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Family Medicine

A Primary Care Approach to Identifying, Investigating and Managing a Patient with Suspected Ovarian Cancer

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Abstract **Case Report**

Ovarian Cancer is one of the leading causes of cancers worldwide associated with high mortality in females. This is due to difficulties in early detection and primary prevention of disease. Most women present with vague gastrointestinal, urological and abdominal symptoms. Conventional diagnosis involves investigating pelvic tumour markers and imaging but in most cases tissue biopsy is the only way to confirm the diagnosis and staging of the disease. Early stage is usually managed with microscopic resection of tumour with consideration to fertility sparing treatment in young women. Advanced ovarian cancer needs primary debulking surgery with or without neoadjuvant therapies. The role of target therapies still faces the challenges of overcoming side effects and toxicity and choosing the correct target populations.

Keywords: Early detection, Primary prevention, Tumour markers, Ovarian Cancer, Staging, Gynaecological cancers, Female mortality, Debulking surgery, Target therapies.

INTRODUCTION

Ovarian cancer is a malignancy arising from the ovary. In the UK, it is the leading cause of death by gynecological cancer (approximately 4000 deaths in UK), and the fifth most common cancer in women, with almost 6500 women diagnosed each year.

The majority of women are postmenopausal, and more than 50 years of age, but younger women can also have ovarian cancer. In UK between 2013-2017 only 35% patients with ovarian cancer survived 10 or more years.

Incidence rates for ovarian cancer are lower in the Asian and Black ethnic groups and in people of mixed or multiple ethnicities, compared with the White ethnic females, in England.

During the last decade, minimal improvement has been observed with ovarian cancer mortality. According to the US Surveillance, Epidemiology and End Results database reports that overall survival for all patients with ovarian cancer is 45.6%, but this can vary considerably on the stage at which the cancer is diagnosed. The 5 year overall survival in patients with stage 1 cancer is 92.1% but is 25% for patients with stage III and stage IV cancer.

Main symptoms of Ovarian Cancer:

- A swollen tummy, or feeling bloated
- Pain or tenderness in the abdomen
- No appetite, or feeling full quickly after eating
- An urgent need to micturate or frequency
- Dyspareunia

CASE

A52 year old lady consults her family medicine physician with abdominal bloating and discomfort, new onset constipation, and unintentional weight loss. She is a known hypertensive, with well controlled BP with medication, and also suffers with occasional migraine (triggered by cheese). Upon examination she is found to have left lower abdominal tenderness. She undergoes investigations, and an abdominal/pelvic ultrasound demonstrates a left ovarian cyst of 5cm diameter, along with raised CA-125. She is then referred to secondary care on an urgent fast track pathway. She further has CT scan which reveals lymphadenopathy and ascites along with a left ovarian mass. Paracentesis along with cytology shows a serous ovarian cancer. Genetic testing does not show any evidence of BRCA1 or BRCA2 mutations. She then underwent debulking surgery including abdominal hysterectomy, bilateral salpingo-oophorectomy and resection of involved lymph nodes. Following this she had chemotherapy, and subsequently

showed no evidence of disease and normalization of ca-125 once the treatment was completed. She is placed on bevacizumab maintenance and remained in remission.

Less common symptoms of Ovarian Cancers:

1. Indigestion
2. Constipation/diarrhea
3. Back pain
4. Feeling tired all the time
5. Unintentional weight loss
6. Postmenopausal bleeding

Risk Factors	
Genetics	BRCA1 and BRCA 2 mutations are the most important and significant genetic risk factors associated with ovarian cancer, and is found in almost 17% of patients. Risk of Ovarian cancer can also be increased by Lynch Syndrome which is an inherited genetic disorder, associated with colorectal, endometrial and ovarian cancer, but can also be associated with cancer of urinary tract, stomach, small intestine and biliary tract.
Oral contraceptives and Hormone Replacement Therapy	In individuals with a germline BRCA1 mutation who used oral contraceptives, the risk of ovarian cancer was reduced. This was also the case in those without genetic predisposition. Serous, endometrioid and clear cell ovarian cancers were also shown to be reduced in those who used oral contraceptives (but not mucinoid) in an analysis from the ovarian cancer cohort consortium. Hormone replacement therapy (HRT) has been shown to increase the risk of developing ovarian cancer in postmenopausal ladies. Interestingly, in women who have been diagnosed with ovarian cancer, and are suffering with severe postmenopausal symptoms, the use of HRT is considered safe and has no effect on overall survival.
Reproductive factors	Women who have never carried a pregnancy to term or have their first full term pregnancy after the age of 35 years, have a higher risk of ovarian cancer.
Age	The risk of developing ovarian cancer increases with age. Ovarian Cancer is rare in women younger than 40 years. Most ovarian cancers develop after 40 years of age. Half of all ovarian cancers are found in women above 63 years of age.
Weight	Obesity has been linked to developing many cancers. Women with BMI of at least 30 have a higher risk of developing cancer but not necessarily the aggressive types such as the high grade serous cancers. Obesity can also have a negative impact on the overall survival of a woman with ovarian cancer.
Using fertility treatment	The use of fertility treatment is thought to increase the risk of 'borderline' or 'low malignant potential' ovarian tumours. However, other studies have not shown risk of invasive ovarian cancer with fertility drugs.

Assesment in Primary care:

- In primary care, measure **CA125IU/ml** in all women with signs and symptoms suggesting ovarian cancer (see signs and symptoms)
- If CA125 is 35IU/ml or greater than, organise an urgent Ultrasound abdomen and pelvis
- If the Ultrasound is suggestive of ovarian cancer, refer the woman to secondary care using suspected cancer pathway.
- For other women, having normal Ca125 or greater Ca125 than 35 iu/ml but normal ultrasound, reassess them for other causes of their symptoms with advice returning to family physician if symptoms persist or become severe.

Establishing diagnosis in secondary care:

Tumour markers:

- In secondary care perform CA125Iu/ml, if not already done
- In women under the age of 40, measure tumour markers alpha fetoprotein (AFP), beta human chorionic gonadotrophin (beta-HCG) as well as Ca125, to diagnose non epithelial cancers.

Imaging in the diagnostic pathway:

- Perform ultrasound pelvis if already not been done, if abnormal tumour markers or ultrasound, arrange urgent CT abdomen and pelvis to assess the extent of disease [2].
- MRI is not routinely recommended in diagnosis of ovarian ca but can be used where ultrasounds is not helpful to confirm the diagnosis especially in young women with solitary pelvis mass who wants to preserve fertility.

Malignancy Indices:

- In women with suspected ovarian cancer, different parameters, like menopausal status, ultrasound characteristics, serum CA125IU/ml levels and performance status, can be combined to provide the malignancy indices to assess the probability of malignancy before surgery [5].
- Risk of malignancy index (RMI) should be calculated and all women with RMI> 250 should be referred to specialised multidisciplinary team (MDT). (see appendix A).

Tissue Diagnosis:

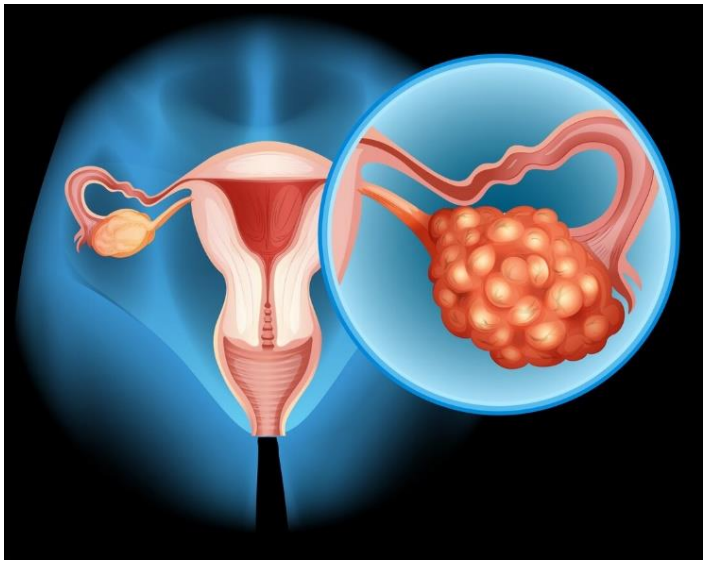
In most cases histology is the only way to determine the type or grade of cancer and rule out other causes like tuberculosis, inflammation and biopsy, there are different ways to get histology like biopsy, laparoscopy and laparotomy. They are all invasive and carry risk.

But in most cases, histology can be safely obtained through ultrasound guided biopsy. Routine use of laparoscopy to obtain biopsy and assess the operability of disease is not recommended [4].

Cytology is usually safer but had lower diagnostic accuracy. If cytology is done for ascitic fluid, absence of malignant cells doesn't not exclude cancer especially in presence of inflammation.

All women with suspected advanced ovarian carcinomas must have confirmed tissue biopsy by histology before offering cytotoxic chemotherapy but in exceptional cases. Cytology alone, along with Ca125/CEA ratio > 25:1may be sufficient in patients with pre-operative poor performance status and where biopsy is not feasible.

In presence of pleural effusion aspiration and cytology of malignant cells should be considered to confirm the staging of cancer.



Types of Ovarian Cancers		
Epithelial Tumours	**Germ cell Tumours**	**Stromal Cell tumours**
This is the most common type of ovarian cancer. About 90% of of ovarian tumours are epithelial and arise from the outer surface layer of cells on the ovary. This cancer is rare in young women, and is usually found in postmenopausal women. There are several types, some of which include : o Serous epithelial ovarian cancers; most common type and are thought to arise from cells at far end of fallopian tube which travel to the ovary and grow. o Endometrioid; second most common type of epithelial tumours thought to be linked to endometriosis, and are usually diagnosed at an early stage and are low grade. o Clear cell ovarian cancers; these are rare and can be linked to endometriosis, venous thromboembolism, paraneoplastic hypercalcemia. o Mucinous cancers; also rare and can arise from the GI tract.	These are less than 2% of all ovarian cancers. They arise from ovarian cells that develop into eggs. They are rare and usually affect women during their teens to their forties. They can be benign or malignant. Mature teratomas (also known as ovarian dermoid cyst) is the most common type of germ cell tumour and is benign. ▪ Malignant germ cell tumours: ▪ Immature teratomas ▪ Dysgerminova ▪ Yolk sac tumour ▪ Non gestational choriocarcinoma ▪ Embryonal carcinoma	These are rare tumours of the ovary which arise from the stroma or sex cords. Most people are diagnosed at an early stage and respond well to treatment. o Pure stromal tumours: fibroma, thecomas o Pure sex cord tumours: adult and juvenile granulosa cell tumours o Mixed sex cord stromal tumours: sertoli-leydig cell tumours

Management of advance ovarian cancer (FIGO II-IV)

Primary debulking surgery is the standard of care where complete or optimal cytoreduction appears achievable in patients with good performance status. Where this is not achievable two randomised trials have showed non-inferiority of the neoadjuvant chemotherapy (NAC) followed by interval debulking surgery.

Following surgery, all patients with FIGO stage II-IV should be offered 6 cycles of platinum-based chemotherapy+/- paclitexal.

Targeted therapies

The success of targeted therapies in other cancers has encouraged the development of these agents for ovarian cancer. Numerous targeted therapies are currently being evaluated in phase I-III studies and should clarify their potential clinical use. The most promising strategies developed so far use the anti–angiogenic approach and PARP inhibitor. Further challenges regarding the success of target therapy to identify the biomarker to guide the management, overcome toxicity and side effects, and choosing the correct target population.

Follow up:

The assessment of new or potential symptoms of recurrent disease and clinical examination is essential at each follow up visit.

The intervals between follow-up visits vary according to local practice, but the most common schedule through convention is every 3 months for the first 2 years and then every 6 months up to 5 years after end of treatment.

Every woman should given clear instruction to contact key work in case of new symptoms of recurrent disease.

Support for women with newly diagnosed ovarian cancer: [7]
All women with newly diagnosed ovarian cancer should have support system to deal with psychosocial and psychosexual issues.

Information should be available regarding

- Stage of disease, treatment and prognosis
- Signs and symptoms of recurrent disease,
- How to deal with side effects of treatment;
- Issues regarding sexuality and sexual activity
- Fertility and hormonal treatment
- Genetics and chances of family members getting ovarian cancer
- Availability of support groups and how to deal with sadness or depression

Appendix A

Risk of Malignancy Index I (RMI I) calculation RMI I combine three pre-surgical features: serum CA125 (CA125), menopausal status (M) and ultrasound score (U).

The RMI I is a product of the ultrasound scan score, the menopausal status and the serum CA125 level (IU/ml).

(31) RMI I = U x M x CA125

The ultrasound result is scored 1 point for each of the following characteristics: multilocular cysts, solid areas, metastases, ascites and bilateral lesions.

U = 0 (for an ultrasound score of 0) U = 1 (for an ultrasound score of 1) U = 3 (for an ultrasound score of 2–5)

The menopausal status is scored as 1 = pre-menopausal and 3 = post-menopausal.

(The classification of 'post-menopausal' is a woman who has had no period for more than 1 year or a woman over 50 who has had a hysterectomy).

Serum CA125 is measured in IU/ml and can vary between 0 and hundreds or even thousands of

Appendix B:

FIGO 2014 FIGO ovarian, fallopian tube, and peritoneal cancer staging system and corresponding TNM

Stage 1: Tumours confined to ovaries or fallopian tubes

FIGO staging	TNM staging	Description
FIGO 1A	T1a-N0-M0	Tumour is limited to one ovary (capsule intact) or one fallopian tube
FIGO 1B	T1b-N0-M0	Tumour is limited to both ovary (capsule intact) or both fallopian tub
FIGO1C1	T1c-N0-M0	Tumour limited to one or both ovaries with surgical spill
FIGO 1C2	T1c-N0-M0	Tumour limited to one or both ovaries where capsule rupture before surgery and tumour on surface of ovary or fallopian tube
FIGO 1C3	T1c-N0-M0	Malignant cells present in ascitic fluid or peritoneal washings

Stage II: Tumour involves one or both ovaries or fallopian tubes with pelvic extension

FIGO IIA	T2a-N0-M0	Extension and/ or implant on uterus and/ or fallopian tubes and /or ovaries
FIGO IIB	T2b-N0-M0	Extension and or implant on other intraperitoneal tissue

Stage III: Tumour involves one or both ovaries or fallopian tubes, or primary peritoneal cancer, with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes

FIGO IIIA1 FIGO IIIA1(i) FIGOIIIA1(ii)	T1/T2-N1-M0	Metastasis to retroperitoneal lymph nodes with or without microscopic peritoneal involvement Metastasis <10mm in its greatest dimension Metastasis >10mmin its greatest dimension
FIGO IIIA2	T3a2-N0/N1- M0	Microscopic extrapelvic (above the pelvic brim) peritoneal involvement with or without positive retroperitoneal lymph nodes
FIGO IIIB	T3b-N0/N1-M0	Macroscopic peritoneal metastasis beyond the pelvis up to 2 cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes
FIGO IIIC	T3c-N0/N1-M0	Macroscopic peritoneal metastasis beyond the pelvis more than 2 cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes (includes extension of tumour to capsule of liver and spleen without parenchymal involvement of either organ.

Stage IV: Distant metastasis excluding peritoneal metastasis

FIGO IVA	Any T, any N, M1	Pleural effusion with positive cytology
FIGO IVB	Any T, any N, M1	Parenchymal metastases and metastases to extraabdominal organs (including inguinal lymph nodes and lymph nodes outside of the abdominal cavity)

Key Points:

Ovarian Cancer is the leading cause of death by gynecological cancer in UK. The incidence is higher in White ethnic females.
The overall survival for women with ovarian cancer can vary on multiple factors, but is approximately 45.6%
Ovarian Cancer typically presents with very vague symptoms i.e. bloating, reduced appetite, lower abdominal discomfort
Epithelial ovarian tumours are the most common cause of Ovarian Cancer.
Ca125 should be measured in Primary Care for all women with signs and symptoms of Ovarian Cancer.
In secondary care further tumour markers are checked and imaging is done.
The Risk of Malignancy Index (RMI) determines referral to MDT
Early stage confirmed disease is usually managed with macroscopic resection of tumour with consideration of fertility sparing treatment if required.
Advanced ovarian cancer consists of primarily debulking surgery with or without neoadjuvant chemotherapy (NAC).
Follow up is usually every 3 months for the first 2 years, and then every 6 months for 5 years after the end of treatment.

REFERENCES

1. Meyer, J. I., Kennedy, A. W., Friedman, R., Ayoub, A., & Zepp, R. C. (1995). Ovarian carcinoma: value of CT in predicting success of debulking surgery. *AJR. American journal of roentgenology*, *165*(4), 875-878.
2. Dowdy, S. C., Mullany, S. A., Brandt, K. R., Huppert, B. J., & Cliby, W. A. (2004). The utility of computed tomography scans in predicting suboptimal cytoreductive surgery in women with advanced ovarian carcinoma. *Cancer*, *101*(2), 346-352.
3. Fischerova, D., Cibula, D., Dundr, P., Zikan, M., Calda, P., Freitag, P., & Slama, J. (2008). Ultrasound-guided tru-cut biopsy in the management of advanced abdomino-pelvic tumors. *International Journal of Gynecological Cancer*, *18*(4), 833-837.
4. Geomini, P., Kruitwagen, R., Bremer, G. L., Cnossen, J., & Mol, B. W. (2009). The accuracy of risk scores in predicting ovarian malignancy: a systematic review. *Obstetrics & Gynecology*, *113*(2 Part 1), 384-394.
5. Banerjee, S., & Kaye, S. (2011). The role of targeted therapy in ovarian cancer. *European journal of cancer*, *47*, S116-S130.nice.org.uk/guidance/cg122/chapter/Recommendations#management-of-suspected-early-stage-iovarian-cancer(7)
6. Willacy H, Tidy C. Ovarian Cancer 2024
7. https://patient.info/doctor/ovarian-cancer-pro
8. https://www.cancerresearchuk.org/about-cancer/ovarian-cancer
9. https://www.rcog.org.uk/for-the-public/browse-our-patient-information/ovarian-cancer/