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The management of ovarian cysts in premenopausal women

Alka Prakash, Tin-Chiu Li, William L Ledger

As high-resolution transvaginal ultrasound becomes more widely available, asymptomatic cysts are diagnosed with increasing frequency. Womens' anxieties centre on the risk of cancer and possible loss of fertility due to the cyst and treatment complications. Investigations include measurement of serum tumour markers, basic assessment of ovarian function, transvaginal ultrasonography and possibly cyst fluid cytology. While a proportion of simple cysts will resolve spontaneously, others require surgical management. Laparoscopic surgery is the treatment of choice in young women at low risk of malignancy.

Introduction

Ovarian tumours can occur at any age in a woman's life but they differ in type, being mostly germ cell tumours in childhood, functional cysts in the reproductive age group (up to 45 years) and becoming increasingly malignant towards and after menopause. Functional ovarian cysts were found to be the fourth most common cause of hospital admission of women in the late 1980s[1] and by the age of 65 years, 4% of all women in England and Wales will have been admitted to hospital for this reason.[2]

The incidence of detection of ovarian cysts has increased dramatically as a result of increased use of transvaginal sonography and computed tomography. Many are asymptomatic although some may require treatment because of pain or perceived risk of torsion. However, the primary task in all cases is to take reasonable steps to exclude malignancy. On the other hand, in younger women it is also desirable to avoid unnecessary surgery so as not to compromise future fertility. In the reproductive age group the incidence of malignant ovarian cysts is reported as being between 0.4–8.9/100 000 women and shows a dramatic increase with advancing age, to 60/100 000 women aged 60–80 years.[3] Malignant ovarian tumours are the most common cause of gynaecological cancer-related deaths in USA and Western Europe.[4]

Evaluation of ovarian masses

A number of methods are available for diagnostic assessment of ovarian cysts, some being more invasive than others.

During clinical examination a large ovarian cyst may be readily detected but small cysts are often missed by routine pelvic examination. It is not always possible to distinguish between ovarian and uterine masses (e.g. fibroids) on clinical examination.

Transvaginal ultrasonography (TVS) provides detailed images of the ovaries and adnexal masses. It has been recommended by the US National Institutes of Health as the preferred method for diagnosis of ovarian cysts.[5,6] The quality of ovarian imaging using TVS greatly exceeds that with transabdominal ultrasonography (TAS). The sonomorphological features suggestive of ovarian malignancy include increased size, presence of septations, papillary formations, echogenic solid areas and free fluid in the pouch of Douglas. However, the specificity of TVS for the detection of malignancy is not sufficiently high for it to be used alone as a screening test.[7] A seven-year prospective study in Germany found that the risk of malignancy developing following detection of a unilocular smooth-walled cyst by sonography was 0.8%. The risk of malignancy declines with decreasing tumour size and decreasing age.[8]

Author details

Alka Prakash MRCOG, *Clinical Research Fellow*, Department of Obstetrics and Gynaecology, Jessop Wing, Royal Hallamshire Hospital, Glossop Road, Sheffield, S10 2JF, UK.

Tin-Chiu Li PhD MRCP MRCPI FRCOG, *Consultant*, Department of Obstetrics and Gynaecology, Jessop Wing, Royal Hallamshire Hospital, Tree Root Walk, Sheffield, S10 2SF, UK.

William L Ledger MA D Phil FRCOG, *Head of Section of Reproductive and Developmental Medicine*, Academic Unit of Reproductive and Developmental Medicine, University of Sheffield, Jessop Wing, Royal Hallamshire Hospital, Tree Root Walk, Sheffield, S10 2SF, UK. email: w.ledger@sheffield.ac.uk (corresponding author)

Levels of the serum tumour marker CA125 are usually elevated in cases of epithelial ovarian cancer. However, an elevated CA125 level is not specific for ovarian malignancy since it may also be raised in benign conditions affecting the peritoneum, such as endometriosis.[9] Serum CA125 levels may also remain low in early ovarian cancer.

The risk of malignancy index (RMI) is a scoring system that combines sonographic findings, menopausal status/age and serum CA125 levels to give an estimate of the risk of malignancy in a woman with an adnexal mass.[10] If the total RMI score is <200 the risk of malignancy is considered to be low. If the score is >200 the chances of malignancy are raised and management should be planned with a gynaecological oncologist.

The role of cytological examination of fluid aspirated from cysts has been examined in several studies.[11] The sensitivity of cytological assessment of cells from aspirated fluid in detecting malignancy has been found to be as low at 25%, with a false positive rate of 73% and false negative rate of 12 %.[11] Cyst aspiration may itself lead to dissemination of malignant cells.

Doppler ultrasound assessment of cyst wall bloodflow does not appear to differentiate between benign and malignant ovarian cysts. This is probably because of the presence of neoangiogenesis in both malignant and functional tumours.[12]

Clinical management

Women with minimal symptoms in whom a simple cyst with no malignant features is detected by TVS and low CA125 levels (RMI <200) may be offered expectant management with a repeat scan three to six months later. Approximately 50% of cysts will resolve spontaneously.

Hormonal suppression, for example with the combined oral contraceptive, may be useful in young women who develop recurrent painful functional cysts in the ovaries. Again, there should be no ultrasound or serum biochemical features of malignancy.

Transvaginal cyst aspiration is a safe and straightforward approach to simple ovarian cysts, using equipment routinely employed for follicle aspiration in IVF treatment. Sadly, there seems to be little advantage of aspiration over regular observation, since the chances of reformation of the cyst are high if the cyst lining is left *in situ*. Aspiration was not found to be superior to regular observation in a randomised study.[13] Cyst aspiration can be considered in selected cases as a temporary solution; for example in the treatment of a simple cyst observed during ovulation induction for treatment of infertility, or in those with symptomatic cysts who are at high risk of medical complications of anaesthesia, provided that the woman is aware of the high risk of recurrence.

Modern surgical management of simple ovarian cysts in premenopausal women is commonly undertaken laparoscopically. Laparotomy may occasionally be necessary in women with a large cyst if there is suspicion of malignancy or if the patient is unfit for laparoscopy because of obesity or extensive abdominal scarring following previous surgery. Fears of finding malignancy during operative laparoscopy in young women are often exaggerated. Nezhat *et al.* found borderline ovarian cancer in only 0.4% of cases in a large series of 1011 women undergoing operative laparoscopy for an adnexal mass.[14] Compared with laparotomy, laparoscopic management of ovarian cysts carries a lower risk of postoperative adhesion formation that may compromise future fertility, decreased blood loss and patient morbidity, with shorter duration of hospital stay. The laparoscopic approach is also frequently preferred by women because of the more acceptable cosmetic results compared with laparotomy. However, in discussion prior to surgery, women should always be informed of the risks of laparoscopy and the chances of requiring a laparotomy should problems arise.[15] In a review of 350 000 laparoscopic procedures, the risk of bowel damage was calculated to be 0.4 in 1000 cases and the risk of major vessel injury to be 0.2 in 1000 cases.[16]

A number of different laparoscopic approaches to ovarian cysts have been described.[17] As the sophistication of laparoscopic surgical instrumentation has increased it has become easier and safer to undertake more complex procedures, with associated reduction in risk of cyst recurrence.

Laparoscopic cystotomy with drainage of cyst fluid is straightforward but, as for aspiration, carries a high risk of recurrence of the cyst.

Cystotomy and ablation of cyst wall has been recommended as a treatment for ovarian endometrioma. The cyst is first aspirated to dryness then opened sufficiently to admit a diathermy or laser. The cyst wall is then destroyed. A proportion of ovarian follicles may also be lost due to thermal injury. Compared with stripping

of the lining of an endometrioma, ablation carries a higher risk of recurrence but may cause less damage to primordial follicles.

Cystotomy and stripping of cyst wall is also used to treat ovarian endometrioma. The cyst is opened and after drainage of 'chocolate' material the internal cyst wall is stripped away from the underlying stroma. Drawbacks to this approach include a higher chance of bleeding from the stripped site and damage to adjacent primordial follicles with possible compromise of ovarian function. Ovarian cystotomy and stripping is also associated with a higher incidence of adhesion formation but decreased risk of recurrence compared with cystotomy and ablation. In practice, it is sometimes straightforward to strip the internal lining of an endometrioma, in which case this is probably the treatment of choice.[18] In other cases the lining seems more adherent and vascular, ablation of the tissue should then be considered.

Cystectomy is the removal of the cyst intact, without prior rupture. Cystectomy is the preferred method for treatment of dermoid cysts, in order to avoid intraperitoneal spillage of cyst content. Cystectomy may also have a place if there is a low but possible chance of malignancy in a young woman wishing to preserve her fertility, again in order to reduce chances of peritoneal seeding.

Oophorectomy may be necessary if the ovary is grossly distorted with multiple endometrioma with complete loss of normal ovarian tissue. Oophorectomy should not be undertaken without careful prior discussion with the woman, particularly if she is young or nulliparous. The discussions should be well documented in the case notes.

Laparoscopic ovarian cystectomy appears to be the treatment of choice in young women, with the stripping technique being relatively tissue sparing.[19] Muzii *et al.* found ovarian tissue in the stripped cyst wall in 36% of cases. However, this tissue did not exhibit the normal follicular pattern seen in healthy ovaries. After the surgical removal of an ovarian cyst, the resulting defect in the ovarian surface may either be closed with sutures, treated with bipolar cautery or left open to heal.[20,21] No method has been clearly shown to be superior in terms of healing and postoperative adhesion formation. It does seem advisable to remove the excised specimen from the peritoneal cavity using an endobag,[20] particularly in the case of dermoid cysts where the contents may be highly irritant and cause chemical peritonitis. Large robust watertight bags (spleen bags) are now available making it possible to remove large cysts intact, without spillage by aspiration of the cyst in the bag. Nehzat *et al.* described the incidence of chemical peritonitis following laparoscopic removal of dermoid cysts to be around 0.2%.[22] The risk of spillage of cyst contents depends on the size of the cyst, the degree of surrounding adhesions and whether previous surgery has been carried out. While a laparoscopic approach may be recommended for a young woman with a relatively small dermoid cyst (less than 8 cm), larger dermoid cysts may be more safely dealt with by laparotomy. Approaches will vary depending on the skill and experience of the surgical team.

Alternative therapies

While the advancement of science has allowed surgeons to improve and refine laparoscopic techniques, modern medicine has also begun to accept its limitations. Many people wish to avoid surgical intervention and there is increasing interest in the systematic evaluation of alternative therapies in reproductive medicine.[23] For example, Wu *et al.*[24] combined laparoscopy with Chinese herbal medicine in the treatment of endometrial ovarian cysts. They reported minimal adverse effects and maximal preservation of reproductive function. Further studies of a high quality are necessary before these approaches can be recommended, but it is possible that novel approaches to ovarian cystic disease will emerge from medical modification of traditional alternative therapies.

Cysts in infertility

Those involved in the treatment of infertility will frequently encounter ovarian cysts, endometriotic or otherwise. The exact incidence of endometriotic cysts is difficult to estimate, however, endometriosis has been described as being found in 21% of infertile women.[25]

A number of treatments for anovulation, including clomiphene citrate and gonadotrophin-induced ovarian stimulation have been linked with increased incidence of ovarian cysts following treatment. This occurs in between 15–50% of women following various forms of stimulation.[26] An association has also been suggested with induction of ovulation and subsequent development of ovarian cancer,[27] although it is not clear whether this association is casual or causal and further prospective studies are needed to examine the nature of this association.

Ovarian cysts can arise during pituitary downregulation with gonadotrophin-releasing

hormone (GnRH) agonist before the start of superovulation for *in vitro* fertilisation (IVF) treatment. The cysts commonly arise as a result of the initial 'flare' of endogenous luteinising hormone and follicle stimulating hormone that precedes pituitary suppression by the GnRH analogue. Such cysts may secrete significant amounts of oestradiol, leading to postponement of the start of stimulation, or may merely complicate ultrasound monitoring of follicle growth by their size and location. Such agonist-induced cysts may resolve spontaneously if downregulation is continued for one to two weeks longer, although cyst aspiration may be necessary. Studies have been carried out to compare expectant management with hormonal suppression in such ovarian cysts, but no clear advantages have been established.[28] It has been suggested that the presence of ovarian cysts prior to administration of GnRH agonists delays downregulation and leads to increased utilisation of gonadotrophins; however, it does not appear to impact on the pregnancy rate.[29] The other circumstance in which ovarian cyst disease may impact on reproductive function is in cases in which ovarian surgery has been previously carried out. Ovarian surgery will inevitably lead to some degree of damage to primordial follicles in adjacent tissue, and may also affect blood supply, compromising the ovarian response to stimulation. The effects of surgery on IVF outcome are still unclear, although some studies did not find significant impact of prior laparoscopic cystectomy/ablation on the numbers of oocytes or embryo quality.[30,31] Further prospective randomised trials are needed to study the effect of surgery for endometriosis on assisted reproductive techniques.

Conclusions

Ovarian cysts are common and distressing to women, particularly to those who wish to preserve future fertility or those with particular anxiety about ovarian malignancy. Where the RMI is greater than 200 the woman's management should be discussed with a gynaecological oncologist. Treatment should be individualised, depending on the findings of diagnostic tests and the patient's wishes. The outcome of laparoscopic surgery is good in skilled hands and should be the treatment of choice in the majority of cases. ■

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