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Gynecological malignancies

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CERVICAL CANCER

The incidence of cervical cancer in the UK and in most of the Western world has declined since the early 1980s when effective cervical cancer screening became the standard of care. In 2005, a total of 2803 cases (8.4 per 100,000) of cervical cancer were documented in the UK, representing about 2% of all female cancers, making cervical cancer the 12th most common cancer in women in the UK[1]. In the US, about 13,000 new cases are recorded every year with a rate of approximately 1 per 21,000 women and a lifetime risk of developing cervical cancer of 1 in 117[2].

Worldwide, cervical cancer remains the major cause of cancer death in women, especially in the developing world[3]. About 0.5 million new cases are seen annually and the condition causes over 0.25 million deaths every year[4]. Of such deaths 80% occur in the developing world where effective cervical cancer screening programs do not exist.

Almost all cases of cervical cancer are due to persistence of the oncogenic human papillomavirus virus (HPV) infection, a form of sexually transmitted disease. The three main risk factors for disease progression are sexual activity, smoking and immune suppression. Oncogenic HPV is detected in approximately 99.7% of all cases of cervical cancer[5–7].

Treatment of cervical cancer and impact on future pregnancy outcome

The standard treatment for cervical cancer is either radical hysterectomy with pelvic lymphadenectomy or radical chemoradiotherapy. A newer type of treatment called radical trachelectomy has recently been developed. This is a fertility sparing procedure that is only feasible for early stages of cervical cancer as described below[8].

With effective screening the majority of cervical cancer cases can be detected in the very early stages, when conservative management and fertility preservation is possible. Such fertility preserving procedures are only possible from stage 1a1 to small volume stage 1b1 disease.

Stage 1a1 disease (invades the cervical stroma to less than 3 mm deep and less than 7 mm wide)

This is the earliest form of the disease. The risk of lymph node involvement is usually less than 0.5%. The majority of cases are usually diagnosed following a large loop excision of the cervical transformation zone (LLETZ) or after a cone biopsy for a severe smear abnormality (Figures 1 and 2).

If the excision margins are clear of the disease and of cervical intraepithelial neoplasia (CIN), no further treatment is necessary apart from management with regular follow-up smears. If the excision margins are involved with CIN, then further loop excision is usually recommended after 4–6 weeks. Usually, the implication for pregnancy outcome following one loop cervical biopsy is negligible. However, after two or more loop excisions there is

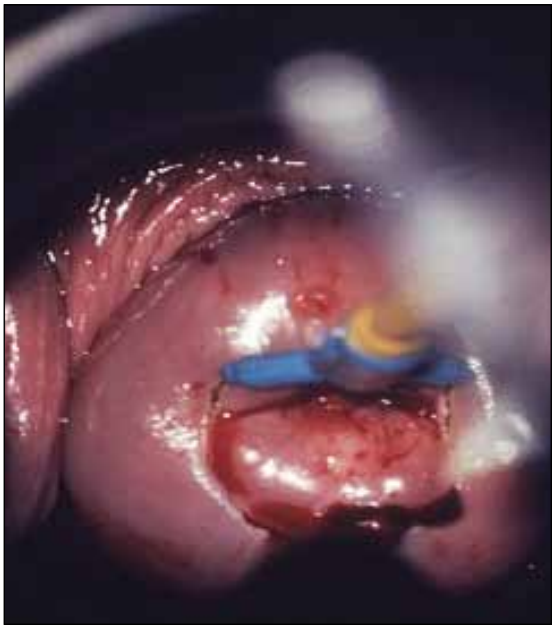

Figure 1 Loop cervical biopsy

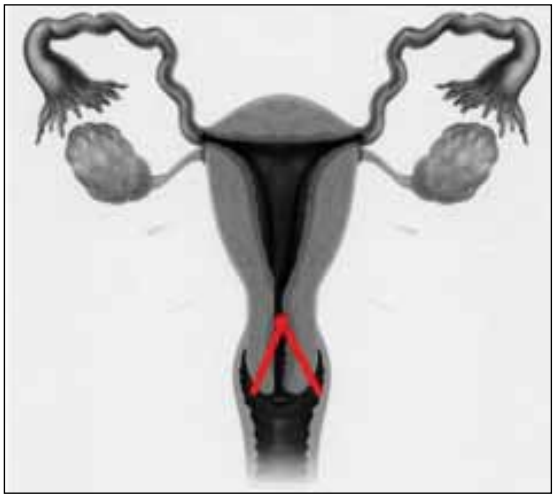

Figure 2 Diagram showing the part of cervix where a cone biopsy is performed

a small but significant risk of late miscarriage and premature labor due to cervical incompetence. Therefore, women who have had two or more loop excisions should be closely monitored by an obstetrician throughout the pregnancy. In the first and second trimesters, the cervical length should be measured at regular intervals with a transvaginal ultrasound scan. The internal cervical os should also be assessed to exclude 'funneling'. If there is evidence of cervical shortening with or without 'funneling', a cervical suture may be inserted in either the late first trimester or early second trimester to prevent premature labor.

Stage 1a2 disease (invades to a depth greater than 3 mm, but less than 5 mm, with horizontal spread not exceeding 7 mm)

The risk of lymph node metastases at this stage is about 5–7.5%. No consensus exists regarding the optimal management of stage 1a2 cervical cancer. Treatment options include:

1. Radical hysterectomy and pelvic lymph node dissection;
2. Radical trachelectomy (Figure 3) and laparoscopic pelvic lymph node dissection;
3. Conization of the cervix followed by laparoscopic pelvic lymph node dissection.

Following radical hysterectomy, assuming pelvic irradiation is avoided, ovarian function is usually preserved thereby preventing the development of premature menopause. Where such women still desire to have children, their only option is surrogacy.

Trachelectomy and cervical conization followed by laparoscopic pelvic lymph node dissection are fertility preserving procedures in women desiring to have children. Careful preoperative counseling (as in radical hysterectomy) is required. The limitations of such a procedure and the fact that no long-term data are available regarding prolonged survival should be carefully discussed with the patient. Radical trachelectomy was first developed by Daniel Dargent as a modification of the radical vaginal hysterectomy described by Schauta[9,10]. It involves removing the cervix, parametria and a cuff of the vagina, thereby preserving

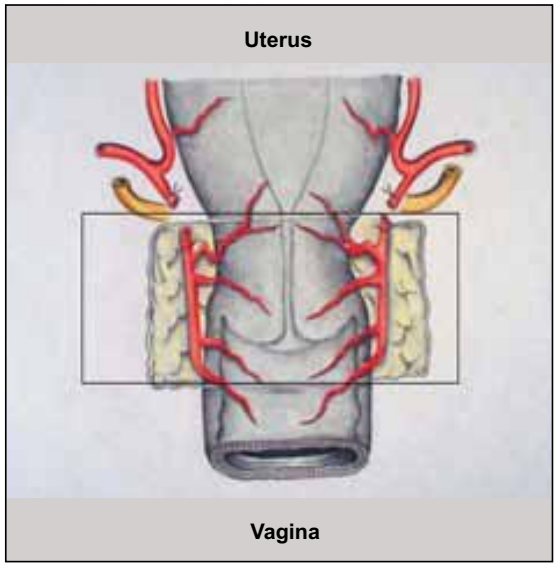

Figure 3 Diagram showing extent of tissue removal during radical trachelectomy for stage 1a2 or small volume stage 1b1 cervical cancer

the body of the uterus for fertility. The procedure is combined with either extraperitoneal or laparoscopic lymphadenectomy. Following radical trachelectomy, a cervical suture is left *in situ* and the vaginal and uterine isthmus is anastomosed, completely burying the suture. The subsequent mode of delivery will be by elective cesarean section. The pregnancy rate amongst women trying to conceive following radical trachelectomy ranges between 53% and 70% within 5 years of trying[8]. Only about half of such pregnancies are carried to term. Approximately 13% are lost in the early second trimester, whilst the rest are usually delivered prematurely due to the presence of an incompetent cervix. Stenosis can also be a major problem following radical trachelectomy, causing menstrual disorders or fertility problems. The majority of such problems are usually resolved following cervical dilatation. On the other hand, if patients succeed in conceiving, they should be warned about the risk of second trimester miscarriage or of premature labor. Close obstetric follow-up throughout the pregnancy is required with careful transvaginal ultrasound monitoring of the cervix.

Small volume stage 1b1 cervical cancer (lesions confined to the cervix more than stage 1a2 but not greater than 2 cm)

For women in the reproductive age group, treatment options are either radical hysterectomy and bilateral pelvic lymphadenectomy or radical trachelectomy followed by laparoscopic pelvic lymphadenectomy[11]. The latter option is recommended for women desiring fertility preservation. However, after radical trachelectomy, the following problems may arise and patients should be counseled beforehand that extra postoperative vigilance will be necessary:

1. Cervical stenosis;
2. Cervical incompetence;
3. Infertility;
4. Difficulty obtaining adequate follow-up cervical smears.

ENDOMETRIAL CANCER

The incidence of endometrial cancer (Figure 4) has gradually increased over the past decade. For example, in 2005 endometrial cancer was the most common gynecological cancer in the UK, accounting for 6891 cases and 1651 deaths[1]; in the US, more than 40,000 new cases and 7470 deaths were recorded in 2004[2]; Canada reported 3800 new cases in 2004[12]; and the annual incidence in Australia is about 1400 new cases[13].

About 70% of cases present with stage 1 disease and treatment with total hysterectomy and bilateral salpingo-oophorectomy provides a cure, so that the overall 5-year survival is about 75%. The majority of cases also present with well or moderately differentiated endometroid type adenocarcinoma which has a good prognosis. Although endometrial cancer

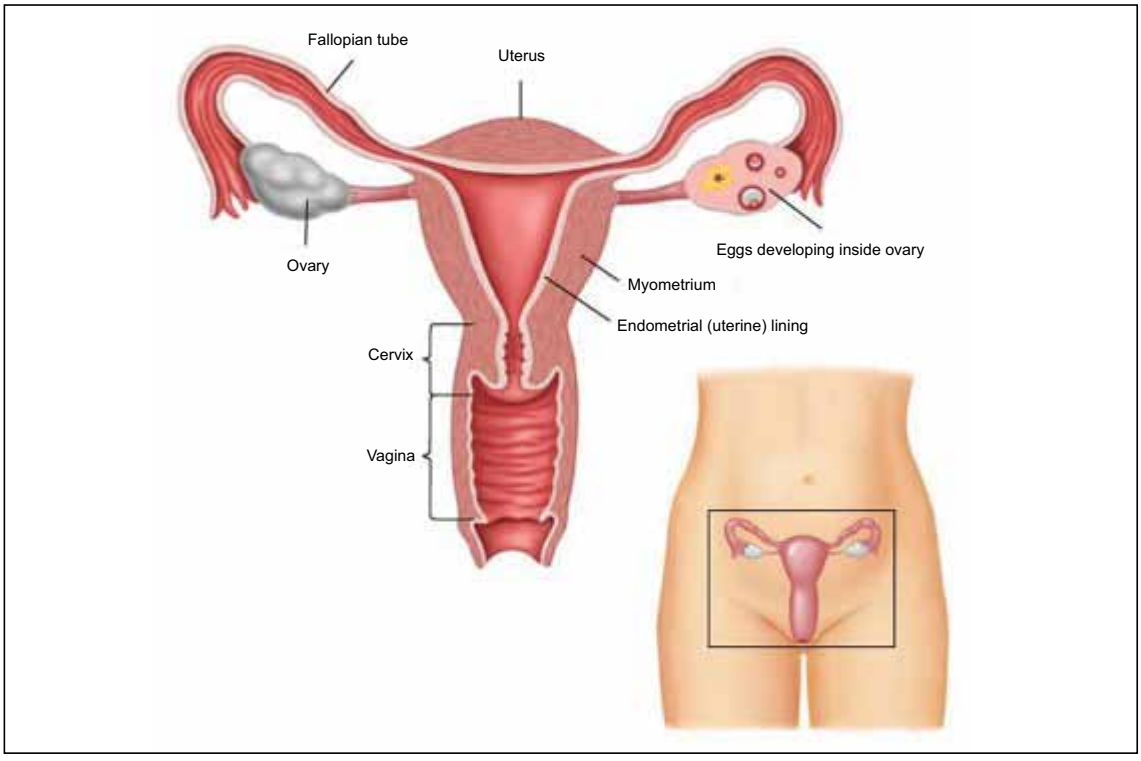

Figure 4 Diagramatic representation of the female anatomy, showing the uterine cavity, cervix and vagina and the position of the tubes and ovaries

is more commonly a disease of postmenopausal women (usually above the age of 60 years), it has been reported in younger women below the age of 45 years and therefore in the reproductive age group. The risk factors for endometrial cancer in premenopausal women include:

1. Polycystic ovarian syndrome;
2. Obesity;
3. Nulliparity;
4. Familial (hereditary non-polyposis colorectal cancer syndrome or the Lynch syndrome);
5. Estrogen secreting tumors.

In hereditary non-polyposis coli, a mismatch repair gene defect increases the risk of endometrial cancer to almost 60%.

Management of endometrial cancer in young women

About 3–14% of all endometrial cancers are diagnosed in women younger than 40 years[14]. The majority of such cases are usually associated with good prognostic features such as degree of differentiation (usually well differentiated), and focal with minimal or no myometrial invasion. Whereas the ideal management of endometrial cancer at any age is total hysterectomy and bilateral salpingo-oophorectomy with or without pelvic/para-aortic lymph node dissection, there are reports of conservative management of very early stage endometrial cancer in young women desiring to preserve fertility[15,16]. It is axiomatic that such women desiring to retain their uterus and ovaries must be properly counseled by both a gynecological oncologist and gynecological oncology

nurse specialist. This decision should not be taken lightly as the long-term implications of such an action remain to be determined.

Prior to instituting conservative management, adequate assessment of the uterine cavity should be carried out with a hysteroscope. This should then be followed by magnetic resonance imaging (MRI) staging assessing the presence or absence of myometrial invasion. Ovarian assessment should also be made using transvaginal ultrasound with or without Doppler studies. Immunohistochemistry studies should be performed on the specimen to determine the hormone receptor status, as progestin sensitivity or uptake is associated with good prognostic outcome. Progestogens have been a mainstay of therapy for women who refuse the standard treatment; although no single protocol represents the standard of care. The overall complete response rate has been reported to be in the region of about 70%[16–19]. The author's suggested treatment protocol is 160 mg of medroxyprogesterone acetate (Megace) orally daily for 90 days followed by further hysteroscopy and endometrial samplings. If there is evidence of complete response (that is absence of tumor in all biopsies), treatment is continued for a further 90 days and then stopped.

The patient is then seen on a 3-monthly basis and undergoes outpatient pipelle endometrial sampling every 6 months indefinitely except if pregnant. On completion of family, or if the patient no longer wishes to have a family, total laparoscopic hysterectomy and bilateral salpingo-oophorectomy should be advised. Some have quoted a pregnancy rate as high as 58% following treatment with progestogens. For those women who do not desire to get pregnant immediately, long-term maintenance therapy with either the combined oral contraceptive pill or the levonorgestrel intrauterine system (Mirena) may be appropriate. Such treatment is discontinued as soon as the patient wishes to conceive.

Another issue that has recently come to the fore is the possibility of ovarian conservation in very young women with early stage endometrial cancer who consent to hysterectomy. If the ovaries are conserved, this would invariably give the patients the option of surrogacy in the future if they so desire. Ovarian conservation would also prevent the devastating effects of menopausal symptoms and estrogen deprivation, in particular osteoporosis. It is important to recognize, however, that approximately 25% of endometrial cancer patients will have coexistent ovarian cancer (either metastatic or primary disease). Under these circumstances, it is vital to discuss ovarian conservation with the patient before her surgery or conservative medical management.

The management of atypical endometrial hyperplasia

Atypical endometrial hyperplasia is characterized by excessive proliferation of endometrial cells associated with cellular stratification, densely eosinophilic cytoplasm, tufting, loss of nuclear polarity, and enlarged and prominent nuclei with increased evidence of mitosis[20]. These nuclear features are more or less similar to what one finds in true cancer cells except that there is no evidence of invasion. The etiological factors are similar to those for endometrial cancer, and young women who are obese and have polycystic ovarian syndrome are particularly affected. The drive for endometrial stimulation is excessive estrogen.

Several studies have shown that complex hyperplasia with atypia has a 30–50% risk of progression to frankly invasive carcinoma if left untreated[21]. The risk of concurrent endometrial cancer at the time of diagnosis varies from as little as 17% to almost 52%. Thus, the recommended treatment standard is total hysterectomy and bilateral salpingo-oophorectomy. However, fertility preservation may represent a huge issue for young women

who have not had children. Once again, hormone treatment, as discussed above, may be a good compromise treatment in this group of patients.

OVARIAN CANCER

Ovarian cancer (Figures 4 and 5) was the second most common gynecological cancer in the UK with a total of 6806 cases in 2005, and 4407 deaths in 2006[1]. In the US, there were 20,095 new cases of ovarian cancer in 2004 and 21,650 cases in 2008; the condition was responsible for 15,520 deaths in 2008[22]. Given these numbers, ovarian cancer causes more deaths than any other cancer of the female reproductive tract. As the symptoms and signs are usually highly non-specific, about 75% of patients present with advanced stage disease where surgery alone is no longer curative. When diagnosed in very early stages, however, treatment is usually very effective. Although the symptoms and signs (such as abdominal swelling, urinary frequency, abdominal pain and alteration in bowel habits) are not specific, it is important to remember that ovarian cancer does cause symptoms and signs. Thus, the notion that ovarian cancer is an absolutely 'silent killer' should be discarded. It is important for every woman to know her body very well and also to know what is normal for her. Indeed, it is important for health care providers to encourage women to become more aware of themselves and their daily functions so that they can notice subtle alterations when they appear. At the same time, clinicians should have a high index of suspicion and should not ignore the so-called 'non-specific' symptoms, especially when they appear in women who have presented without symptoms for years and now complain for the first time. Clinicians should learn to listen more to women when they complain of any of the above symptoms. This means not just to sit across from the patient and let her talk but to follow-up with suitable questions which will illuminate the onset, nature and extent of the symptoms, especially in those who have not been known to complain of anything in the past.

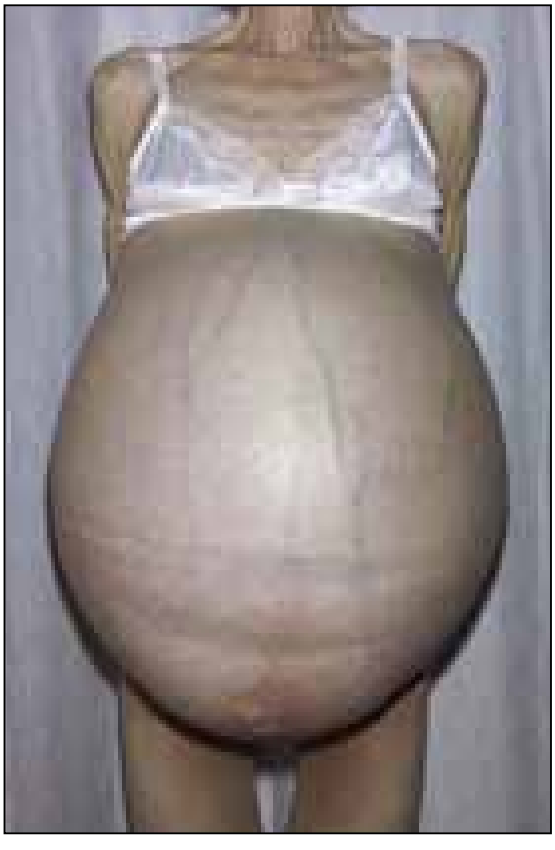

Figure 5 Ovarian tumor and ascites causing markedly distended abdomen with prominent veins, evidence of weight loss and stretched out skin

Ovarian cancer is a disease of older women, and approximately 90% of cases occur in women older than 40 years, with the majority usually above the age of 55 years. Women are only more likely to have ovarian cancer at an earlier age if they are at a high risk, such as having a family history of ovarian or breast cancer and if they are nulliparous. The combined oral contraceptive pill appears to offer some degree of protection against the development of ovarian cancer.

The three main types of ovarian cancer are:

1. Epithelial ovarian tumors – derived from the surface epithelium of the ovary;
2. Germ cell ovarian tumors – derived from the egg (ovum) producing part of the ovary (not all germ cell tumors are malignant);
3. Ovarian stroma tumors – derived from the connecting tissue elements of the ovary.

Epithelial ovarian tumors

Benign epithelial ovarian tumors

The majority of epithelial ovarian cancers are benign, which means they lack cellular atypia and invasive characteristics. Such benign epithelial tumors are serous or mucinous adenomas and Brenner tumors. Therefore, they require conservative management in the young woman with reproductive potential. Unilateral salpingo-oophorectomy or even ovarian cystectomy is all that is required. Such procedures can be undertaken with minimally invasive techniques without need for major laparotomy incisions. The vast majority of these tumors are only diagnosed in postoperative specimens. However, careful preoperative investigations with imaging (ultrasound, computed tomography (CT) or MRI) and tumor markers should lead to a high index of suspicion. Therefore, conservative management can be offered to women desiring to preserve their fertility.

Epithelial ovarian tumors of low malignant potential (borderline ovarian tumors)

These types of epithelial ovarian tumors differ from the typical cancerous ovarian tumors because they appear not to invade the ovarian stroma. They account for about 10–15% of all epithelial ovarian tumors and are usually very slow growing tumors. The majority are diagnosed in the early stages. Even in advanced stages, with spread into the peritoneum or omentum, they usually produce characteristic 'non-invasive' implants. Unlike the frankly invasive epithelial ovarian tumors which affect mainly postmenopausal women, they tend to affect the younger age group of women and those in the reproductive age.

When a complex ovarian mass is found in a young woman of reproductive age, as with any other age, preoperative investigations such as tumor markers (CA125, CEA, β-human chorionic gonadotropin (hCG), α-fetoprotein (AFP)) should be checked and appropriate preoperative imaging should be carried out with ultrasound with or without Doppler imaging, CT scan or MRI. Unfortunately, tumor markers, especially CA125, have been of no value in either the preoperative management or the follow-up of women with borderline ovarian tumors.

Women should be properly counseled prior to surgery. The ideal treatment, even if borderline ovarian tumor is suspected, is total abdominal hysterectomy, bilateral salpingo-oophorectomy and omentectomy. In some cases where there are obvious implants within the peritoneal cavity, these should be excised. The aim should be complete surgical debulking. There may be an argument for pelvic and para-aortic lymphadenectomy for complete tumor staging. However, in young women desiring to preserve their fertility, and when the tumor is unilateral, it may be feasible to carry out conservative surgery such as unilateral salpingo-oophorectomy with the rest of the staging procedures as above. Salpingo-oophorectomy is preferred to cystectomy even if the disease is confined to one ovary, as this is less likely to be associated with risk of recurrence[23]. Cystectomy is more likely to be associated with intraoperative surgical rupture, thus increasing the risk of recurrence. If the contralateral ovary looks normal, there may be no need to biopsy it. On the other hand, if it looks cystic and/or abnormal, a frozen section biopsy should be obtained. If the whole of the ovarian tissue is uninvolved, it may still be

feasible to preserve some of the ovarian tissue. Even if there is the need to remove the contralateral tube and ovary, the uterus does not necessarily need to be removed. This would offer the woman the choice of egg donation and *in vitro* fertilization later in life. Hormone replacement is recommended following bilateral salpingo-oophorectomy to both maintain the endometrium and prevent menopausal symptoms and osteoporosis due to estrogen insufficiency.

Following conservative surgery for borderline ovarian tumors, the patient should be closely followed up at 3-monthly intervals in the first 2 years with 6-monthly pelvic ultrasound scans. Thereafter, she should be followed up 6-monthly with yearly ultrasound scans for a total follow-up period of 10 years, except if she opts for a full hysterectomy and removal of the remaining ovary and tube having completed her family. The place of CA125 monitoring at follow-up is controversial, and the author's personal preference is to only do this in women who have previously had elevated CA125 prior to surgical management.

It is rational to ask if there is a role for adjuvant chemotherapy in borderline ovarian tumors. This remains controversial. No arguments surround the fact that complete surgical debulking should be the goal in both early and advanced stage disease. The overall 5-year survival for women with stage 1 and 2 disease is greater than 90%. Some authors have used chemotherapy for advanced stage disease with invasive implants and have reported varied results. Chemotherapy does not appear to improve the overall survival for disease with non-invasive implants in either the peritoneum or the omentum.

Invasive epithelial ovarian tumors

Epithelial ovarian cancer is relatively uncommon in women below the age of 50 years and even more so below the age of 40 years. Most women have completed their family before the age of 40 years. The management of epithelial ovarian cancer in women who wish to preserve their fertility depends on the stage of the disease. Ideally, following routine preoperative investigations, all women with ovarian cancer should undergo complete surgical staging which includes total abdominal hysterectomy, bilateral salpingo-oophorectomy and omentectomy with pelvic and para-aortic lymphadenectomy. Longer-term survival correlates positively with absence of residual disease following surgery (optimal cytoreductive surgery), younger age of the patient, favorable histological type (apart from serous or clear cell type), early stage disease and good performance status. Conservative management may be considered in younger women with stage 1 disease and favorable histological type as detailed below. Fertility preservation is usually not advisable in women with stage 2 and above irrespective of the histological type.

Stage 1a disease (confined to one ovary without involvement of the surface of the ovary and no ascites) Management of stage 1a disease is by laparotomy via a midline incision to allow complete inspection of the upper abdomen. Peritoneal washings are obtained for cytology, and a unilateral salpingo-oophorectomy and omentectomy are performed. Para-aortic lymph node dissection is also performed to assist in optimal staging.

Stage 1b disease (involvement of both ovaries, but no tumor on the surface of the ovary and no ascites) Management of stage 1b disease is again by laparotomy, peritoneal washings for cytology, bilateral salpingo-oophorectomy, omentectomy and para-aortic lymphadenectomy. The uterus is preserved as this would give the woman the option of egg donation for *in vitro* fertilization. Hormone replacement should be prescribed to maintain endometrial integrity as well as to prevent menopausal symptoms and osteoporosis.

Stage 1c disease (stage 1a or 1b plus one or more of the following – tumor on the surface of the ovary, positive peritoneal cytology or surgical rupture of the cyst) Surgical management for stage 1c disease is as for stage 1a or 1b above but with the addition of adjuvant chemotherapy (single agent platinum or platinum based combination). Once again, in younger women, hormone replacement is usually recommended for the reasons given above.

Germ cell ovarian tumors

These are rare of gynecological tumors. Ovarian germ cell tumors represent about 25% of all germ cell tumors. Other sites where germ cell tumors can be found include the testicle (12%), sacrococcygeal region (40%), brain (5%), and neck and thorax (18%). Not all ovarian germ cell tumors are malignant. The main histological types of ovarian germ cell tumors are the mature teratoma or dermoid cyst which is usually benign, the immature teratoma which is malignant, yolk sac tumors, dysgerminoma, choriocarcinoma, embryonal carcinoma, endodermal sinus tumors and mixed germ cell tumors.

Ovarian germ cell tumors usually affect one ovary and are more likely to be found in girls and women below the age of 40 years. Very rarely, they may also be found in children and elderly women. The symptoms are a feeling of pelvic-abdominal fullness or bloating, abdominal pain, occasional irregular bleeding and urinary frequency due to pressure on the urinary bladder. It is therefore important to have a high index of suspicion as some of these symptoms are non-specific. Abdominal and pelvic examination may reveal a pelvic mass. A pelvic ultrasound would show a complex ovarian mass which is usually unilateral. Blood should be taken for the two main tumor markers, βhCG and AFP. These are very sensitive tumor markers which are usually elevated and are good indicators of complete tumor resection following surgery or response to chemotherapy. They are also very useful for subsequent follow-up after a successful treatment. Pretreatment CT scan of the abdomen, chest and pelvis provides additional evaluation of disease extent (involvement of the omentum or the para-aortic lymph nodes).

Over the past two decades, treatment of ovarian germ cell tumors has improved significantly, and it is now possible to cure most cases in even advanced stage disease. In young women desiring fertility preservation and with stage 1 and 2 disease, unilateral salpingo-oophorectomy should be considered at laparotomy and with full surgical staging. Surgery is usually curative with stage 1 disease. In stage 2 and above, apart from ovarian dysgerminoma where radiotherapy might be considered, combination chemotherapy consisting of cisplatin, etopoxide and bleomycin is usually very effective. Following cessation of chemotherapy, ovarian functioning usually returns over a period of 3–6 months. Other combination chemotherapy has also been used. The use of radiotherapy, however, for advanced stage dysgerminoma would lead to ovarian failure and loss of fertility.

Ovarian stromal (or sex-cord stromal) tumors

These are tumors derived from the connective tissue elements of the ovary. They are rare and account for about 5–10% of all types of ovarian cancers. They occur more often in young girls and women of reproductive age, and only about 10% occur in women above the age of 50 years. Tumors derived from the ovarian stroma may be associated with abnormal production of the sex steroid hormones (progesterone, estrogen, testosterone, androstenedione, dehydroepiandrosterone). The feminizing hormones (progesterone and estrogen) can cause abnormal uterine bleeding or precocious puberty if the tumor develops in children. The

male sex hormones, on the other hand, can cause virilization, hirsutism, greasy skin and infertility.

The most common types are granulosa cell tumor and Sertoli-Leydig tumors. Other types of ovarian stromal tumors include theca cell tumor, fibroma, thecoma, lipid cell tumor and gynandroblastoma. The vast majority of ovarian stromal tumors (approximately 75%) will present with stage 1 disease. Their earlier presentation, unlike their epithelial counterparts, is probably because of the associated symptoms secondary to abnormal hormone production.

Granulosa cell tumors

These tumors account for only about 2% of all ovarian malignancies and usually present early, most typically as complex unilateral ovarian tumors on ultrasound or CT scan. Because of the abnormal hormone production, they may be associated with abnormal uterine bleeding or endometrial hyperplasia. Apart from estrogen, they also produce inhibin, which is a useful tumor marker in subsequent follow-up. Surgery alone is usually curative. Because these tumors tend to present early, unilateral salpingo-oophorectomy and omentectomy with preservation of the contralateral ovary and uterus is all that is required. In advanced stage disease, total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy and surgical debulking of all macroscopic tumor deposits is the aim, because there is no evidence of clear benefit from chemotherapy and radiotherapy in granulosa cell tumor.

Sertoli-Leydig tumors

These tumors account for only 0.5% of all ovarian cancers. By producing male hormones, they can cause virilization and hirsutism. Other symptoms include oligomenorrhea, amenorrhea and infertility. They are a rare cause of precocious puberty in children and infants. About 97% of cases present as stage 1 disease when conservative surgery and fertility preservation would be most appropriate.

VULVAR CANCER

Vulvar cancer is very rare in women in the reproductive age group with only a handful of cases reported in women below the age of 40 years. The majority of cases present as early stage disease where a more conservative approach to management is feasible. Wide local excision of the primary tumor, without the need for radical vulvectomy is all that is usually required. This may be combined with unilateral or bilateral groin node dissection depending on the depth of invasion or the location of the primary tumor in the vulva. With tumor depths greater than 2 mm, groin node dissection is usually recommended. If it is a lateralized disease, then unilateral groin node dissection is performed, and the contralateral groin is preserved except if there is evidence of metastasis in the dissected groin nodes. Nowadays, women with small volume disease can be offered the lesser surgical option of sentinel lymph node dissection of the groin. This is a far less morbid surgical option without the need for extensive groin node dissection.

Wide local excision of the vulvar primary tumor would in most cases preserve the anatomy of the external vulva. Plastic reconstruction may be required to restore any anatomical anomaly, if it should appear postsurgery. In young women still desiring fertility, subsequent deliveries should be by cesarean section as the vulva, although adequate for sexual intercourse, may be too tight for vaginal deliveries. The woman should be appropriately counseled and delivery options carefully explored ideally in the preconceptional period or in the early stages of pregnancy.

Adjuvant radiotherapy is only indicated in women with very close tumor excision margins or involved groin nodes. In those with very close tumor resection margins, the option of further wide local excision should always be considered before resorting to adjuvant radiotherapy. In women requiring groin irradiation, the patient must deal with the risk of irradiating the pelvis as well as with the potential of ovarian tissue damage which can lead to premature menopause. This would, of course, have implications for fertility in women of reproductive age group.

PRECONCEPTION FERTILITY PRESERVATION IN GYNECOLOGICAL ONCOLOGY

So far, we have mentioned radical trachelectomy as a fertility preserving surgical option in the management of the young patient with early stage cervical cancer and conservative management in some women with either early stage endometrial cancer or atypical endometrial hyperplasia after appropriate counseling. However, following the diagnosis of cancer in young women within the reproductive age range, ovarian function is a major issue that merits discussion with the patient and her significant other or family, as appropriate. This is even more necessary if treatment involves radiotherapy and chemotherapy. Radiotherapy treatment, especially external beam irradiation, will most certainly destroy ovarian function, rendering premenopausal women menopausal. Fortunately, major developments in reproductive medicine over the past two decades make it possible to offer women desiring to conceive after cancer treatment options such as:

1. Egg preservation or freezing;
2. Embryo freezing;
3. Ovarian freezing.

Whilst it is important to discuss these options and their relative degrees of success, it is also important for the clinician to consider the overall disease survival and life expectancy of the patient. It may not be ethically justifiable to offer these options to patients with an advanced stage disease where cure rate might be very low. Of the above three options, embryo freezing appears to carry most success and should be the preferred option in women who are in a stable relationship. Until recently, egg preservation or freezing was still experimental; however, it is now increasingly being offered as a realistic option to women in the US and in many European countries. Ovarian freezing is still experimental and reported success rates are low at the time of writing.

Recently, there have been sporadic case reports on whole ovary transplantation and some successes have been reported in identical twins with premature ovarian failure not secondary to cancer or cancer treatment. The technique of transplantation of previously stored ovarian tissue to the same woman has also been reported in the past several years. However, the technique of whole ovary transplantation is totally a new concept. As with any other organ transplantation, the risks of immunosuppression and rejection should be carefully examined. The opinion of the author is that whole ovary transplantation should only be carried out in expert centers and under the auspices of research. Other fertility options are available and should also be considered, including surrogacy and adoption.

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