

Is there an association between septate uterus and endometriosis?

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BACKGROUND: The question of whether Müllerian anomalies are significantly more often combined with endometriosis is a controversially discussed problem. Some publications described this association in patients with obstructive but not non-obstructive Müllerian anomalies or controls without Müllerian anomalies. The aim of this study was to evaluate the incidence of endometriosis in patients with a septate uterus as a non-obstructive form of Müllerian anomalies. **METHODS:** In a retrospective study, we evaluated 120 patients (29.4 ± 4.7 years; mean \pm SD) with a septate uterus. The control group consisted of 486 consecutive infertile patients (30.8 ± 6.3 years) with a normal hysteroscopy and laparoscopy. **RESULTS:** The incidence of dysmenorrhoea was comparable in both groups, but the incidence of endometriosis was significantly higher in patients with a septate uterus (25.8 versus 15.2%, $P = 0.006$). **CONCLUSION:** Our results suggest a higher incidence of endometriosis in patients with a septate uterus. If it can be confirmed by others, the initial finding of a septate uterus in infertile patients should be followed by a combined hysteroscopy and laparoscopy.

Key words: endometriosis/infertility/Müllerian anomaly/septate uterus/uterine malformation

Introduction

There are different explanations regarding the pathogenesis of endometriosis. These include the theories of retrograde menstruation/transplantation, coelomic metaplasia, altered cellular immunity, metastasis, a genetic basis, an environmental basis and a multifactorial mode of inheritance between specific genes and the environment. Furthermore, it was hypothesized that endometriosis is an underdiagnosed disorder with substantial associated morbidity (Giudice and Kao, 2004). One could assume that especially obstructive anomalies in the lower genital tract lead to an intensive retrograde menstruation and cause endometriosis. Data by Olive and Henderson (1987) support the correlation of retrograde menstruation and likelihood of endometriosis. Ugur *et al.* (1995) found a significantly higher prevalence of endometriosis in patients with Müllerian anomalies in comparison with women without such anomalies (controls), but no difference between non-obstructive anomalies and controls. This was confirmed by Fedele *et al.* (1992) comparing the frequency of endometriosis between infertile women with and without non-obstructive Müllerian anomalies.

Others could not repeat these observations consistently. They described obstructive anomalies without endometriosis and non-obstructive anomalies with severe endometriosis (Acien, 1986). It has also been shown that there is a variety of anomalies

(Acien *et al.*, 1992., 2004) which cannot be included in the actual accepted classification (American Fertility Society, 1988).

To clarify this discussion further, the aim of our study was to evaluate the incidence of endometriosis in patients with a septate uterus as a non-obstructive Müllerian anomaly.

Materials and methods

Patients

In a retrospective study, we evaluated all 120 consecutive patients (29.4 ± 4.7 years; mean \pm SD) with a septate uterus according to class V (American Fertility Society, 1988) who were seen by the authors from January 1993 to March 2005. Transvaginal hysteroscopy (two-dimensional) was performed in all patients before operation and a septate uterus was assumed in 68 out of 120 (56.7%). Hysteroscopy and laparoscopy were performed in all 120 patients to exclude tubal factor in patients with primary or secondary infertility and to exclude uterine anomalies in patients with ≥ 2 abortions in the past. All patients had a plane uterine fundus. The septum was complete in 24 out of 120 (20.0%) and partial in 96 out of 120 (80.0%) of the patients. The median septum length was 3.0 ± 1.4 cm (range 2–7.5) and was sonographically measured pre-operatively if possible or estimated intra-operatively. No patient had a vaginal septum. Other causes of infertility were male subfertility (eight out of 120; 6.7%), anovulation (eight out of 120; 6.7%) and tubal factor or myoma (24 out of 120; 20.0%).

After confirmation of a septate uterus, the hysteroscopic septum dissection was performed. Endometriosis was confirmed histologically in all patients. The control group consisted of a random sample of all 486 consecutive infertile patients (30.8 ± 6.3 years) with a normal hysteroscopy and laparoscopy without any Müllerian anomaly who were seen in the time period from January 2003 to March 2005 (Table I).

Statistical analysis

Statistical analysis was carried out using χ^2 test. $P < 0.05$ was considered statistically significant.

Results

The study and control group were comparable regarding age and incidence of dysmenorrhoea. We found a significantly higher incidence of endometriosis in patients with a septate uterus in comparison with the controls (25.8 versus 15.2%, $P = 0.006$). Grade I and II according to the rAFS score (American Society of Reproductive Medicine, 1997) were combined, because it was not possible to distinguish between these two conditions after retrospective evaluation of the operation reports in several patients. The distribution of the degrees of endometriosis was comparable (Table I).

Discussion

The frequency of uterine anomalies in fertile patients is 3.8% and increases to 6.3% in the infertile population. Septate and arcuate uteri represent ~75% of these malformations (Pellicer, 1997). March (1990) reported uterine anomalies in 0.1–2% of all women, in 4% of infertile patients and up to 15% in women with recurrent abortions. Acien (1997) speculated that the true incidence is not known and summarized studies dealing with the incidence in different subgroups of patients. In an earlier study, the same authors showed genital malformations in 4% of their patients with endometriosis. Of patients with malformations, 11.2% had endometriosis independently of the kind of genital anomaly (Acien *et al.*, 1992).

The septate uterus *per se* does not reduce the probability of conception, but septum dissection improves pregnancy outcome (Heinonen and Pystynen, 1983; Grimbizis *et al.*, 2001). Therefore, some authors recommended operation to reduce the risk of abortions in future pregnancies even in nulliparous

women (Mencaglia and Tantini, 1995; Pabuccu *et al.*, 1995; Nawroth *et al.*, 2001), but others disagree with this strategy (Hassiakos and Zourlas, 1990; Corson, 1992; Acien, 1996).

It is well known that obstructive Müllerian anomalies are significantly more often associated with endometriosis, a disease with an adverse effect on fertility (Giudice and Kao, 2004). The underlying pathophysiological mechanism could be the increased risk of retrograde menstruation. Some studies confirmed that the association with endometriosis is present in obstructive Müllerian anomalies but not in non-obstructive malformations (Fedele *et al.*, 1992; Ugur *et al.*, 1995).

In our present series of 120 patients, we describe a significantly higher incidence of endometriosis in patients with a septate uterus in comparison with controls without Müllerian anomaly. We think that uterine septum dissection cannot prevent endometriosis, since a uterine septum and endometriosis are two different things. However, the high coincidence shown in our study may promote the decision to perform an earlier hysteroscopy/laparoscopy to evaluate the presence and extension of endometriosis and to dissect the septum. This strategy would lead to an increased chance of pregnancy in infertile patients by ablative therapy of even minimal or mild endometriosis (Marcoux *et al.*, 1997) and to a lower abortion rate by the dissection of the septum. This is a matter for further debate.

If this association can be confirmed in further studies, additional chronic pelvic pain could support the decision to operate. Carter (1994) found endometriosis in 80% (113 out of 140) of patients with chronic pelvic pain. Consideration of endometriosis and/or a reproductive tract abnormality in the adolescent with persistent pelvic pain was recommended (Sanfilippo *et al.*, 1986). However, the incidence of dysmenorrhoea in our patients with a septate uterus was not significantly different compared with the controls. There are actual available data confirming that ablative therapy of endometriosis is likely to be a beneficial treatment for pelvic pain associated with minimal to moderate endometriosis (Jacobson *et al.*, 2001). However, more studies are necessary to confirm this preliminary conclusion.

Magnetic resonance imaging (MRI) has also been proposed as a means of detecting endometriotic lesions, but its sensitivity depends on the size, location and morphology of the implants. Laparoscopy is the most efficient modality for the detection of peritoneal implants (Philbois *et al.*, 2004).

Table I. Patient and control group characteristics and results of the hysteroscopy/laparoscopy

	Septate uterus ($n = 120$)	Controls ($n = 486$)	P-value
Age (years)	29.4 ± 4.7^a	30.8 ± 6.3	NS
Dysmenorrhoea (%)	25 (20.8)	105 (21.6)	NS
Primary infertility (%)	51 (42.5)	252 (51.9)	
Secondary infertility (%)	36 (57.5)	234 (48.1)	
Repeated miscarriage (≥ 2) (% of patients with secondary infertility)	33 (91.7)	0	
Endometriosis (%)	31 (25.8)	74 (15.2)	0.006
rAFS I/II (%)	31 (100)	71 (95.9)	
rAFS III (%)	0	3 (4.1)	
rAFS IV (%)	0	0	

^aValues are mean \pm SD.

NS = not significant.

A possible higher coincidence of septate uterus with endometriosis cannot be explained by retrograde menstruation due to obstruction. Uterine dysperistalsis was suggested to be the mechanical cause of endometriosis rather than retrograde menstruation (Leyendecker *et al.*, 1996, 2004). One could imagine that uterine anomalies irrespective of their obstructive or non-obstructive character lead to a disturbed peristalsis as a risk factor of endometriosis. Nevertheless, the described studies revealed conflicting results regarding association of uterine anomalies and endometriosis. Therefore, all trials for an explanation are speculative at the moment.

In conclusion, our results suggest a higher incidence of endometriosis in patients with a septate uterus. Further studies are necessary to confirm our results.

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