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Cystic ovarian endometriosis and infertility: arguments for an early but less aggressive surgical treatment

Abstract

Cystic ovarian endometriosis is a cause of pain and infertility. For infertility, surgical treatment has been suggested for cysts larger than 3 or 4cm in diameter only. Surgical treatment is moreover postponed as long as possible or until pain becomes too severe in order to avoid ovarian damage and a decreased ovarian reserve and to avoid recurrences and repeat surgery and adhesion formation.

Our recent understanding of the pathophysiology of endometriosis, of its initiation and its growth, probably permits a more effective prevention of recurrences. In addition, adhesion free surgery has become a reality. We therefore suggest performing surgery for cystic ovarian endometriosis early in life when cysts are small followed by an active prevention of recurrences. When cysts are small superficial destruction instead of excision seems logical. Also, THL and under-water coagulation should be considered

In conclusion, without discussing the management of larger symptomatic cystic endometriosis, we suggest that early surgical treatment of small cyst is the way to go.

Keywords: endometriosis, cystic ovarian, spermatozoa, ovulation, fertility, peritoneal fluid

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Introduction: endometriosis and infertility

Endometriosis and especially cystic ovarian endometriosis are considered a major cause of female infertility. Cystic ovarian endometriosis is moreover generally associated with ovarian and tubal adhesions causing mechanical infertility.[1] Cystic ovarian endometriosis is also associated with superficial pelvic endometriosis and with deep endometriosis.[1,2] It remains debated why endometriosis by itself decreases fertility.[3] The hypotheses vary from an effect on ovarian function and ovulation,[4–6] toxic factors for spermatozoa and oocytes in peritoneal fluid, an altered tubal transport and implantation problems because of immunologic changes, to endometrial changes in endometriosis[7] and a different endometrial microbiome.[8]

The pathophysiology of endometriosis has been updated recently. The Sampson hypothesis of retrograde menstruation and implantation[9,10] cannot explain all clinical presentations of endometriosis and this theory is not compatible with observations as a different clonality of all endometriosis lesions,[11] and endometriosis in the absence of a uterus. The Genetic-epigenetic (G-E) theory[7] is compatible with all observations today. The basic hypothesis is that a specific set of G-E alterations of a body cell, of endometrium, of a stem cell or of a bone marrow cell will induce cellular alterations which make them look microscopically as endometrium, but with a different behaviour as known for the different presentations of endometriosis. These G-E changes are favourised by[7] a predisposition , which are the G-E incidents inherited at birth, by radiation and environmental factors as hormone disruptors, by the oxidative stress of retrograde menstruation and by the endometrial, upper genital tract and peritoneal microbiome.[8] Following the G-E incident the endometriosis lesions will develop according to the type of the incidents into typical, cystic or deep lesions. This development and growth moreover will vary with the woman-specific endocrine and microbiome environment of the peritoneal cavity and with the immunology.[12] Growth is variable but, in most women, self-limiting after a period of growth of 4to 6 years before becoming symptomatic(PK et al submitted). An important consequence of understanding the pathophysiology of endometriosis is that prevention of recurrences after surgery and prevention of growth become conceivable by reducing the oxidative stress after surgery and by preventing ascending infection eventually by changing the peritoneal microbiome by diet and exercise.[8]

This recent understanding of the pathophysiology of endometriosis changes our views on the endometriosis associated infertility and its treatment. First endometriosis becomes an heterogeneous disease.[13] Individual lesions even in the same woman, vary from no to high aromatase activity, from normal progesterone responsiveness to progesterone resistance and thus with a variable response to treatment.[14] We can postulate that endometriosis is not a direct cause of infertility, but that women with a predisposition to develop endometriosis have a decreased fertility, albeit because of the many associated changes in the endometrium,[7] because of a different endometrial microbiota[8] or because of a different immunity.[12] The infertility thus becomes a consequence of the 'endometriotic' constitution rather than a consequence of the endometriosis lesion. This is consistent with the observation that the results of IVF treatment of women with a small endometrioma are similar with or without previous surgery[15] and it explains that the surgical destruction of superficial and/or typical lesions does not clearly improve fertility.[16]

Cystic ovarian endometriosis

In addition of being endometriosis, cystic ovarian endometriosis strongly affects spontaneous fertility because of the associated adhesions[1] and/or by affecting ovulatory function eventually

preventing ovulation.[6] Following surgical destruction or removal of the endometriotic cyst, some 60% of women will conceive spontaneously within 1 year.[17] Since IVF results in women with and without a small cystic ovarian endometrioma do not differ,[18] this suggests that the endometrioma does not affect quality of oocytes and implantation but rather causes mechanical infertility or ovulation impairment.

Surgery for cystic ovarian endometriosis is associated with a variable reduction in ovarian reserve. It remains debated to what extend the cystic ovarian endometriosis decrease oocyte reserve by toxicity or compression and to what extend surgery itself is traumatic;[19–22] this is the unsolved question of the singer versus the song.[23] Whatever the mechanism of the reduction in oocyte reserve size of the cystic ovarian endometriosis matters.[24] Size matters for the decrease in ovarian reserve before surgery, for the difficulty of being complete when superficial destruction of the cyst wall and for the damage to the ovary after surgical excision.

The surgical treatment of cystic ovarian endometriosis remains debated. Superficial destruction by vaporisation or coagulation is less traumatic for the ovary whereas cyst wall excision is associated with a lower recurrence rate.[25,26] However, considering that the endometriosis covering the cyst wall is only superficial with a depth of invasion of only 1 to 2mm.[27–29] the cyst wall seems mainly a fibrotic reaction to the endometriosis and cyst wall removal seems overtreatment. The higher recurrence rate following superficial destruction thus probably is the consequence of an incomplete destruction in some areas.

Management of cystic ovarian endometriosis in infertility

The best approach to cystic ovarian endometriosis and infertility remains unclear. Surgery does not improve the results of IVF treatment,[24] but a sequential use of surgery, and IVF in those that do not conceive spontaneously probably results in slightly higher cumulative pregnancy rates.[30]

IVF in women with a cystic ovarian endometriosis results in spilling of chocolate fluid in the peritoneal cavity. Fortunately, this chocolate fluid does not induce endometriosis as demonstrated in nude mice.[31] However, spilling of this chocolate fluid is expected to increase the oxidative stress while being adhesiogenic.

Considering the risk of ovarian damage during surgery and the excellent results of IVF, actual guidelines[32] therefore have concluded on clinical but arbitrary grounds that small cystic ovarian endometriosis, defined as less than 3-4cm, should not undergo surgery, especially if IVF is indicated.

Adhesion free surgery

Postoperative adhesions remain a major cause of infertility. Although adhesion formation has been considered an inevitable side -effect of surgery, recent understanding begins to permit adhesion free surgery.[33] During surgery, care should be taken not to damage the mesothelial cells by cooling the peritoneal cavity to 30˚C, by adding some 10% of N_2O to the CO_2 pneumoperitoneum,[34] by keeping the insufflation pressure to minimum permitting surgery, by preventing desiccation and by gentle tissue handling together with surgery of a short duration. At the end of surgery, the remaining fibrin and blood should be kept to a minimum, dexamethasone should be administered together with a barrier.

Also underwater surgery during THL is associated with a minimal amount of postoperative adhesions as demonstrated for ovarian drilling.[35]

New approaches to cystic ovarian endometriosis

These new concepts of the pathophysiology of endometriosis and of its growth permitting postoperative prevention of recurrences, together with the new concepts permitting adhesion free surgery, should be considered to change our attitude towards cystic ovarian endometriosis.

Instead of postponing surgery, in order to prevent recurrences with eventual repeat surgery and ovarian damage and adhesions, we might consider early surgical destruction of small cystic ovarian endometriosis. Considering that the endometriosis in cystic ovarian endometriosis is only superficial, a superficial destruction by electrosurgery, CO_2 laser or alcohol should be sufficient.

Therefore instead of letting the cystic ovarian endometriosis grow, while permitting women to develop more lesions, and postponing surgery until pain becomes too severe or until fertility becomes an issue, we suggest early treatment of cystic endometriosis with minimal superficial destruction of the endometriosis together with the destruction of eventual other initiating lesions (Figure 1). Key is this new concept is prevention of recurrences by reducing the oxidative stress of retrograde menstruation and adhesion free surgery. With these concepts, the use of THL in women with infertility should be reconsidered.

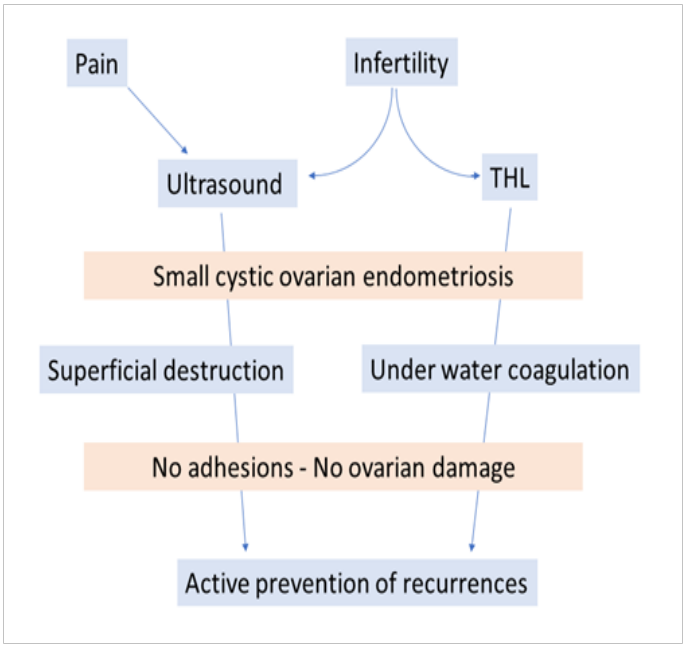

Figure 1 Treatment of cystic ovarian endometriosis. When small cysts are detected by ultrasound, or during laparoscopy of THL, early superficial treatment without adhesion formation, followed by active prevention of endometriosis will result in minimal ovarian damage and maximally preserved fertility.

Transvaginal hydro-laparoscopy (THL)[36–38] offers a minimal invasive procedure for early diagnosis and treatment of small

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endometrioma up to a diameter of 20mm (Figure 2). 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 aggressivity of the disease in these early stages. Dealing with a growing concern of impaired ovarian reserve after surgery, treatment in these early stages and in absence of markers for progressivity, using an ablative technique with a bipolar 5Fr probe causes a minimal trauma and a lower risk for recurrences.[39,40]

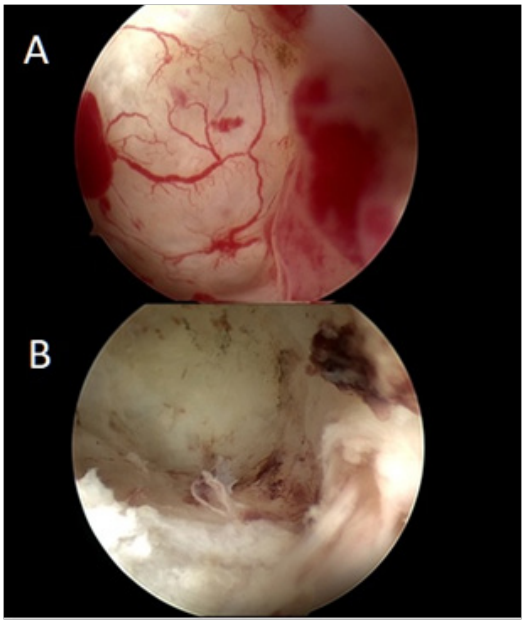

Figure 2 A. Insight view of small endometriotic cyst at THL showing neo-angiogenesis, inflammation and endometrial like tissue. B. View after bipolar coagulation using a 5Fr. coagulation probe causing minimal tissue damage.

Discussion

Considering new possibilities of prevention of recurrences and of growth together with adhesion free surgery, we suggest early and superficial treatment when cysts are still small. The treatment and the technique of surgery of the larger cystic ovarian endometrioma are beyond the scope of this article. In order to keep the message clear, we also will not discuss the management of adolescent endometriosis with pain and/or small cystic ovarian endometriosis and the management of infertility or the role of THL in the work-up.

That the endometriotic constitution increases the risk of endometriosis and the risk of infertility instead of infertility being a consequence of endometriosis can be viewed as a classic example of correlation analysis. During the eighties a strong correlation was observed between dog bites and the selling of roses; this seemed strange until we realised that having a dog and buying roses increased with the standard of living. However strong a correlation might be, it remains difficult to establish causality between the 2 factors and in addition, both can be the consequence of a common factor. For endometriosis and infertility, it becomes logical that surgery of endometriosis does not increase fertility unless during other factors as adhesions and dyspareunia were resolved. It also becomes logical that women with and without endometriosis have a different fertility whether spontaneous of during IVF treatment. With a common causal factors, also all other associated factors will be mutually correlated as recently observed for BCL6.[41]

It is logical that the size of a cystic ovarian endometriosis is important for the oocyte reserve albeit by compression of by toxic factors, and that excision of larger cysts will cause more ovarian damage since the remaining capsule will be less vascularised and thinner, that superficial destruction risks to be less complete and that surgery will take longer. Similar to the volume of a cyst which increases with the third power of the diameter, common sense expects that the relationship between size and these risks will be exponential. Unfortunately, the available data today are limited to educated guesses making classes of less than 3 or 4cm. A simple mathematical analysis indeed would permit to ascertain until which size the relationship with infertility is flat and from which size onwards exponential.

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Conflicts of interest

The author and co-authors have no conflicts of interest relevant to this article.

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