two years after

Discussion

Epithelial ovarian cancer is the 6th most common cancer among women in the UK and it has the highest mortality of all gynaecological cancers, accounting for 6% of all cancer deaths in women.

The most common epithelial ovarian cancer histologic subtype is serous. Approximately 90 percent of serous carcinomas are high-grade, and 10 percent are low-grade. Approximately 60 percent of low-grade serous carcinomas are associated with a serous borderline tumour, which are likely precursor lesions. Clinical studies show that low-grade serous cancers do not convert to high-grade cancers.

Low-grade tumours are distinct from high-grade tumours and have a unique developmental pathway. The Klrsten rat sarcoma viral oncogene homolog (KRAS) and B-Raf proto-oncogene (BRAF) mutations, alteration of the MAP/ERK signaling (mitogen-activated protein kinases, originally called extracellular signal-regulated kinases), are frequent in low-grade tumours and exceptionally rare in high-grade cancers. Mutations in tumour protein p53 (TP53), a hallmark of high-grade serous ovarian cancer are not found in low-grade cancers.

LGSOC patients are younger than those with ovarian cancer of all types. The median age at diagnosis is 43 to 46.5 years of age. The clinical presentation may range from an asymptomatic adnexal mass to significant symptomatology

consisting of bloating, early satiety, urinary urgency, and abdominal or pelvic pain. In more advanced cases, women may also present with a pleural effusion or bowel obstruction. Approximately 90 percent present with disseminated disease (International Federation of Gynaecology and Obstetrics [FIGO] stage II to IV).

The diagnosis is based on histologic evaluation performed following removal of the ovaries and/or biopsies of the peritoneum. In most cases, low-grade serous carcinoma is characterized by low Ki-67 proliferative rates, wild-type p53 expression, and oestrogen receptor (ER) expression.

Women suspected of having ovarian/peritoneal cancers should be evaluated with imaging studies of the chest, abdomen, and pelvis. A baseline serum cancer antigen (CA) 125 should be drawn prior to surgery. Approximately 85 percent of women with low-grade serous carcinoma have an elevated serum CA 125 preoperatively.

The management of LGSOC is predominantly surgical. Primary surgery is the recommended approach. For patients with early stage 1 disease, comprehensive surgical staging is recommended. In selected young patients with unilateral ovarian involvement, fertility-sparing surgery may be feasible. Because stage I, low-grade serous carcinoma is extremely rare (2 to 6 percent), no definitive information exists regarding standard adjuvant therapy.

For those patients with stage II to IV, maximum cytoreductive surgery to achieve minimal residual disease is the standard. The cytoreductive procedure may occur as primary cytoreductive surgery or as interval cytoreductive surgery following neoadjuvant chemotherapy. Following surgery, adjuvant systemic therapy consisting of a taxane/platinum regimen is often administered, alternative options is endocrine monotherapy therapy.

A large meta-analysis showed a response rate to platinum-based chemotherapy of approximately 24% in patients with advanced primary low grade advanced ovarian cancer after upfront surgery. Hormonal maintenance strategies after completion of platinum-based chemotherapy seem to have a survival benefit in retrospective series.

LGSOC is relative chemoresistance and the more effective therapy for the first-line treatment is still at the research area. Endocrine therapy also is an option as evidence indicates that a very high proportion of these tumours express the oestrogen receptor. MEK (mitogen-activated protein kinase enzymes MEK1 and/or MEK2) inhibitors are emerging as active agents and may become an effective therapeutic strategy in the near future.

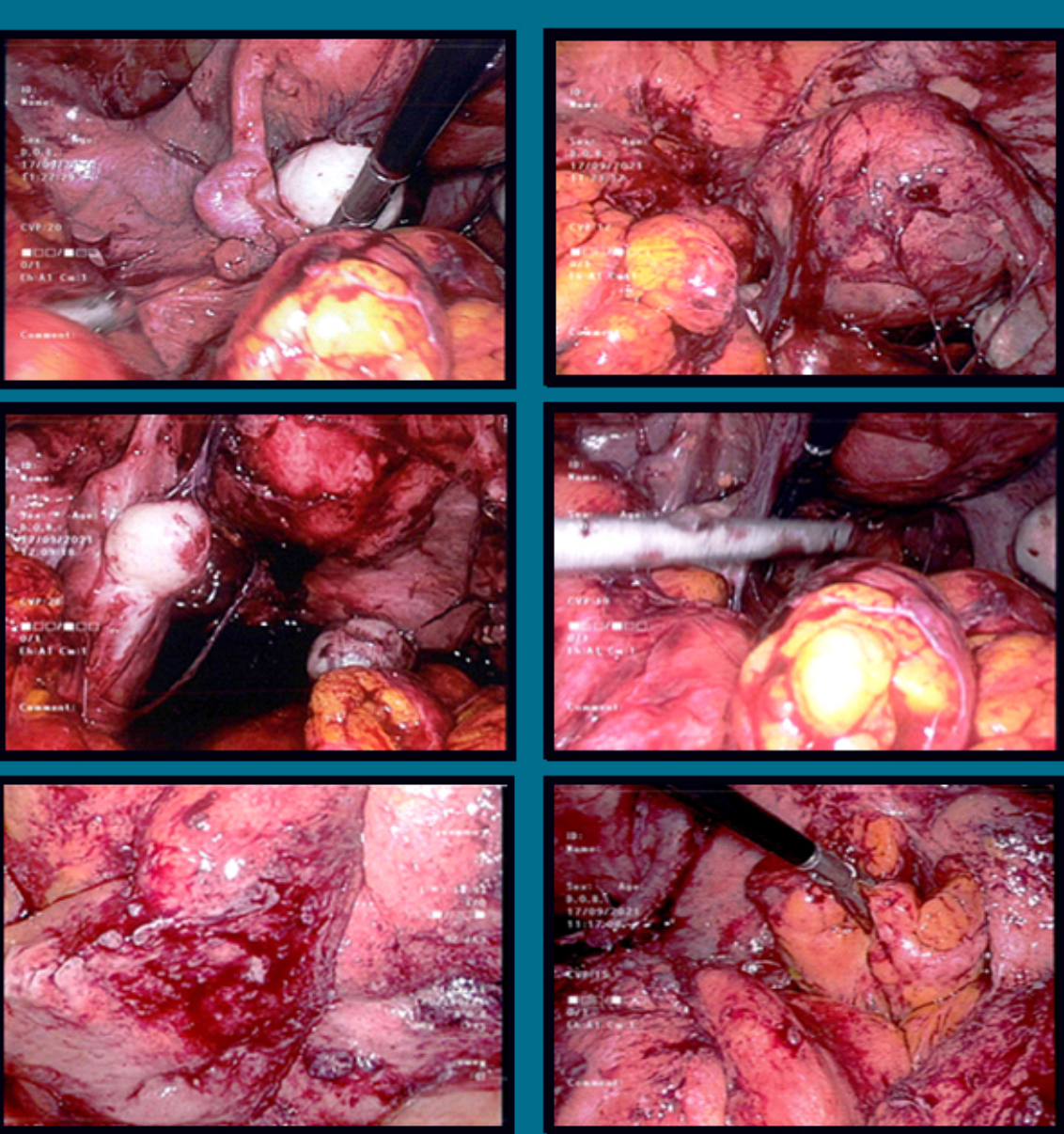
Several options exist for women with recurrent, low-grade serous carcinoma of the ovary or peritoneum. These include possible secondary cytoreductive surgery, chemotherapy, endocrine therapies, or targeted agents such as angiogenesis inhibitors, or others available on clinical trial.

Women with low-grade, serous carcinoma have a substantially prolonged overall survival time compared with women with high-grade serous carcinoma.

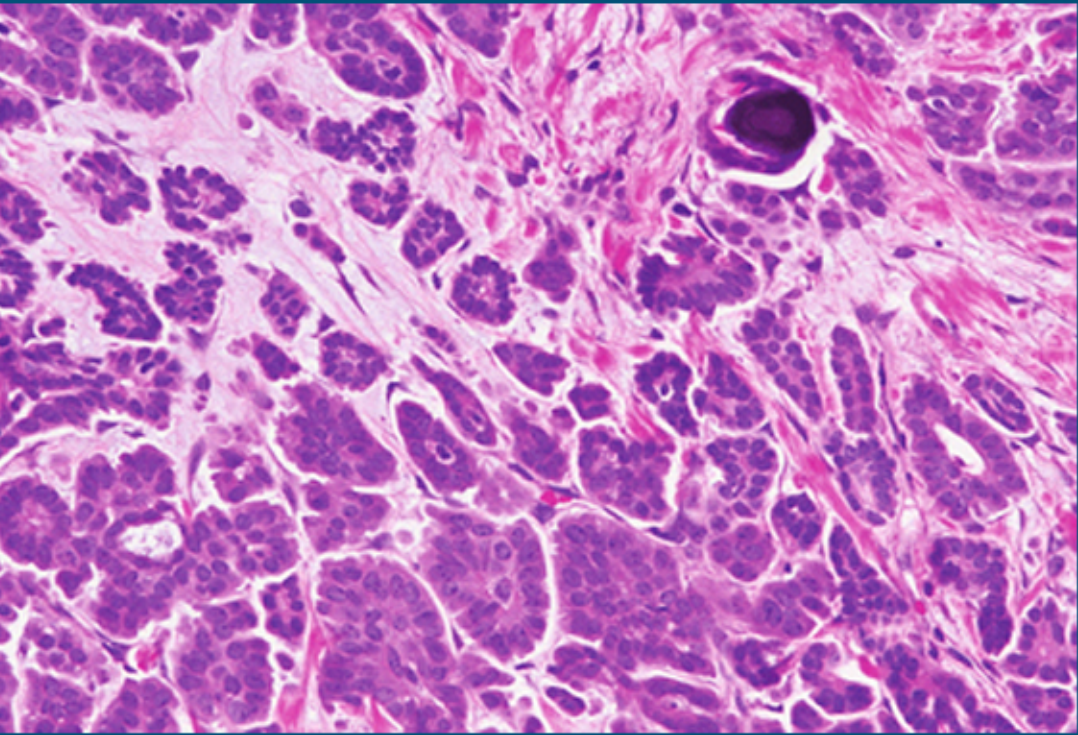
Our generally well patient started with very vague abdominal and pelvic pain with mildly raised CA 125 without any other significant signs and symptoms and later she developed bowel symptoms. It was initially convinced to start with the conservative management as CA 125 level was fluctuating and the imaging reports did not specify the identifiable pathology. The very non-specific symptoms and unclear results in the investigations delayed in proceeding for the diagnostic surgery. It took 14 months to reach to the point of the diagnostic laparoscopy and proceed. The diagnosis could be missed if the case is not monitored properly. Involvement of the multidisciplinary team from the tertiary centre was pivotal in managing this case. There were extensive flimsy adhesions in the abdomen and pelvis but no grossly identifiable tumours and the histology confirmed the advanced stage of the disease. She was counselled for the debulking surgery and chemotherapy, but she decided to avoid these extensive surgeries, chemotherapy due to the chemoresistance nature of the disease and chose for the endocrine therapy. It has been nearly two years after the surgery, and she has been stable with no signs of recurrence.

Conclusion

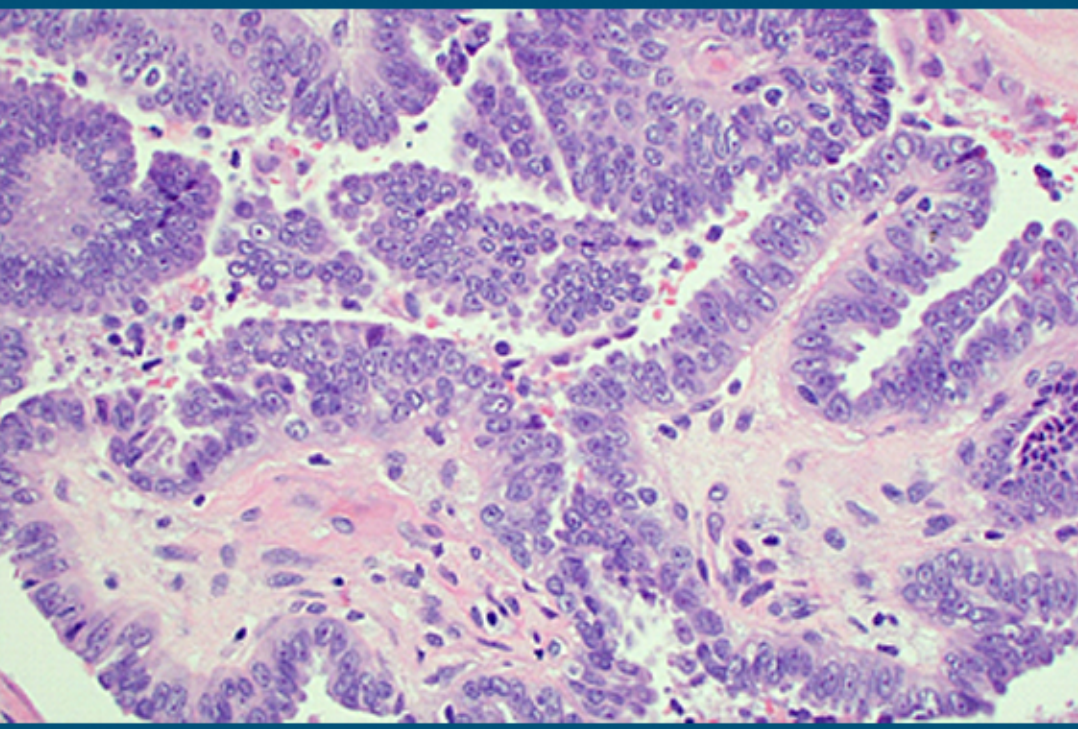
LGSOC can present with vague symptoms, mildly raised CA 125 and non-specific findings in the imaging which can delay in getting the diagnosis and starting the specific treatment. Vigilant monitoring with multi-disciplinary team involvement is crucial in management of these cases.



Picture 3 - Image records of laparoscopic operation, LGSOC (Noble's Hospital, Isle of Man, 2021)



Picture 1- H&E staining of low-grade serous ovarian carcinoma (Ovarian Cancer Genetics: Subtypes and Risk Factors, University of Kansas Medical Center)



Picture 2 – Histology of LGSOC -MyPathologyReport.ca

References

1. Patient's medical records (Noble's Hospital, Isle of Man)
2. Up To Date -Management of low-grade, serous carcinomas of the ovary
3. British Gynaecological Cancer Society (BGCS)- Epithelial Ovarian/Fallopian Tube/ Primary Peritoneal Cancer Guidelines: Recommendations for Practice 2017
4. Pictures
Picture 1 & 2 from google.

