Ovarian cancer

Diagnosis and management

BACKGROUND
Epithelial ovarian cancer presents most often as late stage disease due to a lack of effective screening tests and vagueness of symptoms.

OBJECTIVE
This article outlines the diagnosis and management of ovarian cancer.

DISCUSSION
Women with suspected ovarian cancer are best managed in a gynaecological treatment unit offering multidisciplinary care. Surgery is usually needed both to make a diagnosis and for definitive treatment and referral to a specialty trained gynaecological oncologist is appropriate. Most women will also require chemotherapy. Ovarian cancers have good sensitivity to several drugs but relapse rates are high. This means that ovarian cancer is now seen as a chronic disease with often several episodes of remission, relapse and treatment. The psychological impact of this diagnosis both on the woman and her family are significant and best dealt with proactively.

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In 1999, ovarian cancer was the eighth commonest cancer and the sixth most common cause of death from cancer in Australian women (*Table 1*).[1] This in no small way reflects the late presentation for the majority of women.

Symptomatology

Epithelial ovarian cancers tend to occur most commonly in the peri- and post-menopausal woman. Symptoms are usually vague – accounting for the late presentation – and may include:

- pressure symptoms – bladder, bowel
- increased abdominal girth
- fatigue
- gastrointestinal symptoms – indigestion or lack of appetite, change in bowel habits, constipation, or
- less commonly, pain.

Vine et al[3] reported that 92% of women with invasive ovarian tumours and 84% of borderline cases have symptoms with a median duration of 4 months.

Obviously not all peri- or post-menopausal women with these symptoms will have ovarian cancer, but symptoms which persist (eg. for 1 month) should be investigated. The question should always be raised: 'Could this be ovarian cancer?'

The thought that a woman may have a psychosomatic problem should not overrule clinical suspicion of malignancy in women with persistent symptoms. A high level of suspicion is a useful adjunct in making the diagnosis of ovarian cancer particularly:

- in women with a family history of ovarian cancer
- women over 45 years of age, or
- where symptoms appear to persist in the absence of any alternative explanation.

Investigation

Clinical examination, including a pelvic examination may reveal:

- increased girth either ascites, or
- an abdominal mass (omental cake), and/or
- pelvic mass – filling the pouch of Douglas (best felt by recto-vaginal examination).

Depending on findings and symptomatology, a transvaginal ultrasound or computerised tomography (CT) scan of the abdomen and pelvis may confirm any physical findings.

Gastrointestinal symptoms may frequently lead to a referral for endoscopy – which will be negative. Both the general practitioner and the endoscopist need to consider ovarian cancer in these cases where symptoms persist and are not explained.

Tumour markers (CA-125) may be elevated (see the article by Neesham this issue about the role of CA-125 in ovarian cancer screening).

Diagnosis

The definitive diagnosis is made surgically. Where suspicion is high, surgery is best performed by a gynaecological oncologist with training in all aspects in the management of ovarian cancer. At this surgery, staging is also undertaken as well as definitive treatment.[4]

A total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy, examination of pelvic and para-aortic lymph nodes, as well as a careful search throughout the peritoneal cavity to detect and remove any tumour deposits will be undertaken. Occasionally where tumour affects the bowel, bowel resection, usually with primary reanastomosis, may also be necessary.

The aim of the surgery therefore, is to remove all tumour deposits as much as possible to leave no or minimal tumour burden remaining. The stage of the tumour is therefore determined at this surgery and gives a guide to prognosis. The stage of the tumour acts as a guide to further management (*Table 2*).

What is 'standard management'?

Ideally each woman should be managed in the setting of a multidisciplinary team, where each member has expertise in ovarian cancer care specifically, as well as their own field. There is evidence that outcomes for women in this setting are maximised.[5,6]

With exception of certain women whose disease is still stage I, the majority of women will expect to be offered chemotherapy after surgery. The gold standard currently is paclitaxel and carboplatin combination.[7] The standard dose of paclitaxel of 175 mg/m^2 and carboplatin AUC x 6 given every 3 weeks is generally well tolerated.[8] This is given usually in a day centre one day every 21 days for six cycles. Blood tests to ensure bone marrow recovery before each cycle are undertaken. A consultation also occurs before each cycle to investigate the efficacy of the treatment as well as management of any side effects from chemotherapy. Tumours have a good sensitivity to these drugs and about three-quarters may expect a positive response.

Chemotherapy usually commences as soon as practical after surgery when bowel function has recovered. There is no advantage in delaying chemotherapy because of wound healing. There is also no evidence to suggest that more than six cycles of chemotherapy offer any further advantage.

As well as monitoring bone marrow function the tumour marker CA-125 can be used as an additional means of assessing response. CA-125 has a half life of approximately 6 days. Provided the CA-125 continues to fall, treatment should continue to maximum of six cycles.

Table 1. Ovarian cancer in Australian women in 1999[1,2]

- 1173 women diagnosed with ovarian cancer
- 731 women died from ovarian cancer
- 5948 years of life lost under the age of 75 years
- Relative survival nationally of 42% at 5 years after diagnosis in 1992–1997
- The most common cause of death from gynaecological malignancy

Follow up after primary treatment

Present evidence does not support the use of any maintenance or consolidation therapy after initial treatment.[9] CA-125 is also used to monitor for tumour relapse. A rise to more than twice the upper limit of normal during follow up accurately predicts tumour relapse.[10]

Despite the relatively high response to chemotherapy, the majority of advanced ovarian cancer patients will relapse. The interval between the end of first line therapy and relapse (the so-called 'treatment free interval') is of prognostic significance. The longer the treatment free interval, the higher the likelihood of a further worthwhile response.[11] Experience would suggest that a treatment free interval greater than 12 months is associated with a significant number of patients deriving worthwhile benefit from re-treatment. Women whose disease recurs in less than 6 months (platinum refractory) usually do not respond to other forms of therapy. In all cases of second line therapy, it is important to monitor patients carefully and only continue treatment if there is objective evidence of response. It is essential that the quality of life of the woman is a major part of assessment.

Radiation therapy

Following surgery, chemotherapy has been the major thrust of treatment, however, radiation therapy has been useful in some women. The systematic study of radiation therapy has been hampered by poor accrual to large randomised trials. Whole Abdominal Radiotherapy (WART) has been used in patients with stage I, II and III disease with no macroscopic disease in the upper abdomen after completion of surgery.[12] The amount of radiation delivered to the abdomen is limited by the normal organs in the field. The dose is limited to 45–50 Gy in relatively low fractions of up to two Gy per fraction. Most patients experience acute side effects including nausea, vomiting and diarrhoea. Myelosuppression has been a common reason for treatment interruptions. Up to 10% of patients do not complete therapy. The late complications of WART include chronic diarrhoea, transient liver enzyme disturbance, basal pneumonitis, cystitis and bowel obstruction.

Common side effects of therapy

Surgery

The common postsurgical problems of infection, thrombosis and poor wound healing are similar to any other surgery. Postoperative ileus may be higher because of bowel involvement with tumour.

Chemotherapy

With the advent of modern antinausea medication, nausea and vomiting are usually a thing of the past when undergoing chemotherapy. Medication will include a 5HT3 antagonist and possibly also an anxiolytic. Both paclitaxel and platinum can produce peripheral neuropathy and women must be warned of this possibility. The neuropathy may often not appear until quite late in the cycle of chemotherapy or even after it is completed. Paclitaxel can also cause muscle and joint pain that may last from a few hours to several days in the first week after therapy.

Bone marrow suppression may occur. Carboplatin may be more responsible for platelet depletion whereas both drugs equally will affect neutrophils.

Prognosis

The majority of patients will present with stage III or IV disease (about 75%). While the response rates to primary chemotherapy with paclitaxel and carboplatin are relatively high, the majority of women will eventually relapse and succumb to their disease. Survival rates are in the order of 40%.

Quality of life

Ovarian cancer should be seen as a chronic disease with often several episodes of remission, relapse and treatment. It is essential that the quality of life of women with ovarian cancer is a major part of assessment and consideration of quality of life issues underpin any treatment decisions.

There is Level one evidence that psychosocial intervention can result in lower rates of anxiety and depression, and nausea and vomiting for patients with cancer.[13] Psychosocial interventions can include counselling and relaxation therapy, education programs to improve pain control, and cognitive behavioural interventions, all of which have shown positive benefits.

Table 2. Staging of ovarian cancer

Stage I	Growth limited to ovaries only
Stage IA	One ovary, no ascites, no tumour on external surface, capsule intact
Stage IB	Both ovaries involved, no ascites, no tumour on external surface, capsule intact
Stage IC	IA or IB with tumour on surface, capsule ruptured, malignant ascites or positive washings
Stage II	Pelvic extension only
Stage IIA	Extension and/or metastasis to uterus and/or fallopian tubes
Stage IIB	Extension to other pelvic tissues
Stage IIC	IIA or IIB with tumour on surface or capsule ruptured, malignant ascites or positive washings
Stage III	Tumour involving one or both ovaries with peritoneal implants outside the pelvis and/or positive retroperitoneal or inguinal nodes
Stage IIIA	Tumour grossly limited to the true pelvis with negative nodes but histologically confirmed microscopic seeding of abdominal peritoneal surfaces
Stage IIIB	Tumour involving one or both ovaries, histologically confirmed implants on abdominal peritoneal surfaces <2 cm
Stage IIIC	Abdominal implants >2 cm and/or positive retroperitoneal or inguinal nodes
Stage IV	Growth involving one or both ovaries with distant metastasis. If pleural effusion present, positive cytology; parenchymal liver metastasis

Conclusion

In women with epithelial ovarian cancers symptoms are usually vague and as a consequence presentation and/or diagnosis is often late. A high level of suspicion is important in making the diagnosis of ovarian cancer particularly in the peri- and post-menopausal woman, those with a family history of ovarian cancer, and when symptoms persist for more than 1 month. Women with suspected ovarian cancer are best managed in a gynaecological treatment unit offering multidisciplinary care. Surgery is usually needed both to make a diagnosis and for definitive treatment. Most women will also require chemotherapy. Ovarian cancers have good sensitivity to several drugs but relapse rates are high.

Conflict of interest: none declared.

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