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Antimullerian Hormone Level and Endometrioma Ablation Using Plasma Energy

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ABSTRACT

Objective: To investigate the impact of ovarian endometrioma vaporization using plasma energy on antimullerian hormone (AMH) level.

Method: We report a prospective, noncomparative series (NCT01596985). Twenty-two patients with unilateral ovarian endometriomas ≥30 mm, with no surgical antecedent and no ongoing pregnancy, underwent vaporization of ovarian endometriomas using plasma energy during the period of November 29, 2010 to November 28, 2012. We assessed AMH levels before surgery, 3 months postoperatively, and at the end of follow-up.

Results: The mean length of postoperative follow-up was 18.2 ± 8 months. AMH level significantly varied through the 3 assessments performed in the study, as the mean values $\pm$ SD were 3.9 ± 2.6 ng/mL before the surgery, 2.3 ± 1.1 ng/mL at 3 months, and 3.1 ± 2.2 ng/mL at the end of the follow-up ($P = .001$). There was a significant increase from 3 months postoperatively to the end of follow-up (median change 0.7 ng/mL, $P = .01$). Seventy-one percent of patients had an AMH level >2 ng/mL at the end of the follow-up versus 76% before the surgery ($P = 1$). During the postoperative follow-up, 11 patients tried to conceive, of whom 8 (73%) became pregnant.

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Conclusions: The ablation of unilateral endometriomas is followed in a majority of cases by a significant decrease in AMH level 3 months after surgery. In subsequent months, this level progressively increases, raising questions about the real factors that impact postoperative ovarian AMH production.

Key Words: Ablation, Antimullerian hormone, Endometrioma, Plasma energy, PlasmaJet, Vaporization.

INTRODUCTION

Surgical management of ovarian endometriomas is mainly performed by 2 procedures: cystectomy leading to the excision of the cyst wall, and ablation, which aims to destroy the inner surface of the cyst wall in situ, without removing it. Increasing evidence suggests that endometrioma cystectomy negatively affects the ovarian reserve, as revealed by decreased antimullerian hormone (AMH) levels at various points in time after surgery.[1–11] As part of our search for an alternative procedure to cystectomy able to better preserve the ovarian parenchyma underlying the cyst, we evaluated a new ablation technique using PlasmaJet (Plasma Surgical, Inc, Roswell, Georgia) similar to that of the CO_2 laser.[12] Our evaluation began by an assessment of the histological effects of the procedure on the ovarian parenchyma,[13] followed by measurement of the ultrasonographic parameters of the operated ovary.[14] We pursued our clinical evaluation with a retrospective, comparative study that suggested PlasmaJet ablation may spare the ovary to a greater extent than cystectomy does,[15] and with a retrospective analysis of recurrences and pregnancy rates, which were both found to be very satisfactory.[16] Despite these encouraging preliminary data, we are aware that further studies are required before advocating the routine use of PlasmaJet vaporization for the management of ovarian endometriomas in women with pregnancy intention.

The aim of the present prospective study was to investigate the impact of endometrioma vaporization on the ovarian reserve, using consecutive assessment of the AMH level before and after surgery.

MATERIALS AND METHODS

The study protocol was written in 2010. The aim was to compare women managed by PlasmaJet ablation to those managed with cystectomy, with surgery performed uniquely by surgeons with proven experience in endometriosis (NCT01596985). At this time as the first author (H.R.) was the only surgeon experienced in PlasmaJet ablation, the study was designed as a multicentric study with patients managed by ablation at Rouen University Hospital and by cystectomy at Clermont-Ferrand University Hospital. The sample size was estimated at 25 patients for each arm. The inclusion criteria, which allowed unilateral cysts only with no ovarian surgery antecedents, proved too limiting in Clermont-Ferrand, where most patients are second or third referrals, and resulted in numbers that were too disproportionate for valid comparison (25 ablations vs 4 cystectomies). Therefore, the comparative design was abandoned, and the study is presented as a prospective, monocentric series of 25 women managed by ablation using plasma energy.

Women included in the study were managed for unilateral ovarian endometriomas using plasma energy from November 29, 2010 to November 28, 2012. Inclusion criteria were the following: age between 18 and 45 years, no ovarian surgery antecedents, no ongoing pregnancy, surgical treatment required on the basis of pain or infertility, preoperative magnetic resonance imaging revealing a unilateral endometrioma ≥30 mm, and patient informed consent. Exclusion criteria concerned unexpected ovarian endometrioma or bilateral endometrioma found intraoperatively. All patients wished to conserve the possibility to conceive, although the desire for pregnancy was not necessarily immediate.

The main outcome was measured by variation in AMH level (3 months postoperatively vs preoperatively). Secondary outcomes were intraoperative incidents, postoperative complication, and pain assessed 3 months after surgery. The study received institutional review board approval in September 2010. Later research suggested that assessment of AMH level 3 months after surgery might be too early and that after 3 months these levels may improve or decrease over time.[2,17] Consequently, following institutional review board approval for a study amendment in March 2013, AMH values were also assessed at >6 months postoperatively during the period April to August 2013.

Patients were seen preoperatively by the surgeon (H.R.) who checked inclusion and exclusion criteria and presented study information and objectives. Patients who gave informed consent underwent an AMH test the day before surgery, along with a beta human chorionic gonadotropin test to rule out ongoing pregnancy. Preoperative hormonal treatment (gonadotropin-releasing hormone agonists [GnRHa] and add-back therapy, progestins, or continuous contraceptive pill intake) was proposed in all patients, to prevent menstruation immediately before and after surgery. GnRHa were systematically proposed in patients with associated deep endometriotic lesions.

Surgery was performed laparoscopically beginning with an exhaustive examination of all intraabdominal and subperitoneal endometriosis lesions. Data from patients where unexpected endometriotic lesions were found on a supposed healthy contralateral ovary were not included in the analysis. The use of plasma energy in ovarian endometrioma ablation has been previously described (**Figure 1**).[13–16] The origin of cyst invagination is identified after lysis of the adhesions between the ovary and the adjacent broad ligament, leading to the characteristic "chocolate fluid" evacuating from the cyst. In the few cases where major ovarian adhesions are not found, the invagination site is located on the antemesial part of the ovary and the cyst is directly opened. Once the cyst is open, the surgeon attempts to turn it completely inside out via the original invagination site of diameter averaging 1 to 2 cm. Ablation of the inner surface of the cyst is performed using plasma energy in coagulation mode set at 10 to 40, at a distance averaging 5 mm from the tip of the hand piece. Plasma is applied for 1 to 2 seconds on each site. Care is taken to treat all areas and to ablate the edges of the invagination site and the corresponding peritoneal implants on the adjacent broad ligament. When cyst reversion is not fea-
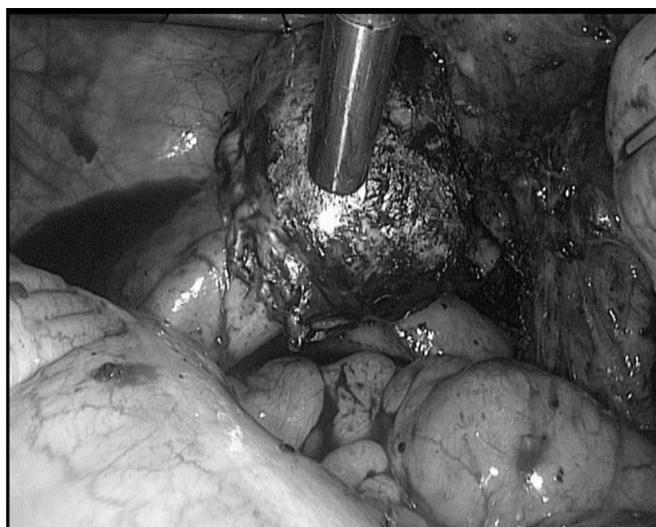

Figure 1. Ovarian endometrioma ablation using PlasmaJet.

Table 1.
Main Characteristics of Patient and Intraoperative Findings

	N = 22 (%)	Mean ± SD
Patient characteristics		
Age, yrs		30.6 ± 4.8
Surgical antecedents	5 (23)	
Open surgery	0	
Laparoscopy	5 (23)	
Surgical antecedents related to endometriosis	4 (18)	
Obstetrical antecedents	9 (41)	
Deliveries	4 (18)	
1 child	3 (14)	
2 children	1 (5)	
Preoperative infertility care	9 (41)	
Infertility assessment without performing ART	5 (23)	
Stimulation	2 (9)	
Insemination	2 (9)	
Dysmenorrhea	22 (100)	
VAS of dysmenorrhea		6.9 ± 1.9
Sexual intercourse during previous 12 mo	17 (77)	
Deep dyspareunia	11 (65)	
VAS of dyspareunia		4.5 ± 3.3
Intermenstrual pelvic pain	12 (55)	
VAS of intermenstrual pelvic pain		6 ± 1.7
Preoperative AMH level		3.9 ± 2.6
<1 ng/mL	1 (5)	
1–2 ng/mL	4 (18)	
2–6 ng/mL	14 (62)	
> 6 ng/mL	3 (14)	
Intraoperative findings		
Ovary involved		
Right	9 (41)	
Left	13 (59)	
Preoperative medical treatment	20 (91)	
GnRH analogs	16 (80)	
Oral contraceptive pill in continuous intake	1 (5)	
Progestin in continuous intake	3 (14)	

Table 1 continued in next column.

Table 1. (continued)
Main Characteristics of Patient and Intraoperative Findings

	N = 22 (%)	Mean ± SD
Duration of preoperative medical treatment (mo)		2 ± 0.7
rAFS score		42 ± 18
Associated endometriotic lesions		
Douglas pouch obliteration	12 (55)	
Peritoneal implants	20 (91)	
Diaphragmatic implants	5 (23)	
Bladder nodule	1 (5)	
Small bowel lesions	1 (5)	
Appendix lesions	1 (5)	
Sigmoid colon lesions	4 (18)	
Rectal nodules	6 (27)	
Deep nodules without digestive or urinary involvement	16 (73)	
Vaginal nodule	3 (14)	
Adhesiolysis	19 (86)	
Endometrioma diameter, mm		43 ± 14
30–39 mm	10 (45)	
40–49 mm	6 (27)	
50–59 mm	2 (9)	
60–85 mm	4 (18)	
Exposition of the cyst		
Inside out inversion of the inner cyst wall	18 (59)	
No inversion	9 (41)	
Surgeon assessment of the extent of vaporization		
Complete	21 (95)	
Incomplete	1 (5)	
Bipolar coagulation required at the end of the procedure		
No	19 (86)	
Yes	3 (14)	
Duration of endometrioma vaporization (min)		11 ± 4
5–10 min	12 (55)	
11–15 min	7 (31)	
>15 min	3 (14)	

Abbreviations: ART, assisted reproductive technology; GnRH, gonadotropin-releasing hormone; rAFS, revised American Fertility Society; VAS, visual analog scale.

sible, the surgeon progressively exposes the cyst interior to apply the plasma at an angle perpendicular to the inner surface of the cyst. Plasma energy is also used in dissection, to excise or to ablate superficial implants and deep nodules, and to perform rectal nodule shaving.[18] All surgical procedures were fully recorded and are available for review upon request. Intraoperative incidents and postoperative complications were also recorded. Patients were seen 3 months after surgery (between 11 and 13 weeks). The AMH value was assessed in women who were not pregnant.

All patients were also included in and followed up through the CIRENDO database (the North-Western Inter Regional Female Cohort for Patients with Endometriosis), a prospective cohort financed by the G4 Group (The University Hospitals of Rouen, Lille, Amiens, and Caen), and coordinated by the first author of the present study (H.R.). The database includes surgical and histological findings, as well as information based on self-questionnaires that the patients complete preoperatively and 12 and 36 months postoperatively. Data recording, patient contact, and follow-up were carried out by a clinical research technician.

From April to August 2013 at 6 months or more postoperatively, the patients were called back, a clinical examination was performed, and a third AMH assessment was proposed. In patients who accepted this new AMH test, the blood sample was obtained during the visit.

Statistical analysis was performed using Stata 9.0 software (Stata Corporation, College Station, Texas) and SAS 9.3 (SAS Institute, Cary, North Carolina). The Wilcoxon test for dependent samples was used to compare pre- and postoperative AMH values, and the Friedman test was used to evaluate whether or not the 95% confidence intervals (CIs) of median AMH values change between consecutive time points. The sign test was performed to calculate P values corresponding to variations of median value change over time.[19] Because the third AMH assessment was performed at patient-specific intervals, the hypothesis of independence between AMH level and time lapse between surgery and the day of the assessment was measured using the Spearman rank correlation coefficient.[19] The threshold for statistical significance was set to $P < .05$.

RESULTS

Twenty-five patients who met inclusion criteria were preoperatively enrolled in the study. Eligible patients repre-

sented 20.1% of the 124 patients managed for endometriosis, presenting with ≥1 ovarian endometriotic cyst at our institution between November 29, 2010, and November 28, 2012. The 99 women not included had previous antecedents of ovarian surgery, presented with bilateral localizations, or the cyst diameter did not exceed 30 mm (in the latter, the existence of ovarian endometrioma only could not justify surgery).

Analysis was ultimately performed in only 22 patients. Three patients were followed up without analysis of data. In 2 of these patients, contralateral small ovarian endometriomas were intraoperatively revealed, requiring bilateral ovarian ablation by plasma energy. Unexpectedly, the third patient was found to be pregnant several weeks after surgery and therefore at 10 days' gestation pregnant on the day of surgery. As her preoperative urinary pregnancy test had been negative, she received preoperative hormonal treatment and was initially included in the study. The patient gave birth vaginally at our facility at 41-week gestation to a healthy newborn weighing 3.320 g. On the basis of AMH level variations during pregnancy,[20] the patient was not included in the analysis.

The study sample main characteristics are presented in **Table 1**. Mean age was 30.6 ± 4.8 years and 13 women (59%) were nulligesta. Three women were homosexual (14%) and wished to conceive using an assisted reproductive technique. Preoperative infertility care was recorded in 9 patients (41%). Although 41% of women had been pregnant, the rate of live births was only 29%.

All procedures were performed laparoscopically (**Figure 2**). Preoperative GnRHa were administered in 17 patients with associated deep endometriosis (77%), whereas preoperative continuous macro-progestin intake was recorded in 5 women (23%). Two patients presenting with large rectal involvements were also included in the ENDORE (Functional Outcomes of Surgical Management of Deep Endometriosis Infiltrating the Rectum) randomized trial[21] and benefited from colorectal resection.

One postoperative complication was recorded in a patient presenting with ovarian and deep endometriosis of the sigmoid colon treated by colorectal resection. The patient suffered from a transitory muscular palsy of the left leg, due to the intraoperative compression of the left external sciatic popliteal nerve. The palsy resolved spontaneously within 5 days. The complication was unrelated to endometrioma ablation or to the use of the PlasmaJet.

Pre- and postoperative AMH values are presented in **Tables 1** and **2**. The Friedman test revealed that median
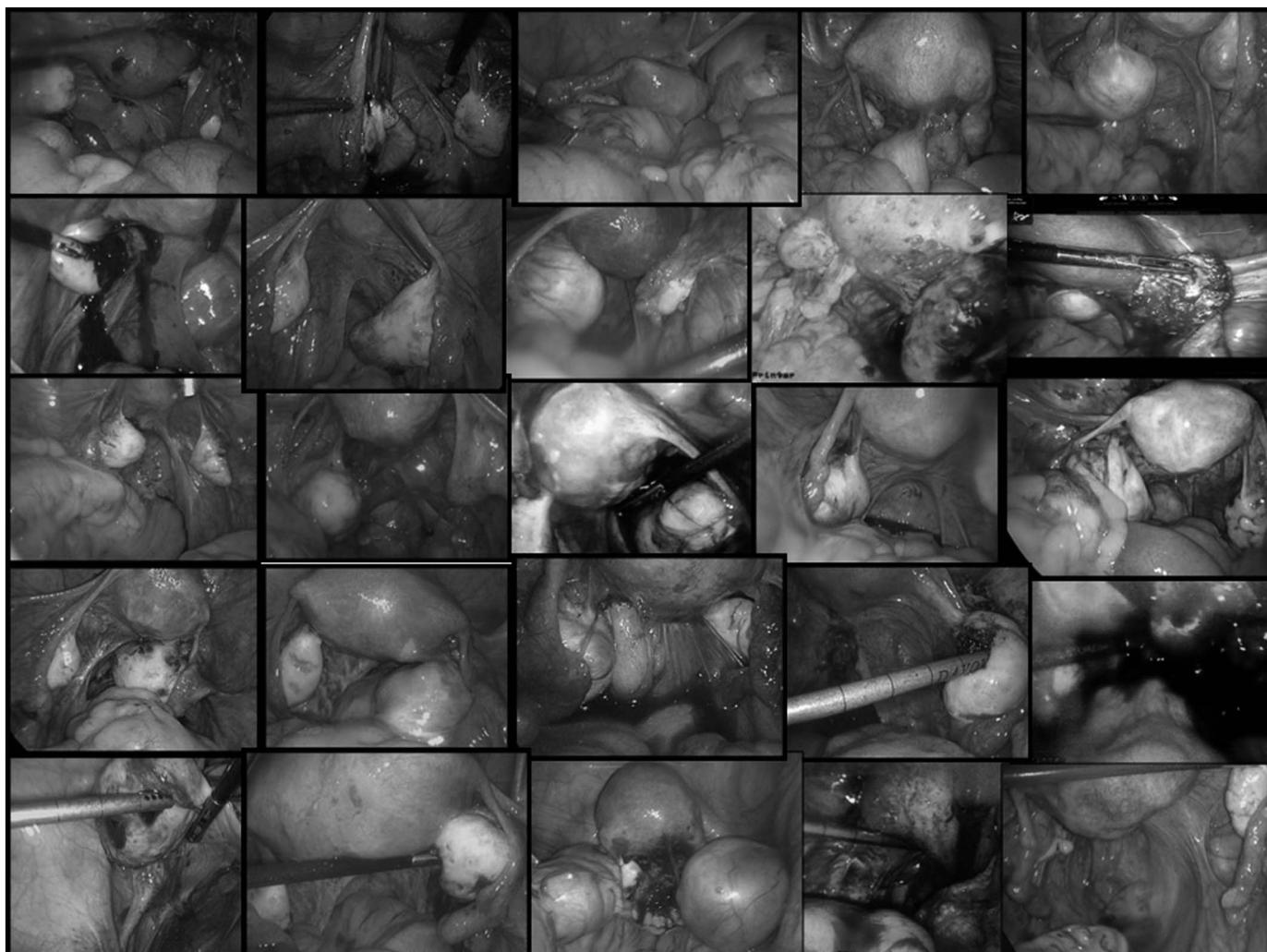
Figure 2. Intraoperative findings in 22 patients included in analysis.

values of AMH level and their 95% CI varied significantly during follow-up. In 5 patients (24%), the preoperative value was inferior to 2 ng/mL. When compared with preoperative values, the AMH levels at 3 months postoperatively decreased on average by 1 ng/mL (median value). In a 43-year-old nullipara, the preoperative value was as low as 0.1 ng/mL, increasing 3 months later to 0.4 ng/mL, and remaining unchanged thereafter. In 2 patients, the 3-month AMH values slightly increased, but in 1 patient it remained unchanged.

Three normal-weight women presented with high preoperative AMH values, >6 ng/mL. In all 3 cases, the 3-month postoperative values dropped considerably by 57% to 75%.

Clinical evaluation at 3 months revealed that only 6 women did not benefit from therapeutic amenorrhea, 3 of whom experienced dysmenorrhea with visual analog scale (VAS) scores respectively of 2, 3, and 5. Among the 15 women who had sexual intercourse, only 3 experienced dyspareunia with 10-point visual analogue scale scores of 2, 3, and 7 respectively. Seven women still had intermenstrual pain with a median value of VAS scores of 4 (range 2 to 7).

The mean follow-up, from the day of surgery to the last visit, was 18.2 months (SD 8 months, range 7 to 29 months). All patients but 1 agreed to undergo a third AMH assessment, which was performed no earlier than 6 months postoperatively. The patient who refused was nullipara, without immediate pregnancy desire, and considered the assessment to be of no benefit. This patient accepted a consultation with the surgeon, during which a

Table 2.
Postoperative Outcomes

	N = 22 (%)	Mean ± SD
Follow-up, mo		18.2 ± 8
Patients with pregnancy intention during follow-up	11 (50)	
Pregnancy	7 (64)	
Delay between arrest of medical treatment and onset of pregnancy, mo, mean (range)		4.4 (2–11)
Live birth	5 (45)	
Pregnancy conception		
Spontaneous	3	
Insemination	2	
IVF	1	
Transfer of frozen embryos, former IVF	1	
Pelvic pains		
Patients with periods during previous 12 mo	11 (50)	
Dysmenorrhea	10 (45)	
VAS of dysmenorrhea		4.6 ± 2.2
Sexual intercourse during previous 12 mo	13 (59)	
Deep dyspareunia	6 (27)	
VAS of dyspareunia		2.1 ± 0.8
Intermenstrual pelvic pain	12 (55)	
VAS of intermenstrual pelvic pain		5.2 ± 1.6
3-mo assessment	22 (100)	
AMH assessment		2.3 ± 1.1
<1 ng/mL	3 (14)	
1–1.9 ng/mL	3 (14)	
2–6 ng/mL	16 (72)	
>6 ng/mL	0	
Third AMH assessment at end of follow-up	21 (95)	
AMH assessment		3.1 ± 2.2
<1 ng/mL	2 (10)	
1–1.9 ng/mL	4 (19)	
2–6 ng/mL	13 (61)	
>6 ng/mL	2 (10)	

Abbreviations: AMH, antimullerian hormone; IVF, in vitro fertilization; VAS, visual analog scale.

clinical assessment was carried out. AMH level variation from 3 months postoperatively to the last follow-up visit (> 6 months postoperatively) is shown in **Table 3**. When compared with the AMH value at 3 months, a median increase in AMH level of 0.7 ng/mL was recorded. Of the 21 patients who consented to a third AMH assessment, 15 had a normal AMH level >2 ng/mL (72%). The sign test revealed that the median values of AMH levels significantly decrease at 3 months postoperatively ($P = .003$), then significantly increase ($P = .01$) (**Table 4**). As the Spearman rank correlation coefficient was $rs = +0.099$ ($P = 0.67$), the hypothesis of the independence of AMH values at the third assessment could not be rejected, meaning that delayed postoperative AMH values were not

Table 3.
AMH Values Before and After Surgery

	Preoperative	3 Mo After Surgery	Third Assessment	*P Value*
Number of patients with AMH assessment	22	22	21	
Median AMH value, ng/mL	3.2	2.2	2.7	.001
25th and 75th percentiles of median AMH value, ng/mL	2.2, 5.2	1.9, 2.8	1.9, 3.4	
95% CI of median AMH value, ng/mL	2.2–5.2	2–2.8	1.9–3.4	

Abbreviations: AMH, antimullerian hormone; CI, confidence interval.

Table 4.
AMH Level Variations Between 2 Assessments

	3-Mo vs Preoperative	*P* Value	Third Assessment vs. 3-Mo	*P* Value	Third Assessment vs. Preoperative	*P* Value
Median AMH level variation, ng/mL	−1	.003	0.7	.01	−1	.26
95% CI of the median AMH level variation, ng/mL	−2.3 to −0.2		0.1 to 1.4		−2 to 0.2	

Abbreviations as in Table 3.

significantly impacted by the length of time between surgery and the third assessment. When comparing AMH values at the first and the third assessment using the sign test, 95% CI of difference included 0, thus the difference was not statistically significant. Stratification of patients by age (cut-off value at 30 years) and cyst diameter (cut-off value at 40 mm) did not alter the statistical significance of the results.

The AMH values were compared between patients who received and patients who did not receive preoperative GnRHa treatment. Differences were not statistically significant 3 months after surgery (*P* = .38) or at the end of the follow-up (*P* = .17).

Pelvic ultrasonographic examination was performed in all patients to check for recurrent endometriomas. Only 1 patient (5%) presented with a 16-mm cyst on the contralateral ovary, the characteristics of which suggested endometrioma recurrence, 17 months after surgery. The patient had not been on contraceptive pill during the postoperative period. As a homosexual, she did not attempt spontaneous pregnancies but only underwent an unsuccessful intrauterine insemination.

Pelvic pains were checked pre- and postoperatively (Tables 1 and 2). There was a statistically significant decrease in VAS for dysmenorrhea in women who had periods during the previous 12 months (*P* = .001). The rates of patients with pre- and postoperative dyspareunia and intermenstrual pain were comparable (respectively, *P* = .30 and *P* = 1). Comparison between the pre- and postoperative VAS for dyspareunia and intermenstrual pain did not reach statistical significance either (respectively, *P* = .16 and *P* = .25).

Eleven of 22 patients (50%) tried to conceive postoperatively. Eight of them (73%) became pregnant, and the median (range) of the delay from the arrest of postoperative hormonal treatment to conception was 4.4 months (2 to 11 months). Three of the 8 conceived spontaneously, 2 after insemination (in 1 case, homosexuality was the sole reason for insemination), 2 after in vitro fertilization (IVF), and 1 following frozen embryo transfer. Five gave birth to healthy babies, one pregnancy is ongoing, one experienced miscarriage and the last patient underwent first trimester medical abortion for severe hygroma. The other 3 patients failed to conceive. Two homosexual women underwent unsuccessful inseminations, and one patient was referred for IVF due to abnormal sperm parameters, respectively.

DISCUSSION

This is the first prospective assessment of AMH level variation following the management of ovarian endometriomas by ablation using plasma energy. Our results

suggest that even though the contralateral ovary is healthy, ablation of a unilateral endometrioma is followed in a majority of cases by a significant decrease in AMH level 3 months after surgery and that this initial decrease is followed by a significant, progressive increase in values. In general, AMH levels at the third assessment carried out >6 months postoperatively did not reach the preoperative level, though this difference was not statistically significant.

Although preliminary, our study presents several limitations that could impact the results. The comparative design was abandoned, and the lack of a control group does not allow us to draw conclusions on the technique's benefits and risks versus those of endometriomas cystectomy. The sample size is small, thus estimation of results may be less precise. As usual in endometriosis series, there is a heterogeneity in the localizations: Several women also present with deep disease, but others do not. Even though associated deep localization may not influence AMH variations and cyst recurrences, it can impact secondary outcomes such as postoperative pain scores. The follow-up and the interval from the second to the third AMH assessment is variable and provides only a trend for AMH evolution over 6 postoperative months. The inclusion criteria, which limited enrollment to only women with a single, unilateral endometrioma and no prior ovarian surgery, preclude extrapolation of the study findings to the whole population of patients managed for ovarian endometriomas.

High preoperative AMH levels in 3 patients bear witness to the existence of ovarian polycystic syndrome. It is likely that ablation played a similar role to unilateral ovarian drilling, leading to a decrease in AMH level.[22] Logically, the starkest decrease in AMH level in our series was observed in these women.

The third AMH level assessment was carried out after a postoperative delay varying from 7 months to 2.5 years. It has been previously shown that AMH value depends on age, decreasing by –1 pmol/L/year at 30 years and –3 pmol/L/year at 40 years.[23] This natural age-related decrease may influence values at the third assessment. However, in our sample, the relationship between AMH values and length of time from surgery to the third assessment was not statistically significant.

Based on the presumption that PlasmaJet vaporization seldom involves underlying ovarian parenchyma, the observed fall in AMH values 3 months after surgery was unexpected. We recently observed that depth of necrosis induced by PlasmaJet vaporization in ovaries man-

aged by ablation followed by immediate ovarian-sparing cystectomy seldom exceeded the thickness of the cyst fibrous wall.[13] In cases where necrosis extended into the ovarian parenchyma, it represented on average 10% of the ovarian tissue inadvertently removed with the cyst during cystectomy leading to the conclusion that ovarian reserve should be better preserved by the ablative technique than by cystectomy. This hypothesis was supported by a retrospective comparison of the ultrasonographic parameters of ovaries managed respectively by ablation or cystectomy.[15] We previously observed a high likelihood of postoperative pregnancy in patients having undergone ovarian endometrioma ablation using PlasmaJet, with a rate of pregnancy reaching 73% 2 years after surgery, despite a high prevalence of unfavorable associated factors (deep and colorectal endometriosis, bilateral ovarian localization, surgical antecedents, and previous infertility care).[16] A recent randomized trial comparing cystectomy and vaporization using the CO_2 laser, which has a comparable effect to that of PlasmaJet, also revealed a significantly improved postoperative AMH level following vaporization.[4] In the present study, as only 1 ovary was treated, we further expected to reveal only slight postoperative variations in AMH level following PlasmaJet ablation. In our opinion, the 30% decrease in value observed at 3 months raises questions about the real factors that impact postoperative ovarian AMH production.

AMH is produced by the granulosa cells of primary, preantral, and small antral follicles. Serum concentrations of AMH appear to be gonadotropin-independent and therefore remain relatively consistent during the menstrual cycle, both in normally ovulating and in infertile women.[24] It has been emphasized that AMH levels are not affected by the use of hormonal treatments, and they are sensitive to changes in ovarian reserve correlating well with antral follicle counts. However, recent data, unavailable at the time of the study inclusions, has suggested that administration of GnRH agonists could decrease the AMH level several days after drug administration.[25] As 17 patients (68%) presenting with associated deep endometriosis received 11.25 mg GnRHa and add-back therapy just before PlasmaJet vaporization, the decrease observed in 3-month AMH levels may also be linked to the use of hormonal therapy.

When ovarian endometriomas are removed by cystectomy, some underlying ovarian parenchyma is inadvertently excised along with the cyst wall. This inadvertent excision is not unexpected considering the lack of a histologic cleavage plane between the cyst wall and the

ovarian cortex and is frequently revealed by histologic examination of specimens. The excision of ovarian cortex alongside the cyst is responsible for a significant reduction in ovarian reserve, in patient responsiveness to ovarian stimulation, and in likelihood of subsequent pregnancy. Several studies have investigated AMH-level variations following excision of endometriomas, the results of which have been included in a recent meta-analysis.[3–11] Despite considerable heterogeneity between the studies included, the pooled analysis of 237 patients revealed a significant decrease in AMH level following cystectomy: –1.13 ng/mL on average (95% CI, −0.37 to −1.88), up to 40% of the baseline AMH value.[3] Two studies totaling 53 patients showed that AMH assessments performed 6 to 9 months post cystectomy still found a statistically significant fall in AMH level of –1.49 ng/mL (95% CI, −0.86 to −2.12).[3,4,7] The only study that included successive assessments at 3 and 9 months postoperatively reported constant values of AMH levels, respectively, 1.4 ± 0.2 and 1.3 ± 0.3 (baseline values 3 ± 0.4).[7] The postoperative fall in AMH level was statistically significant in the subgroup analysis, with studies involving only women younger than 40 years, with endometriomas exceeding 5 cm in diameter, or with a baseline AMH ≥3.1 ng/mL. The postoperative fall in AMH in women undergoing bilateral endometrioma cystectomy was even greater (−44%), though this difference was not statistical significant.[3]

Unexpected results have recently been reported by Celik et al [2] who performed cystectomies for ovarian endometriomas with AMH assessments preoperatively and 3 and 6 months postoperatively. Like preceding investigators, they observed a decrease in AMH level between the baseline and the 3-month postoperative value (1.78 ± 1.71 vs 1.32 ± 1.29), with a continuing decrease over the subsequent 3 months (6-month value at 0.72 ± 0.79). When compared with the baseline value, the 6-month level showed an average 61% decrease and was starker in bilateral endometriomas (29% of patients) and in women with endometriomas measuring >5 cm in diameter (61.5% of patients). However, the loss of 40% of patients from follow-up between the third and sixth postoperative month prevents definitive conclusions from being drawn.

To date, we are unable to provide an explanation for the fall in AMH level 3 months after PlasmaJet ablation, or its subsequent rise. The variation may be due to transitory inflammation following ovarian manipulation, adhesiolysis, and vaporization. To date, little data exists on the impact of inflammatory processes on AMH level. It has recently been shown that inflammatory

bowel disease and systemic lupus erythematosus are associated with low AMH values.[26–28] AMH levels were decreased in women with high levels of cytokines such as tumor necrosis factor, interleukin 15, and granulocyte-macrophage colony-stimulating factor, even though the ovarian reserve did not appear clinically decreased.[29] It is possible that postoperative ovarian inflammation can either decrease AMH secretion by granulosa cells or can modify follicle development with a transitory decrease in the activity of a number of primary, preantral and small antral follicles. Plasma energy itself could have a negative effect on the early follicles in the surrounding ovarian tissue, despite the lack of histologically documented necrosis.

To provide strong arguments to the debate concerning the best treatment of ovarian endometriomas in women intending to conceive, a further randomized, controlled trial is required. Based on recent, published data regarding clinical outcomes in patients managed by ablation using plasma energy, a multicenter, prospective, randomized trial is planned to compare the rate of pregnancies and that of cyst recurrences in patients managed by either cystectomy or ablation using PlasmaJet. Patients' enrollment in the trial is expected to start by the end of 2014, with full reporting in 2018.

CONCLUSIONS

We believe that ablation using PlasmaJet may play a role in the management of ovarian endometriomas in women wishing to conceive. Although frequently advocated cystectomy fails to prevent recurrences in almost 29% of cases within 2 years[30] and can lead to a dramatic decrease in the ovarian reserve and significantly impair IVF results.[31] This evidence should push surgeons to seek out alternative techniques to cystectomy, in the interest of young infertile women affected by bilateral or recurrent ovarian endometriomas and at risk of premature ovarian failure.

Conflict of Interest

Dr Roman received an honorarium for his participation at a symposium and master class, where he presented his clinical experience with the PlasmaJet. This remuneration remains independent of the submitted work.

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