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Research article

Myometrial smooth muscle cells spillage during open myomectomy: Is it True or a myth?

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ABSTRACT

Background: Uncontained morcellation of myoma during laparoscopic surgery has been discouraged because of unknown malignancy. Even the safety of contained morcellation has been questioned because muscle cells have been detected in washings obtained during laparoscopic procedures. The possibility of myoma cell dissemination has been observed in open abdominal surgery, even after hysterectomy. Thus myomectomy would be unsafe from an oncological point of view, regardless of surgical approach.

Methods: This is an observational cohort study involving 30 patients who underwent open abdominal myomectomy. Peritoneal abdominal washings were obtained two times during the open abdominal myomectomy: before uterus incision and after the myomectomy itself. Cytological, cell block, and immunohistochemical evaluations were performed.

Results: All washings obtained immediately after abdominal peritoneal cavity opening were negative for fibroid cells. Both the first and second washings were free of myoma cells. Cytologic evaluation did not reveal any smooth muscle cells. The results of desmin and smooth muscle actin staining, performed on the pre- and post-myomectomy samples, were negative.

Conclusion: Our results demonstrated, for the first time to our knowledge, that there is no dissemination of myoma cells during conservative abdominal surgery. It could represent an additional oncological safety. Further data are needed.

1. Introduction

Uterine leiomyoma is the most common benign tumor. In symptomatic patients, leiomyomas can cause abnormal uterine bleeding, infertility, and pelvic pain. Myomectomy is performed by laparoscopy, laparotomy, or hysteroscopy depending on the location, size, and number of myomas and the age of the woman.

The benefits of laparoscopic surgery compared with open abdominal surgery are well established: a shorter hospital stay, faster recovery time, less morbidity, and fewer complications and postoperative adhesions.[1–3] In the last few decades, laparoscopic myomectomy has been performed worldwide, even though some gynecologic surgeons consider laparoscopic myomectomy to be a challenge because of the need for suturing skills and limits in terms of number (<4) and size (8–10 cm).[4,5] Retrieval of enucleated myomas during laparoscopic myomectomy invariably requires mechanical morcellation. Nevertheless, in 2014 the US Food and Drug Administration (FDA) "discouraged the use of laparoscopic power morcellation during hysterectomy and myomectomy for uterine fibroids" because of the oncological risk.[6] The reason for this recommendation was that the use of a morcellator in patients with unsuspected uterine malignancy could disseminate malignant cells in the pelvis and abdomen and decrease the overall survival rate. Furthermore, the morcellation process may leave myoma fragments in the peritoneal cavity. These fragments could survive through attachment to the peritoneal surface and develop

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into parasitic myomas, which are not malignant but could potentially threaten the health of the patient.

To bypass these concerns, the gynecological community has continued to seek alternatives to morcellation or a device for safe contained morcellation, such as a surgical specimen bag.[7] Transvaginal removal has been proposed as a new way for specimen safety.[8] Furthermore, the open abdominal approach has been upgraded, with the loss of the well-established advantages of minimal invasive surgical approaches.

Some researchers have identified myometrial smooth muscle cells in peritoneal cavity and pelvic washings, even in patients who underwent laparoscopic or open abdominal myomectomy without any morcellation or when washings were collected before morcellation.[9,10] If myomatous tissue dissemination occurs during myomectomy alone and uterine manipulation is confirmed, there would not be any reason for the use of contained morcellation, vaginal extraction,[8] or an open abdominal surgical approach.[11] Furthermore, if tissue spillage is considered potentially harmful and if it occurs during myomectomy independently of the surgical route, it could be questioned whether, from an oncological point of view, myomectomy is a safe technique. Sandberg[10] hypothesized that dissemination of smooth cells occurs during myoma resection and not only during morcellation. The results of their study confirmed the presence of myoma cells in peritoneal washes collected after open abdominal surgical procedures. Nonetheless, it is unclear whether these positive cytology results have any clinical or oncological relevance.

Leiomyoma cell spillage has been postulated by other researchers because of the occasional diagnosis of parasitic myoma after abdominal myomectomy, confirming the occurrence of peritoneal dissemination due to uterine incision and myoma manipulation.[12] In light of these considerations, we hypothesized that myoma cell dissemination may occur during uterine/myoma manipulation and that it may not be due to power morcellation.

The aim of the present study was to detect the presence of myomatous cells and/or tissue during open abdominal myomectomy by performing peritoneal washings at the beginning and the end of the surgical procedure.

2. Materials and methods

This is an observational cohort study involving open abdominal myomectomies consecutively performed at S. Antonio Abate Hospital of Trapani (Italy) between October 2019 and March 2020. Because standard surgery was performed and the diagnostic procedure was considered to pose no additional risk, no ethical committee approval was required. Inclusion criteria were as follows: age >18 years, informed consent was given, and symptomatic intramural fibroids were >10 cm or >3 cm in women older than 40 years old. Women who met all inclusion criteria were informed about the surgical procedure and asked to participate. The surgical procedure was performed by two skilled gynecological surgeons (LG and VI) according to standard approaches and in agreement with current guidelines, with the exception of the washing, which was performed before and after myoma enucleation. The standardized techniques were performed as follows: general anesthesia, Trendelemburg position, Pfannenstiel incision, peritoneal washing with 100 ml of sterile saline solution in the anterior and posterior pouch of Douglas before any surgical maneveur, identification of myomas (with sonographic guide), vertical uterine incision, enucleation of myoma(s) with a tenaculum and blunt dissection, myoma removal, double layer suture of the uterine wall with absorbable sutures, peritoneal washing with 100 ml of sterile saline solution, hemostasis check was achieved, and abdominal wall closure with multilayer sutures.

The 100 ml pre- and post-myomectomy washings were completely aspirated, and samples were collected separately in sterile bags for cytological analysis. Washing saline solution obtained pre- and post-myomectomy were analyzed by pathologists. For each sample, smear slides were prepared and a immunohistochemical staining was performed for vimentin, actin, desmin, HBME1, and caldesmone in order to identify and differentiate mesothelial cells and muscle cells. Demographic information (Table 1), information about surgical procedures, and histological reports were prospectively collected.

3. Results

Thirty patients who met the inclusion criteria were recruited to the study between October 2019 and March 2020. Characteristics of the study cohort are shown in Tables 1 and 2. The median age was 36 ± 5 years. The size of the largest myoma removed was 18 cm. All fibroids were intramural/subserosal. Eighteen (60%) women had a single myoma, 3 (10.0%) had 2 myomas, and 9 (30.0%) had between 3 and 6 myomas. The most common symptoms reported were abnormal uterine bleeding (26.7%), abdominal pain (23.3%), infertility (13.3%) and/or pregnancy desire (20.0%), fast growth (3.3%), and frequent voiding (3.3%). Only 1 (3.3%) woman received a blood transfusion after surgical intervention, 3 patients out of 30 (10.0%) had postoperative fever, 3 (10.0%) had a significant reduction of hemoglobin level not requiring transfusion but were treated with 50 mg ferric carboxymaltose intravenous infusion, and 1 (3.3%) patient had ileus, which spontaneously resolved after 48 h.

All of the washings obtained immediately after abdominal peritoneal cavity opening were negative for fibroid cells. Cytologic evaluation did not reveal any smooth muscle cells. Results of desmin and smooth muscle actin staining, performed on the pre- and post-myomectomy samples, were negative.

4. Discussion

The risk factors for tissue dissemination are recognized in surgical procedure, morcellation, hormonal milieu and/or genetic characteristic of myomas.[9–11,13] Takeda et al.[14] hypothesized that smooth muscle cell

Table 1
Demographic characteristics, myoma features, and surgical outcomes of 30 women included in the cohort study.

Age (years)	36 ± 5
BMI (kg/m^2)	25.7 ± 3.4
Nulliparous	15 (50.0)
Married	20 (66.7)
Ethnicity	
Caucasian	25 (83.3)
Afro-american	3 (10.0)
Asian	2 (6.6)
Indication for myomectomy	
Abnormal uterine bleeding	8 (26.7)
Abdominal pain	7 (23.3)
Pregnancy desire	6 (20.0)
Infertility	4 (13.3)
Abdominal mass	1 (3.3)
Dyspareunia	1 (3.3)
Fast growth	1 (3.3)
Frequent voiding	1 (3.3)
Number of fibroids	
1	18 (60.0)
2	3 (10.0)
3	3 (10.0)
4	2 (6.7)
5	2 (6.7)
6	2 (6.7)
Fibroid larger diameter (cm)	11.4 ± 3.1
Preoperative treatment with GnRHa/UPA	0 (0.0)
Surgical complications	
Fever	3 (10.0)
Blood transfusion	1 (3.3)
Anemia	3 (10.0)
Ileus	1 (3.3)

Data are given as n (%) or mean ± SD. GnRHa: analogs of GnRH; UPA: ulipristal acetate.

Table 2
Characteristics of the specific cases included in the study.

	Age (ys)	BMI	Parity	Ethnic	Marital status	Indication for myomectomy	Number of fibroids	Size of fibroids (cm)	GnRHa/UPA (preoperative treatment)	Surgical complications
1	44	22.6	Yes	Caucasian	M	Abdominal pain	1	16	No	Postop fever
2	45	24	Yes	Caucasian	D	Abnormal uterine bleeding	1	9	No	None
3	40	27	Yes	Caucasian	M	Infertility	4	7.5, 6,5,5	No	None
4	41	30	Yes	Caucasian	M	Abnormal uterine bleeding	4	7, 6,5,4	No	Hb levels ↓
5	38	28	No	Caucasian	S	Abnormal uterine bleeding	1	8.5	No	None
6	28	21	No	Sri lanka	M	Abdominal pain	1	14	No	None
7	37	24	Yes	Caucasian	M	Abdominal pain menorrhagia	1	11	No	Hb levels↓
8	43	22	No	Caucasian	M	Abdominal mass	1	9.5	No	None
9	35	26	No	Caucasian	S	Pregnancy desire	6	7,5,4,4,3,2	No	None
10	42	27	Yes	Caucasian	S	Abnormal uterine bleeding	1	8	No	None
11	32	21	Yes	Caucasian	M	Pregnancy desire	1	14	No	None
12	30	20,5	No	North african	M	Pregnancy desire	1	15	No	None
13	36	23	No	Caucasian	D	Abdominal pain	1	12	No	Ileus
14	33	31	No	Caucasian	S	Pregnancy desire	4	8,8,6,4	No	Postop fever
15	30	28	No	Caucasian	M	Infertility	3	10,5,5	No	None
16	52	29	No	Caucasian	S	Abdominal pain	1	16	No	None
17	39	25	Yes	Caucasian	D	Abnormal uterine bleeding	1	10	No	None
18	31	22	No	Caucasian	S	Abdominal pain	2	12,8.7	No	None
19	30	20	Yes	North african	M	Pregnancy desire	1	14	No	None
20	41	28	No	Caucasian	M	Pregnancy desire	1	18	No	Blood transfusion
21	28	33	Yes	Caucasian	M	Abnormal uterine bleeding	4	10,9,5,4	No	None
22	34	30	No	Caucasian	M	Abdominal pain	2	13,8	No	None
23	42	29	No	Caucasian	M	Fast growth	1	16	No	None
24	39	25	Yes	Chinese	M	Infertility	1	15	No	None
25	36	24	Yes	Caucasian	S	Abdominal pain	3	9,8,5	No	None
26	31	23	Yes	Caucasian	M	Frequent voiding	1	12	No	None
27	42	24	Yes	Caucasian	M	Abdominal pain	6	10,7,5,5,3,3	No	HB levels↓
28	37	28	No	Caucasian	M	Abnormal uterine bleeding	2	12,10	No	No
29	40	26	Yes	Caucasian	M	Dyspareunia	1	11	No	None
30	28	29	No	North african	M	Infertility	3	9,8,8	No	Postop fever

aGnRH: analogs of GnRH; UPA: ulipristal acetate; M: married; S: single; D: divorced.

dispersion occurs in the peritoneal cavity when the uterus is incised to reach the myomas, when a surgical instrument fixes myoma, and when sharp or blunt dissection is performed. This occurs whether the operation is performed without tissue morcellation or before tissue morcellation.[14] Washes containing smooth muscle cells have been found even with contained morcellation during robotic laparoscopic myomectomies.[14] Previous studies have demonstrated that tissue spillage from leiomyoma(s) occurs even during open abdominal myomectomy.[10] The clinical relevance of this dissemination is unclear but it is not possible to exclude the risk from an oncological point of view. Some researchers have postulated theories in order to explain the presence of parasitic myomas after open abdominal myomectomy.[12,13] Consequently, technological efforts to design bags for contained morcellation would be useless. Otherwise, myomectomy itself would become a dangerous surgical procedure, with possible leiomyoma tissue dissemination.

Our observational study demonstrates for the first time the absence of any fibroid cell dissemination due to open abdominal myomectomy. This finding is in contrast to that of a previous study,[10] in which washings containing fibroid cells were obtained solely during uterine incision. If our results are confirmed by other studies, open myomectomy would be considered safe, without the oncological risk of malignant cell spillage. How we use these data to "morcellation" and "laparoscopic myomectomy" is another matter; however, these data may be useful to develop strategies for laparoscopic myomectomy with/without morcellation.

5. Conclusion

We are aware of the limitation of our results: a small group of patients is represented. Furthermore, this is an observational not randomized study, and thus is weak from a methodological point of view. But in light of our results it can be questioned whether laparoscopic myomectomy and contained morcellation guarantee any oncological safety. Further studies are required to ensure that the surgery women undergo is safe.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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