

Dilemma in Management of Endometriotic Ovarian Cyst

Tahira Shahzadi* and Shazia Maqsood

Department of Obstetrics and Gynaecology, Dr. Sulaiman Al Habib Hospital, Saudi Arabia

***Corresponding author:** Tahira Shahzadi, Department of Obstetrics and Gynaecology, Dr. Sulaiman Al Habib Hospital, Khurais Road, Ar Rayan, Riyadh, Saudi Arabia



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ABSTRACT

A commonly diagnosed form of endometriosis is Endometriotic ovarian cyst or Endometriomas, once diagnosed incidentally may cause anxiety. Treatment of endometrioma can be conservative, medical, or surgical and Sclerotherapy. Aim of treatment is to control symptoms and recurrence. Surgical treatment is done if symptoms are severe to minimize damage to ovaries, recurrence, and formation of adhesions. Older age, pseudo capsule stripping and large cyst size may result in reduced ovarian reserve. If Endometrioma is found incidentally then clinical dilemma is when and how to treat. Recommendations based on previously published guidelines are available for treatment of endometriosis but without recommendations on the practical aspects of endometrioma surgery. Mostly these recommendations are based on clinical expertise. Clinical dilemma is debate between planning early treatment and surgery should not be planned if size is less than 3 cm.

Introduction

Ovarian endometrioma or chocolate cyst is ectopic endometrial tissue lining ovarian cyst [1]. Presence of endometrial glands and stroma outside the uterine cavity is known as endometriosis [2]. Endometriosis may present as peritoneal lesions, deep endometriosis and ovarian endometriomas. Due to relative ease of diagnosis endometriomas are the most diagnosed form of endometriosis. Endometriosis have been reported in 17-44% [3]. With 10-20% in women in reproductive age most commonly between 40 and 44 years and approximately 17% of women suffering from infertility [4]. This condition is prevalent among the East Asian race [5]. Endometriosis and endometriomas have the multifactorial ethology [6]. Endometriomas are mostly unilateral, commonly left-sided, they are either asymptomatic or may present with symptoms. It is not infrequent to have under diagnosis or misdiagnosis and this is quite common in adolescent women [7]. Treatment of endometrioma is a clinical dilemma that

if found in imaging then whether to treat or not and if yes then how to treat. Symptoms of a patient will guide for available options either conservative, medical, surgical or combination of both or sclerotherapy [8].

Discussion

The presence of ovarian endometrioses has been found to be associated with deep endometriosis and multifocal deep lesions [9]. Endometriomas are mostly unilateral, commonly left-sided [10]. Left sided predisposition is explained by anatomic barriers like sigmoid colon that may delay in eliminations of endometriotic tissue from left side of pelvis and promotes left sided cysts, in support this is explained by theory of retrograde menstruation [11]. The pathogenesis of endometrioma is explained as implantation of endometrial cells on ovarian surface via tubular lumen that causes persistent inflammation, bleeding, cyst formation at implantation site resulting invagination of ovarian cortex, adhesions secondary

to metaplasia which may result in progressive damage of healthy ovarian tissue [12]. Endometrioma pseudo capsule is ovarian epithelium containing oocytes and follicular structures. The reason of endometrioma-related infertility remains unclear. Possible theories may be damage to affected ovary or tubo-ovarian distortion anatomy and cellular damage resulting in follicular loss [13]. Other factors may be involved including immune factors, inflammatory factors, environmental toxins, and genetic factors [14]. Endometrioma may present with dyspareunia, dysmenorrhea, pelvic pain, bleeding, infertility, and dysuria. It is not infrequent to have under diagnosis or misdiagnosis and this is quite common in adolescent women. Ovarian endometriomas may predispose to ovarian malignancies, especially clear cell carcinoma and endometrioid adenocarcinoma.

For Endometrioma diagnosis, transvaginal ultrasonography is a very sensitive and specific. Unilocular cyst with a "ground glass" homogeneity, low levels of echogenicity, and poor vascularization, one to four compartments and no papillary structures with detectable blood flow [15], which had been adopted in the ESHRE guidelines [16] are typical ultrasound characteristics of endometriomas [17]. One useful diagnostic indicator is immobility as adherent to pelvic side wall. Diagnosis and treatment of endometrioma another useful tool is laparoscopy. A new promising biomarker is Human epididymal secretory protein E4 used in the differential diagnosis of endometriosis cyst. The combination of HE4 and CA 125 assay could discriminate ovarian endometriosis cysts from malignant ovarian tumours effectively [18]. The advantage of HE4 over CA125 is mainly in the detection of borderline ovarian tumours and early-stage epithelial ovarian and tubal cancers. After diagnosis, possible options are either expectant management or treatment depending on symptoms, age, fertility concerns, ovarian reserve and previous history of treatment with specific reference to past surgical interventions; nature of the cyst; and the fertility wishes of the woman [19]. Treatment of incidental disease in otherwise asymptomatic women is currently not recommended, as still the natural progression and development history of endometriomas is not well understood.

Treatment of endometrioma is a clinical dilemma that is found in imaging then whether to treat or not and if yes then how to treat. Symptoms of a patient will guide for available options either medical treatment progestins, oestrogen suppression or surgical or combination of both. An incidental finding of an ovarian endometrioma in young women with regular menstrual cycles and without suspicion of malignancy who wish to conceive should be encouraged for natural conception before seeking fertility treatment. While the evidence of the impact of an endometrioma on spontaneous conception is limited. Aim of surgical treatment

is removal of endometriotic tissue, to have sufficient sample for histopathology and to preserve maximum ovarian tissue in cases where fertility is desired and to avoid risk of menopause. With surgical treatment risk is unintentional removal of ovarian follicles which is later shown by reduced levels or antral follicle count on ultrasound or reduction in serum anti-Müllerian hormone (AMH) [20]. To reduce recurrence after surgery medical therapy may be used. Recurrence rate of endometriomas after surgical treatment are 30-40% [21]. So to delay recurrence of ovarian endometrioma in 2014, European Society of Human Reproduction and Embryology (ESHRE) recommended for ovarian cystectomy instead of drainage and coagulation of endometriosis in cases of surgical treatment, since ovarian cystectomy can reduce endometriosis-associated pain and recurrence rate effectively [22]. Fertility is affected by presence of endometrioma [23], while after IVF overall pregnancy rates are unaffected [24]. Any surgical intervention to remove endometrioma may be associated with decrease ovarian reserve and possible recurrence [25]. At present, no consensus has been reached on the timing of surgery in young women; whether surgery should be delayed in infertile women planning IVF is still debated [26].

Possible complications with non-surgical approach are:

- 1) Difficulties during oocyte retrieval
- 2) Progression of endometriosis
- 3) Missing an occult early-stage malignancy
- 4) Risk of development of a pelvic abscess or rupture of the endometrioma
- 5) Follicular fluid contamination with endometrioma content

Most common mode of treatment is surgical which is laparoscopic cystectomy, benefit is reduced pain symptoms and recurrence. Excision of endometrioma in comparison with drainage of endometrioma with or without ablation of pseudo capsule is associated with better outcome and higher pregnancy rates [27]. However, ovarian cystectomy can lead to decreased ovarian reserve or due to excessive coagulation can be reason [28]. So to attain follicular development, increased amounts of gonadotropins are needed [29]. Laparoscopic cyst fenestration and ablation of the cyst capsule is another alternative method which improve pelvic pain and result in high patient satisfaction but high recurrence. That's why opinion shifted towards more conservative approach. In 2013, The European Society of Human Reproduction and Embryology guideline suggested that surgery should be considered only if size of endometrioma is >3 cm, to improve access to follicles or pain [30]. Size play an important role in decrease ovarian reserve before

surgery and difficulty for complete removal in case of superficial destruction as well as damage to ovary in case of surgical excision. Post-operative medical treatment markedly reduces the recurrence rate of endometrioma [31]. Therefore, long-term medical treatment to prevent recurrence is routinely recommended [32]. Post-operative medical treatments including oral contraceptives GnRH agonists, and progesterone commonly used to suppress possible residual lesions due to the oestrogen-reducing effects [33]. However, each of these treatments has reported adverse effects. Post operative medication needs, or efficacy was not studied in women aged 40 year or more.

Medical treatment used for treatment of endometrioma include Oral contraceptive pills, progestins, gonadotropin-releasing hormone agonists [34] as well as aromatase inhibitors are helpful to reduce size, symptoms, and post-surgery recurrence [35]. However, problem is reappearance of symptoms after stopping medical treatment [36]. To reduce recurrence after aspiration another promising method is sclerotherapy [37]. It involves injecting into cyst cavity a sclerosing agent which can be either removed by washing or left within cyst. It is thought that it will work by causing inflammation and fibrosis causing destruction of epithelial lining of cyst and at the end will cause obliteration of cyst [38]. It has been shown that sclerotherapy is cost effective method for endometrioma but not widely used [39]. Pain improved in 68-96% independent from duration of ethanol inside endometriotic cyst. Compared to laparoscopic cystectomy, with sclerotherapy number of oocytes retrieved during IVF treatments was higher but no difference in pregnancy rates after sclerotherapy and untreated cases. Sclerotherapy was found to be safe with possible complication of transient abdominal pain. After sclerotherapy difference in the recurrence rate in studies can be due to variation in selection criteria (cyst size and number of cysts), technique used (sclerosing agent, concentration, installed volume, and retention time), duration of ethanol inside the endometrioma and the follow-up time. Risk of unexpected malignancy with typical features of endometrioma has been found in 1% in patients [40]. Other factors will influence the decision in an asymptomatic patient like the rate of growth, the age of patients, personal and family history of breast and ovarian malignancies [41].

Other alternative is phytotherapeutic options obtained from plants or herbal preparations some of them work by influencing apoptosis, epigenetic factors, angiogenetic processes, cell survival, oxidative stress and oestrogen modulation [42]. During course of fertility treatment, endometrioma often present a clinical dilemma due to uncertainty regarding decision of either to operate or manage conservatively while balancing possible risk of surgery on ovarian reserve. So far guidance available from either small and/

or retrospective controlled studies. Surgery does not improve the results of IVF treatment [43], but a sequential use of surgery and IVF in those that do not conceive spontaneously probably results in slightly higher cumulative pregnancy rates [44]. There may be spilling of chocolate fluid of endometrioma in peritoneal cavity in women undergoing IVF. This fluid may not induce endometriosis but is adhesiogenic [45]. Considering the risk of ovarian damage during surgery and the excellent results of IVF, actual guidelines [46] therefore have concluded that if IVF indicated then should not undergo surgery if size of endometrioma is < than 3-4cm. Surgical treatment of endometriomas prior to IVF is widely practiced, [47] although debatable on its effect and need. To date, there has been no evidence that surgical treatment improves reproductive outcome of women treated with the use of ART, no difference in the clinical pregnancy rate and the number of oocytes retrieved from women who had surgical treatment compared with those with intact endometrioma. Cancellation rate and number of retrieved oocytes were comparable. After surgical treatment of endometrioma there is lower antral follicle count and higher doses of gonadotrophins required for ovarian stimulation.

Women of advanced reproductive age, asymptomatic, those with reduced ovarian reserve, bilateral endometriomas or a history of prior ovarian surgery may benefit from proceeding directly with IVF, as Ovarian reserve may be compromised further after surgery. In case of symptomatic women, large endometrioma, intact ovarian reserve, suspicious features of cyst on radiological investigations or with clinical features surgery may be considered. There is risk of Infertility and Premature Ovarian failure after treatment of endometrioma in very young women. Pathophysiology and manifestation of endometriomas in adolescents may be different than adult women [48]. The diagnosis of endometriosis in adolescents is often delayed due to several factors. Regarding early diagnosis followed by surgical removal of endometriomas in the adolescent population, currently no original studies are present as fertility is a major concern as well as future recurrence. New concept is early treatment instead of postponing surgery to prevent adhesions, ovarian damage and recurrence. Considering that the endometriosis in cystic ovarian endometriosis is only superficial, a superficial destruction by electro surgery, CO₂ laser or alcohol should be sufficient before the development of more lesions and size of endometrioma is getting more or symptoms becoming more severe or concern of fertility arises. With these concepts, the use of THL in women with infertility should be reconsidered. Transvaginal hydro-laparoscopy (THL) [49,50] offers a minimal invasive procedure for early diagnosis and treatment of small endometrioma up to a diameter of 20 mm not seldom these small endometriotic cyst are missed at routine vaginal ultrasound examination in approximately 50% of the cases.

It is always surprising after opening of such small cysts to see the pronounced presence of inflammation and neo-angiogenesis, a signature for the aggressiveness of the disease in these early stages. Due to concern of ovarian reserve early stages treatment using ablative technique with a bipolar 5Fr probe causes a minimal trauma and a lower risk for recurrences [51]. In absence of suspicious radiological, clinical features chances of missing an occult malignancy in an endometrioma is extremely low and surgery is not advised. But in later life risk of developing ovarian cancer can be a concern with the lifetime probability increasing from 1% to 2% in the presence of an endometrioma [52].

Conclusion

Need clear guidelines for when to treat, when to stay conservative and if need treatment then what mode of treatment out of available options should be used keeping in view risk of recurrence, reduced ovarian reserve and fertility concerns. All available options have their own benefits and risks. So in current circumstances we need to decide either to stay conservative or treatment depending on symptoms or need for intervention.

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Tahira Shahzadi. Biomed J Sci & Tech Res



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