Review Article

Iatrogenic Myomas: New Class of Myomas?

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ABSTRACT

Parasitic myomas, defined as extrauterine seeding of leiomyoma, have been reported since the early 1900s. These myomas were thought to be spontaneously occurring, separate from the uterus but still hormone-dependent and can cause symptoms. What seemed to be a rare disorder developing from the natural history of pedunculated myomas has become increasingly reported over the last decade. Because it is still a rare disorder, the literature is limited to case reports. Herein, we review the literature and provide an analytic review of recent case reports, with emphasis on etiology, trends, and risk factors, to increase awareness of this problematic entity. Journal of Minimally Invasive Gynecology (2010) 17, 544–550 © 2010 AAGL. All rights reserved.

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Uterine myomas are benign monoclonal tumors that arise from smooth-muscle cells of the myometrium. They occur in approximately 25% of women of reproductive age, and are noted at pathologic examination in approximately 80% of surgically excised uteri [1,2]. Myomas are typically classified according to location, and include submucous, intramural, and subserosal subtypes. A fourth class of rare myomas, known as parasitic myomas, was first reported in the literature in the early 1900s [3]; these were traditionally thought to be pedunculated subserous myomas that lost their attachment to the uterus and became parasitic on surrounding organs. Thus, these myomas exist free and separate from the uterus but are still responsive to the hormonal milieu.

While diagnosis of parasitic myomas has often been incidental at surgery for other indications, they are also known to cause symptoms and to require surgical management themselves [4,5]. What appeared to be a rare entity that could develop naturally from pedunculated myomas has been increasingly reported over the last decade. Because the entity is still rare, the literature is limited to case reports. A strong association among these cases is a history of surgery, and in more recent reports, a history of laparoscopic surgery involving morcellation of the uterus or myomas. In addition, a related but distinct entity, peritoneal leiomyomatosis or leiomyomatosis peritonealis disseminata (LPD), has also been increasingly reported in the literature and is associated with morcellation. Herein, we present a comprehensive review of the literature on parasitic myomas and provide an analytic review of recent case reports to increase awareness and theorize potential causes.

Are We Witnessing a Trend?

Described by Kelly and Cullen [3] in 1909 as “myomata that have for some reason become partially or almost completely separated from the uterus and receive their main blood supply from another source,” parasitic myomas attracted some attention in the early 1900s and were written about in the literature of that time [4]. One report in 1953 described a similar entity of a 6-cm myoma attached to the omentum [4], and in the 1990s, there were 2 reports of acute abdomen with suspected ovarian torsion that were found to be torsed parasitic myomas [5,6]. Such cases were presented as interesting and confounding manifestations of a rare entity that grew out of a natural history of myomas.

However, in the last 10 years, there has been an increase in the reports of parasitic myomas in the literature, and they are largely found to be associated with previous surgery. Most of these cases are parasitic myomas found after laparoscopic myomectomy and supracervical hysterectomy, and even 1 case occurring after vaginal hysterectomy. Similarly, over the last 3 years, several case reports of “disseminated
peritoneal leiomyomatosis” and “parasitic peritoneal leiomyomatosis” have been noted in the literature. These reports also individually suggest an association with previous laparoscopy.

We also present our experience with 2 novel cases of parasitic myoma formation, 1 occurring after administration of gonadotropin-releasing hormone agonist, and 1 after magnetic resonance–focused ultrasound (MR[f]US) treatment of uterine myomas [7]. These cases from our institution suggest a similar pathogenesis as that of the parasitic myomas traditionally described in the literature; that is, when the uterine blood supply is diminished to the myoma, it may find an adjacent organ from which to obtain blood supply and thereby become parasitic on this nonuterine source. In contrast to the cases described by Kelly and Cullen [3], these cases seem to represent iatrogenically induced conditions that precipitate formation of these myomas.

Thus, parasitic myomas seem to fall into 3 broad categories: spontaneous development of parasitic myomas from pedunculated myomas; myomas associated with previous uterine surgery, in particular, morcellation; and myomas associated with restriction of blood supply to the uterus. Concern increases in the last 2 groups, and leads us to ask whether we are iatrogenically creating a new class of myomas.

Spontaneous Parasitic Myomas

In their 1909 text, Myomata of the Uterus, Kelly and Cullen [3] include a chapter on parasitic myomas and report a series of 37 parasitic myomas. They subscribe the cause of such myomas as “inherent in the myomata and not in the surrounding organs,” and surmise that the uterus, as it tries to “naturally get rid of its interstitial nodules,” contracts until a submucous myoma becomes pedunculated, and finally the mass of the myoma creates such traction on its pedicle that it becomes separated from it. At this point, the omentum “fulfilling its useful function of guarding other abdominal organs” attaches to the detached myoma and provides it blood supply; if this does not occur, the myoma “may become a parasite upon the intestines or bladder for its sustenance” [3].

In their series, the authors describe mainly pedunculated myomas, which are still partially attached to the uterus but gain their main blood supply from other organs. In 1953, the topic is revisited with a case report in which Brody [4] describes a pedunculated myoma that became detached and parasitic to the omentum. No doubt, in the intervening years, there was evidence of torsion of a parasitic myoma around a thin stalk of omentum to which the myoma had parasitized. Other signs and symptoms included abdominal mass, urinary retention, and menorrhagia. In 1 patient without symptoms, the mass was incidentally found at routine pelvic examination.

The mean age at diagnosis was 38 years. In 11 of 16 patients, previous pelvic surgery was confirmed, with a mean of 26 months between the surgery and the diagnosis of parasitic myoma. Four cases were categorized as “unspecifed” because there was no information about surgical history. Eight of 16 patients had a history of previous laparoscopic myomectomy; in 1 of these, a gasless laparoscopic technique was used [16]. Six of 16 patients had undergone some form of electric morcellation during the previous procedures, and 5 others had undergone some unspecified form of morcellation.

Six cases were diagnosed intraoperatively, 4 during laparoscopy and 2 during laparotomy. In 7 cases, preoperative ultrasound was performed, which suggested the presence of an abnormal mass that was confirmed as a parasitic myoma at surgery. The remaining 3 cases were first detected as abnormal masses at examination, although parasitic myomas were not considered in the differential diagnosis. Nearly all of the case reports suggest that parasitic myoma was not included in the differential diagnosis before intraoperative evaluation. When indicated in the case report, the leading diagnoses were uterine myomas, ovarian torsion, and unspecified abnormal pelvic or abdominal mass demonstrated at ultrasound or physical examination.

Eight cases were managed laparoscopically, and 4 patients underwent exploratory laparotomy for resection of the parasitic myomas. Two patients with port-site myomas
<table>
<thead>
<tr>
<th>Source, Year</th>
<th>Symptom</th>
<th>Diagnosis</th>
<th>Age at Diagnosis, y</th>
<th>Previous surgery</th>
<th>Electric morcellation</th>
<th>Interval</th>
<th>No. of myomas</th>
<th>Location</th>
<th>Size, cm</th>
<th>Presence of uterine myomas</th>
<th>Method of resection</th>
<th>Histopathologic findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brieger et al [5], 1995</td>
<td>Pain</td>
<td>Torsion of parasitic myoma</td>
<td>41</td>
<td>NA</td>
<td>No</td>
<td>NA</td>
<td>1</td>
<td>Pouch of Douglas, attached to omentum</td>
<td>10</td>
<td>No</td>
<td>L/S</td>
<td>Myoma with necrosis</td>
</tr>
<tr>
<td>Brody [4], 1953</td>
<td>Pain</td>
<td>Parasitic myoma</td>
<td>31</td>
<td>NA</td>
<td>Yes</td>
<td>NA</td>
<td>1</td>
<td>Omentum</td>
<td>8 × 6</td>
<td>No</td>
<td>X-lap</td>
<td>Fibroleiomyoma</td>
</tr>
<tr>
<td>Epstein et al [8], 2009</td>
<td>Pain</td>
<td>Parasitic myoma</td>
<td>31</td>
<td>L/S MMX</td>
<td>Yes</td>
<td>18 mo</td>
<td>2</td>
<td>Omentum</td>
<td>3</td>
<td>Yes</td>
<td>L/S</td>
<td>NA</td>
</tr>
<tr>
<td>Hutchins and Reinoehl [9], 1998</td>
<td>Pain</td>
<td>Retained myoma</td>
<td>42</td>
<td>LSH</td>
<td>Yes</td>
<td>1 mo</td>
<td>1</td>
<td>Sigmod</td>
<td>8</td>
<td>Yes</td>
<td>X-lap</td>
<td>Infarcted leiomyoma</td>
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<tr>
<td>Kumar et al [10], 2008</td>
<td>Pain, SOB</td>
<td>Disseminated peritoneal leiomyomatosis</td>
<td>24</td>
<td>L/S MMX</td>
<td>Yes</td>
<td>11 mo</td>
<td>7</td>
<td>Omentum and peritoneum of descending colon</td>
<td>30 – 20</td>
<td>Yes</td>
<td>X-lap</td>
<td>Leiomymoma</td>
</tr>
<tr>
<td>Lurie et al [6], 1991</td>
<td>Pain</td>
<td>Paratonic leiomyoma</td>
<td>40</td>
<td>NA</td>
<td>NA</td>
<td>Unspecified</td>
<td>1</td>
<td>Near uterine fundus</td>
<td>11–12</td>
<td>No</td>
<td>X-lap</td>
<td>Leiomymoma</td>
</tr>
<tr>
<td>Moon et al [11], 2008</td>
<td>Palpable mass</td>
<td>Paratonic leiomyoma</td>
<td>34</td>
<td>L/S MMX</td>
<td>Unspecified</td>
<td>3 yr</td>
<td>1</td>
<td>Subfascial, near LLQ port site</td>
<td>3.2 × 2.2 × 2</td>
<td>Yes</td>
<td>Open excision</td>
<td>Leiomymoma</td>
</tr>
<tr>
<td>Ostrzenski [12], 1997</td>
<td>Pain</td>
<td>Uterine leiomyoma particle</td>
<td>43</td>
<td>L/S MMX</td>
<td>Unspecified</td>
<td>“Fragmentation”</td>
<td>9 mo</td>
<td>Embedded in rectus muscle at suprapubic scar</td>
<td>2.5 × 2.5</td>
<td>Yes</td>
<td>Open excision</td>
<td>Leiomymoma</td>
</tr>
<tr>
<td>Paul and Koshy [13], 2006</td>
<td>NA</td>
<td>Multiple peritoneal parasitic myomas</td>
<td>30</td>
<td>L/S MMX</td>
<td>Yes</td>
<td>2 1/2 yr</td>
<td>3</td>
<td>Parietal peritoneum at port site</td>
<td>NA</td>
<td>Yes</td>
<td>L/S</td>
<td>Leiomymoma</td>
</tr>
<tr>
<td>Sinha et al [14], 2007</td>
<td>AUB</td>
<td>Parasitic myoma</td>
<td>40</td>
<td>L/S MMX; CD × 2</td>
<td>NA</td>
<td>5 yr</td>
<td>2</td>
<td>Under right dome diaphragm</td>
<td>5</td>
<td>Yes</td>
<td>L/S</td>
<td>Leiomymoma</td>
</tr>
<tr>
<td>Sinha et al [14], 2007</td>
<td>Pain</td>
<td>Postlaparoscopic hysterecomy disseminated Leiomyomas</td>
<td>48</td>
<td>L/S MMX, TLH</td>
<td>Unspecified</td>
<td>morcellation</td>
<td>3 yr</td>
<td>3</td>
<td>Rectovaginal septum</td>
<td>15</td>
<td>Yes</td>
<td>L/S</td>
</tr>
<tr>
<td>Sinha et al [15], 2007</td>
<td>“Symptoms of mass”</td>
<td>Same</td>
<td>41</td>
<td>CD × 2, L/S MMX, LSH</td>
<td>Unspecified</td>
<td>morcellation</td>
<td>8 mo</td>
<td>1</td>
<td>Right lateral pelvic wall</td>
<td>7</td>
<td>8 × 6</td>
<td>Yes</td>
</tr>
<tr>
<td>Takeda et al [16], 2007</td>
<td>Asymptomatic, found at routine examination</td>
<td>Parasitic peritoneal leiomyomatosis</td>
<td>39</td>
<td>Gasless L/S MMX</td>
<td>Yes</td>
<td>6 yr</td>
<td>5</td>
<td>Left broad ligament; right round ligament; left pelvic sidewall; vesicouterine pouch; Pouch of Douglas</td>
<td>1–6</td>
<td>Yes</td>
<td>Gasless L/S</td>
<td>LM, ER+/PR+</td>
</tr>
<tr>
<td>Yeh et al [17], 1999</td>
<td>Pain</td>
<td>Torsion of parasitic leiomyoma</td>
<td>33</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>1</td>
<td>Broad ligament</td>
<td>15</td>
<td>Yes</td>
<td>NA</td>
<td>Leiomyma with hemorrhagic infarction</td>
</tr>
<tr>
<td>Yeh et al [17], 1999</td>
<td>GI symptoms</td>
<td>Parasitic leiomyoma</td>
<td>34</td>
<td>Vaginal hysterectomy</td>
<td>NA</td>
<td>Unspecified</td>
<td>morcellation</td>
<td>3 mo</td>
<td>1</td>
<td>Left broad ligament</td>
<td>29 × 17</td>
<td>Yes</td>
</tr>
<tr>
<td>Agostini et al [18], 2005</td>
<td>Pain</td>
<td>Parasitic myoma</td>
<td>51</td>
<td>Vaginal hysterectomy</td>
<td>NA</td>
<td>Unspecified</td>
<td>morcellation</td>
<td>3 mo</td>
<td>1</td>
<td>Vaginal dome</td>
<td>8 × 5.5</td>
<td>Yes</td>
</tr>
</tbody>
</table>

AUB, abnormal uterine bleeding; CD, cesarean delivery; ER, estrogen receptor; GI, gastrointestinal; LLQ, left lower quadrant; L/S, laparoscopy; LSH, laparoscopic supracervical hysterectomy; MMX, myomectomy; NA, not applicable; PR, progesterone receptor; RUQ, right upper quadrant; SOB, shortness of breath; TLH, total laparoscopic hysterectomy; X-lap, exploratory laparotomy.

* Time between last surgery and diagnosis of parasitic myoma.
underwent open excision with sedation and local anesthesia. One case report did not specify the method of myoma resection. Only 1 case was managed before the widespread popularization of laparoscopic techniques [4].

The parasitic myomas ranged in greatest diameter from 1 to 30 cm. Most were located in the pelvis, although 3 were observed in the right upper quadrant near the gallbladder and liver. Three myomas were found near port sites, 1 suprafascial and 2 subfascial; all of these manifested as anterior abdominal wall masses appreciable at examination. Parasitic myomas were found most frequently parasitizing to the omentum, then to the sigmoid colon. These findings in the individual case reports are consistent with the results of our case series of 12 patients from our single institution [7].

Parasitic Myomas after Surgery

While most cases reported are associated with laparoscopic myomectomy, some cases have occurred with supracervical hysterectomy, total laparoscopic hysterectomy, and vaginal hysterectomy [9,13,18]. Unless a colpotomy is performed, both laparoscopic myomectomy and supracervical hysterectomy usually require abdominal morcellation to remove the specimens. Although “lost” fragments associated with laparoscopic resections were reported as early as 1997, including 3 myomas lost in the abdominal cavity and knowingly left behind during myomectomy [19], more likely surgeons are unknowingly leaving behind small fragments of tissue.

In the past, laparoscopic morcellation involved bivalving and fragmentation with a knife or other cutting instrument [20]; however, with the advent of laparoscopic electric morcellators in 1993, more efficient removal of tissue can be performed [21]. Despite its advantages, electromechanics morcellators fragment myomas or the uterus, and because of the rotating blade, may then seed in any area of the peritoneal cavity with small fragments of tissue. If these fragments are not identified and removed, they may then implant on any organ and form parasitic myomas (Figs. 1–3). Unlike the parasitic myomas described in the past and found in the pelvis, more recent cases describe myomas in far reaches of the peritoneal cavity including under the diaphragm [14], on the liver [19], and attached to the gallbladder [9]. In our institution’s experience with parasitic myomas, 2 were identified retroperitoneally, 1 of which was embedded in the bladder wall [7].

Not only can parasitic myomas develop from peritoneal seeding, they may also be pulled into port sites when withdrawing laparoscopic cannulas. One case described a 2.5-cm mass that was found in the scar of a suprapubic incision. Symptoms of pain at the scar site developed 2 months after laparoscopic myomectomy during which a 40-g myoma was fragmented intraabdominally and removed through the suprapubic port. The author does not indicate whether electric morcellation was used, but speculates that during fragmentation, a small fragment of myoma was stuck on the cannula sleeve, and when the sleeve was removed, the myoma was trapped in the abdominal wall incision [12].

Although they are largely found at surgery for myoma-related symptoms, parasitic myomas may manifest with symptoms. Several cases describe substantial pain, and some with peritoneal signs [4,5,8,9].

Though no cases were found in the setting of previous open myomectomy or open hysterectomy, a parasitic myoma was found to be associated with vaginal hysterectomy. In 1 case, a 140-g parasitic myoma was identified at the vaginal cuff 3 months after vaginal hysterectomy of a large uterus involving cervical amputation and vaginal morcellation [18]. Thus, parasitic myomas may not only be a risk associated with laparoscopic procedures of the uterus, but vaginal procedures as well. These minimally invasive methods attempt to extract large masses through small incisions and thereby require some form of morcellation, with the potential for fragmentation in the peritoneal cavity. Although some centers advise that morcellation be performed within an endoscopic bag to prevent seeding of fragments, this can be cumbersome and may make morcellation even more challenging. Furthermore, some minimally invasive methods,
particularly the vaginal approach and gasless laparoscopy, provide a limited view of the abdominal cavity and may thereby increase the risk of incomplete resection and leaving tissue and even entire myomas behind.

**Nonsurgical “Iatrogenic” Parasitic Myomas?**

In a pathophysiologic process such as that described by Kelly and Cullen [3], in theory, parasitic myomas may be formed by any process that restricts blood supply to the uterus. Therapeutic administration of gonadotropin-releasing hormone agonists has become increasingly popular as a temporizing method to diminish uterine volume. Restriction of blood supply is intended to occur and, thus, treat the symptoms of a myomatous uterus. Analogously, other minimally invasive procedures such as uterine artery embolization and MR(f)US are also used to manage symptomatic myomas.

At our institution, we observed 1 parasitic myomas free from the uterus after leuprolide acetate administration, and 1 after an MR(f)US procedure. After being treated with leuprolide acetate for 3 months, a 26-year-old nulliparous woman with no surgical history was found to have a 790-g myoma completely parasitized to the anterior abdominal wall [7]. Pretreatment magnetic resonance imaging revealed a 6-cm right-sided pedunculated myoma. At surgery, within 6 months of the first leuprolide acetate injection, the patient was found to have a parasitic myoma of the same approximate size as seen on the magnetic resonance image. Given the time course and imaging, we theorize that the gonadotropin-releasmg hormone agonist diminished hormonal stimulation of the uterus and thereby decreased blood supply to the pedunculated myoma. We propose that the myoma had existed in close proximity to the anterior abdominal wall, it parasitized to that area until it obtained its primary blood supply from the anterior abdominal wall, and with uterine blood supply decreased and abdominal wall supply established, the stalk of the pedunculated fibroid likely necrosed.

In a similar, not previously reported case from our institution, a 41-year-old woman who underwent MR(f)US for management of symptomatic myomas 11 months before surgery was incidentally found to have a 1.2-cm parasitic myoma on the posterior wall of the vagina. Both novel cases describe parasitic myomas in women with no surgical history, occurring after processes that restrict blood supply to the uterus. Although causality cannot be established in these cases, the association exists. No reports were found in the literature; however, it is possible that a similar process could occur with uterine artery embolization or any other intervention that would decrease uterine blood supply. Thus, with modalities that diminish blood supply to the uterus, we may observe an increasing frequency of iatrogenically formed parasitic myomas.

**Iatrogenic Nodules**

Not unrelated, leiomyomatosis peritonealis disseminata (LPD) is a rare, typically benign condition characterized by multiple peritoneal smooth-muscle, myofibroblastic, and fibroblast nodules on the peritoneal surfaces of the pelvic and abdominal cavities [22], often studding the surface of the uterus, intestines, and abdominal walls. The condition typically develops in women of reproductive age. Theories for the pathogenesis of LPD include metaplasia of pluripotent mesenchymal stem cells, which are particularly sensitive to the influence of hormonal factors [23]. Case reports of LPD associating with previous morcellation have been increasingly reported in the literature. Since 2007, at least 5 case reports of the condition have associated the development of LPD with previous laparoscopic surgery [10,15,16,21,23]. Thian et al [24] reported the case of a premenopausal woman who underwent laparoscopic myomectomy with morcellation and “slicing.” Sonographic evidence of soft-tissue masses developed within 10 months of the initial surgery. Thirty-one months after the initial laparoscopic myomectomy, the patient was found to have more than 50 soft tumor masses scattered throughout the lower abdomen, as well as a periumbilical subcutaneous parasitic myoma.

Histopathologically, LPD and leiomyoma are identical, consisting of fascicles of smooth-muscle cells without mitotic figures or nuclear pleomorphism [25]. Although LPDs have been traditionally believed to develop de novo from pluripotent stem cells, the appearance and location of these masses suggest the possibility of iatrogenic formation and seeding with morcellation. The authors point out that the clustering of LPD and parasitic myomas at the umbilicus and pelvis are consistent with “tract seeding” [24]. Another recent case report by Miyake et al [22] reports a similar finding of both myomas and LPD resected 2 and 6 years after an initial laparoscopic myomectomy involving morcellation of an 18-cm myoma. In this report, identical molecular genetic analysis patterns corroborate that the nodules and the myomas resected with the subsequent surgeries originated from a single myoma that was morcellated during the initial surgery [22]. The immunohistochemical analyses performed in this study provide further evidence for a causal relationship.
between laparoscopic morcellation and development of parasitic myomas, as well as LPD.

Discussion

Although still rare relative to the ubiquity of leiomyomas, we believe that a review of the recent literature reveals substantial potential for development of a new class of myomas, that is, iatrogenically formed myomas. While the establishment of causality requires more robust evidence than simple correlation, the totality of the case reports and case series describing parasitic myomas as well as LPD begin to illustrate something more than a trend, and the criteria of Hill [26] for the establishment of a causal relationship. Consistency, temporality, strength of association, specificity, and biological plausibility emerge when this once rare entity is examined comprehensively. The report by Takeda et al [16] illustrating histologic consistency between parasitic myomas and original myomas strengthens the evidence for a biologically plausible relationship. Furthermore, the use of molecular genetic analyses looking for identical patterns to determine the origin of parasitic myomas and LPD nodules by comparing the patterns with the original myoma not only provides more robust support but evidence for a relationship [21].

We propose the institution of a registry so that the scientific community may better understand this rare entity, its risk factors, and natural history. We also support performing hormone receptor analyses of the parasitic myomas and comparing them with the hormonal status of uterine myomas, and if possible, application of molecular genetic analyses to the parasitic tissue and the original tissues to further characterize the myomas or nodules.

If the increasing frequency of similar case reports heralds a new classification of myomas, it is beholden on us as physicians and surgeons to maintain awareness of this potential risk to our patients. Perhaps something as “benign” as inadvertently leaving behind small fragments of myoma may lead to a more sinister pathologic condition. Endometriosis, adenomyomas, cervical tissue, and even uterine cancer have been reportedly spread in the abdominal cavity after morcellation procedures [27–30].

Laparoscopic management of parasitic myomas is feasible and safe. More than half of the cases in the literature and all of our reported cases were diagnosed and managed laparoscopically. With increased magnification and access to the entire abdominopelvic cavity, a laparoscopic view may be more beneficial for diagnosis of unknown or unsuspected masses, as well as prevention.

In conclusion, meticulous surgical technique with systematic surveying of the entire cavity and complete retrieval of even small fragments of morcellated tissue should be practiced so as not to iatrogenically increase the risk of morbidity associated with parasitic myomas. Increased awareness of parasitic myomas as a pathologic entity warrants thorough exploration of the abdominopelvic cavity at surgery.

References


