Near lethal endometriosis and a massive (64 kg) endometrioma: case report and review of the literature

S.V. Sakpal, *M.D.*; **C. Patel,** *M.D.*; **R.S. Chamberlain,** *M.D., M.P.A., F.A.C.S.*

Department of Surgery, Saint Barnabas Medical Center, Livingston, New Jersey (USA)

Summary

A 51-year-old morbidly obese, hypertensive, anemic, and amenorrheic female presented with anuria and respiratory symptoms. The patient had a distinctly massive abdomen with necrotic anterior abdominal wall, and laboratory findings revealed a leukocytosis, profound anemia, coagulopathy and renal failure. An abdominal sonogram showed a large, complex intra-abdominopelvic mass and ascites. At surgery, a massive, cystic left ovarian mass, 37 l of ascitic/cyst fluid, and several peritoneal nodules were removed- a total of 64 kg of tumorous tissue. Histopathological evaluation of the mass revealed an endometrioma. We present this rare case of severe endometriosis in a morbidly obese patient who presented with an exceptionally large endometrioma (64 kg), multifactorial respiratory and renal failure, coagulopathy, and profound anemia.

Key words: Ascites; Endometriosis; Endometrioma; Renal failure.

Introduction

Endometriosis is the presence of ectopic endometrial tissue, particularly in the peritoneal cavity and adnexa. Ovarian endometriotic tissue may organize into a complex cyst-an ovarian endometrioma. Variable in size, endometriomas may very rarely exceed > 20 cm in diameter. We report an exceptionally large endometrioma (64 kg) in a 51-year-old female who presented with rare symptoms of the disease. Multiple theories have proposed likely pathophysiology of endometriosis, but the growth and development of endometriotic implants appear multifactorially regulated. In the majority of women endometriosis is asymptomatic, but some may present commonly with complaints such as dyspareunia, pelvic pain and infertility. Dyspnea secondary to ascites and/or pleural effusions is very rare in endometriosis. Characteristic ultrasound (US) findings – homogeneous, echolucent fluid-filled cyst – may suggest the diagnosis of an endometrioma, however magnetic resonance imaging (MRI) serves the same purpose with higher sensitivity, specificity and accuracy. Malignant transformation of endometrioma is extremely rare but a possibility. Hence, precise histopathological scrutiny of endometriotic tissue is essential. Both medical and/or multi-step surgical therapy may be implemented in endometriosis to alleviate symptoms, and most importantly restore fertility and prevent near-lethal complications of the disease.

Case Report

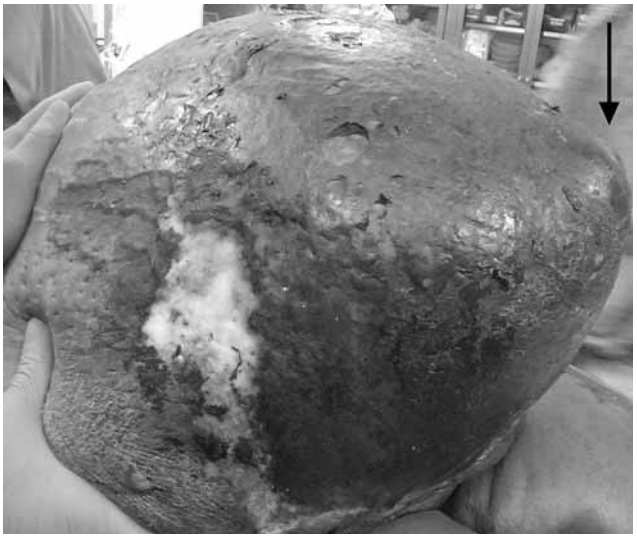
A 51-year-old morbidly obese (264 kg) African-American female was admitted with dyspnea, productive cough and anuria of three days duration. Her past medical history included hypertension treated with hydrochlorothiazide-losartan combination and hypochromic microcytic anemia secondary to a two-year history of a suspected leiomyomatous uterus that was being treated with subcutaneous erythropoietin and occasional intravenous iron. Casarean section was the only surgical procedure she underwent in the past. In addition to a leiomyomatous uterus, she reported 12 months of amenorrhea at admission as part of her gynecologic history. She refused surgical intervention and blood products on religious grounds in the past. There was no significant family history except for diabetes and hypertension. The patient denied a history of cigarette smoking, alcohol consumption or illicit drug use.

On admission, she was pale in appearance, afebrile, tachycardic (100-110 beats/min) and tachypneic (22 breaths/min). Chest examination revealed diffuse bilateral rhonchi with decreased bibasilar breath sounds. The abdomen was massive, distended and tense with significant abdominal varices. The skin over her lower abdomen was edematous and necrotic with significant seepage of serous fluid. The umbilicus was everted and necrotic over an area of 60 x 35 cm (Figures 1 and 2). Laboratory findings revealed a leukocytosis (WBC 17,200/mm^3), microcytic hypochromic anemia (Hgb 7.0 g/dl & Hct 22.9%), coagulopathy (INR 1.5), and elevated serum urea-nitrogen and creatinine levels (BUN 51 mmol/l & Cr 4.44 μmol/l). An electrocardiogram revealed sinus tachycardia. Chest roentgenography demonstrated bilaterally hypoinflated lungs with a probable right-sided infiltrate. Except for a limited abdominal US, radiological testing to evaluate intraabdominal pathology or rule out pulmonary embolism could not be performed due to her morbid obesity (264 kg). Sonogram revealed moderate, loculated ascites throughout the abdomen in addition to a large, complex, heterogenous, intraabdominal mass arising from the pelvis. Although very limited, the study revealed no evidence of apparent hydronephrosis. She was treated with hemodialysis for her acute renal failure. Broad spectrum antibiotics were started for a presumptive pneumonia/bronchitis and a necrotic anterior abdominal wall. The treatment of her coagulopathy and profound anemia was initially supportive only.

An abdominal paracentesis was performed which revealed no malignant cells in the peritoneal fluid. The patient's body habitus disqualified cystoscopic evaluation for post-renal uropathy. Though initially deferring blood products, the patient and her family decided to accept transfusion and invasive interven-

Revised manuscript accepted for publication May 8, 2008

Fig. 1



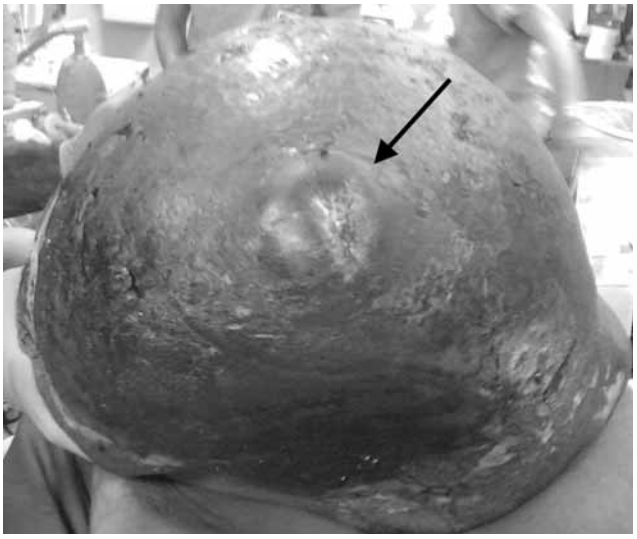


Fig. 2

Figure 1. — Right anterolateral view of the patient's massively distended abdomen with ulcerated, necrotic skin spread circumferentially over an area of 60 x 35 cm. A hard necrotic everted umbilicus is noticeable at the black arrow.
Figure 2. — Caudal to cranial view of the patient's abdomen exhibiting circumferential necrotic skin, and an everted umbilicus (black arrow) at the center.

tion. Worsening multifactorial respiratory failure, renal failure, and persistent ascites in the presence of worsening anemia led to a steep deterioration in her clinical status. Severe sepsis culminating in respiratory failure and shock led to endotracheal intubation and mechanical ventilation, as well as the administration of pressor support. Worsening acidosis (pH = 7.30), leukocytosis (WBC 48,000/mm^3) and the development of profuse vaginal bleeding, in the wake of a necrotic abdominal wall and unknown intraabdominal/pelvic pathology led to surgical exploration.

At surgery, the patient underwent a panniculectomy to excise the necrotic skin areas over the abdominal wall that extended down to the fascia (measuring 60 x 35 x 3.5 cm and weighing 4,500 g). Exploratory laparotomy revealed a massive extraperitoneal cystic mass arising from the left ovary. Extirpation of the mass without decompression was not feasible. At decompression, approximately 37 l of thick grey-brown ascitic/cyst fluid was removed. Multiple irregular, tan-red, necrotic, tumorous peritoneal nodules were excised (measuring 50 x 30 x 15 cm and weighing in excess of 9 kg). In total, tumoral tissue including ascitic fluid removed weighed 64 kg. The stage of endometriosis was thought to be IV based on R-AFS (revised-American Fertility Society) classification (Table 1).

Histopathological examination identified the mass as an ovarian cyst (endometrial glandular epithelium and stroma) with organized hemorrhage, suggesting an endometrioma. The skin, fascia and peritoneal specimens revealed inflamed, necrotic tissue with no evidence of malignancy.

Postoperatively, the patient followed a critical course complicated by a novel episode of hemorrhagic shock secondary to a bleeding duodenal ulcer requiring a second laparotomy, oversew of the ulcer bed and pyloroplasty. At that time, 7 l of new ascitic fluid was aspirated from the abdominal cavity. Right thoracostomy drainage for pleural effusion, tracheostomy, percutaneous endoscopic gastrostomy, and multiple dialysis catheter insertions and abdominal wound debridements were also performed. She was eventually discharged on tracheostomy collar tolerating full-strength tube feeds and purée diet on hospital day 57. Vacuum assisted closure (VAC) therapy was applied to the abdominal wound and a sacral decubitus.

Table 1. — *American Fertility Society's scoring system for staging endometriosis. Cumulation of points based on descriptive findings of endometriosis and adhesions determines the stage of the disease. Stage I (minimal): 1-5; Stage II (mild): 6-15; Stage III (moderate): 16-40; and Stage IV (severe): > 40. Highlighted numbers in the table represent findings in our patient.*

	Endometriosis	< 1 cm	1-3 cm	> 3 cm
Peritoneum	Superficial	1	2	4
	Deep	2	4	**6**
Ovary	R Superficial	1	2	**4**
	Deep	4	16	20
	L Superficial	1	2	4
	Deep	4	16	**20**
Posterior Culdesac obliteration			Partial 4	Complete **40**
	Adhesions	< 1/3 cm Enclosure	1/3-2/3 Enclosure	> 2/3 Enclosure
Ovary	R Filmy	1	2	4
	Dense	4	8	16
	L Filmy	1	2	4
	Dense	4	8	**16**
Tube	R Filmy	1	2	4
	Dense	4	8	16
	L Filmy	1	2	4
	Dense	4	8	**16**

Discussion

Endometriosis is the presence of ectopic endometrial tissue, particularly in the peritoneal cavity or adnexa. Although extrapelvic endometriosis is possible, it is very rare. The incidence of endometriosis is unknown, but in women undergoing evaluation for infertility and for dysmenorrhea/pelvic pain, it is approximately 30% and 40-50%, respectively [1]. Like uterine endometrium, endometriotic tissue responds to ovarian cycles. Under hormonal influence, ovarian endometriotic tissue may

organize into a complex hemorrhagic mass known as an ovarian endometrioma or commonly referred to as "chocolate cyst". Out of the two-thirds of women with endometriosis who have ovarian enlargement, only 5% are detectable on pelvic exam [2]. Endometriomas vary from 1-5 mm in diameter, superficial, blue-black implants to 5-10 cm in diameter, multiloculated cysts. Endometriomas > 20 cm in diameter are extremely rare.

The two widely accepted theories explaining the pathophysiology of endometriosis are the Sampson theory and the metaplasia theory [3]. The Sampson theory suggests that viable endometrial cells shed by retrograde menstruation into the peritoneal cavity, implant and grow within the peritoneum, whereas metaplasia explains endometriosis in an amenorrheic state. Neither of these two theories explains the growth and development of endometriotic tissue. Compartmentalized peritoneal fluid with higher than plasma concentrations of steroid hormones, along side cellular elements and their secreted cytokines, growth factors and angiogenic factors suggests a tumor mechanism – mass formation, extracellular matrix degradation and immunologic defense – in the growth of endometriotic implants. Similarly, high intraovarian concentrations of steroid hormones may be vital in the development of ovarian endometriosis via direct membrane effects of estrogens and immunosuppressive effects of progesterone. Also, enhanced expression of proteolytic enzymes, fibronectin receptors, and angiogenesis by endometriotic cells, in addition to the local ovarian and peritoneal fluid milieu may suggest a genetic contribution. Hence, development of endometriotic disease is likely multifactorial.

The majority of women with endometriomas are asymptomatic. When patients are symptomatic, dyspareunia, pelvic pain, and infertility are the most common complaints. Despite its antagonistic effects on fertility, endometriosis or endometrioma may nevertheless yield a successful pregnancy. Birken et al. reported a successful conception, pregnancy, and vaginal delivery of a third child by a mother who underwent right ovarian cystectomy (10 x 12 cm endometrioma) in the second trimester as well as left salpingo-oophorectomy for severe endometriosis in the past [4]. Severe symptoms such as abdominal distention and dyspnea are very rare with endometriomas. Dyspnea, if persisting, is usually due to pleural effusions caused by direct extrapelvic endometriotic implants and/or from abdominal distention caused by ascites in severe endometriosis. Elevated intraabdominal pressure causing transudation of transdiaphragmatic lymphatics also may result in pleural effusions. Cytological diagnosis of pleural or peritoneal endometriosis can be difficult since non-specific hemosiderin-laden macrophages may be the only cells identified [1].

Endometriomas may be solid, mixed or cystic. A homogeneous, echolucent fluid-filled cyst is a characteristic sonographic finding of an endometrioma. Although complete radiological imaging was difficult in our case, Togashi *et al.* reported that MRI enabled accurate diagnosis of 77 of 86 endometrial cysts and exclusion of diagnosis in 263 of 268 other gynecologic masses, with or without internal hemorrhage. Thus, MR imaging is an acceptable modality for endometriomas with diagnostic sensitivity, specificity, and accuracy of 90%, 98% and 96%, respectively [5]. On histopathology, endometrial columnar glandular epithelium, stroma, and hemosiderin-laden macrophages may be identified in endometriotic tissue [6]. Fibrosis from inflammation may also be seen and is usually present in symptomatic cases when the ovaries adhere to surrounding structures resulting in tender, fixed ovaries.

In many ways, symptoms of severe or extrapelvic endometriosis may mimic neoplastic disease, especially advanced ovarian malignancy. However, tumor markers such as CA-125, CEA and CA19-9 are normally not helpful in distinguishing between those entities. Interestingly, Goumenou *et al.* reported a case of endometriosis, in which the patient presented with massive ascites, pleural effusions and extremely elevated CA-125 and CA19-9 levels. Chemotherapy (carboplatin and taxol) was administered based on the presumptive diagnosis of an ovarian neoplasm, however subsequent total abdominal hysterectomy, bilateral salpingo-oophorectomy, lymphadenectomy, omentectomy, peritoneal biopsy and appendectomy revealed no evidence of malignancy [1].

Malignant transformation of endometrioma is rare but is a recognized event, with the ovaries being the most common site. Criteria for establishing the diagnosis requires 1) coexistence of carcinoma and endometriosis at the same site, 2) similar histological pattern, 3) exclusion of another malignancy elsewhere, and 4) morphologic demonstration of continuity between benign and malignant endometrioid epithelium. Moll et al. were among the first few to report a case of invasive clear-cell adenocarcinoma three years after diagnosing and treating an endometrioma containing a focus of severe epithelial atypia in the same ovary [7]. Hence, precise histopathological scrutiny of endometrioid tissue for atypia is essential.

Medical or surgical intervention, or a combination of both may be applied to the management of large ovarian endometriomas. Medical therapy involves ovarian estrogen suppression and induction of amenorrhea by using gonadotropin-release hormone (GnRH) agonists. The surgical approach may involve radiologically-guided cyst drainage, and/or open or laparoscopic cystectomy with ablation of the residual tissue as well as excision of endometriotic implants from other tissue surfaces. Brosens *et al.* have proposed a 2-step laparoscopic technique of ovarian reconstruction in large endometriomas based on the concept that typical endometriomas are extraovarian pseudocysts formed by invagination of the ovarian cortex [8]. The first step involves ovarioscopy, biopsy and pseudocyst exposure allowing spontaneous regression and eversion, followed by a second laparoscopy at two to three months involving adhesiolysis and coagulative destruction of neovascularization and implants on the exposed pseudocyst cortex. Of the (n = 18) patients (age range 26-41 years) who underwent both

steps, no recurrences were noted between 26 and 42 months of follow-up except for the development of a contralateral ovarian endometrioma in a single patient. Donnez *et al.* reported on patients with endometriosis who were initially treated with laparoscopic cyst (> 3 cm) drainage, followed by a second laparoscopy to assess endometriosis and perform CO_2 laser vaporization of the internal ovarian cyst wall (site of active implants). In between these two procedures, patients were administered a 12-week regimen of GnRH agonist. They reported a significant decrease in the number and size of endometriotic implants, and a pregnancy rate of > 51% (majority in first 10 months after surgery) in patients followed-up for a period of two to 13 years [9].

As mentioned earlier, endometriomas > 20 cm in diameter are extremely rare. Our extensive literature search revealed only a handful (n = 3) of super-sized endometriomas. Roth *et al.* reported on a large left ovarian endometrioma (18 x 11 x 5 cm) in an adolescent girl [10], and Reuter *et al.* reported a large right ovarian endometrioma (measuring 20 x 30 cm and weighing 2,750 g) in a premenopausal woman [6]. A right ovarian endometrioma (measuring 24 x 15 x 15 cm and weighing 3,121 g) in a postmenopausal woman published by Bellina *et al.* was the largest until now [11]. In the case presented, the endometrioma measured 89 x 76 cm prior to decompression and weighed a mammoth 64 kg. No similar instance of such an oversized – both in weight and size – endometrioma has ever been reported.

Conclusion

Endometriosis although asymptomatic in the majority may exhibit severe, progressive symptoms in rare instances. In our morbidly obese patient, an enormous endometrioma and associated ascites that initially presented with dyspnea and anuria led to extreme clinical deterioration. The result was almost lethal-septic shock, mutifactorial respiratory failure, renal failure, anemia and coagulopathy. Although infeasible in our case, a precise diagnosis of endometriosis with radiological diagnostic modalities (US or MRI) and biopsy is essential since it most commonly affects women of reproductive age. Despite its rarity, malignant degeneration of an endometrioma is also a possibility and must be excluded. Hence, accurate histopathological scrutiny is vital. Defining the extent of endometriotic progression may help stage the disease and categorize the patients (Table 1). Accordingly then, implementing appropriate and timely therapeutic interventions – GnRH agonist administration or multi-step surgical therapy, or a combination of these – may not only prevent lethal complications, but also decrease disease recurrence and restore fertility. We believe self-neglect and the reluctance to accept medical and surgical intervention previously led to an aggressive and severe progression of endometriosis in our patient. We recommend early diagnosis followed by necessary treatment to avoid severe, near-lethal complications that may arise from this disease.

References

[1] Goumenou A., Matalliotakis I., Mahutte N., Koumantakis E.: "Endometriosis mimicking advanced ovarian cancer". *Fertil. Steril.,* 2006, *86,* 219.
[2] Lobo R.: "Endometriosis: etiology, pathology, diagnosis and management". In: Comprehensive Gynecology, 5th ed. Katz V.L., Lentz G.M., Lobo R., Gershenson D.M. Philadelphia: Mosby-Elsevier, 2007, 473.
[3] Koninckx P.R., Kennedy S.H., Barlow D.H.: "Pathogenesis of endometriosis: the role of peritoneal fluid". *Gynecol. Obstet. Invest.,* 1999, *47,* 23.
[4] Birken R.A., Stern S.E., Halipoto M.H.: "Case report: large endometrioma in pregnancy". *Tex Med.*, 1982, *78*, 50.
[5] Togashi K., Nishimura K., Kimura I., Tsuda Y., Yamashita K., Shibata T. *et al.*: "Endometrial cysts: diagnosis with MR imaging". *Radiology*, 1991, *180,* 73.
[6] Reuter K.L., Davidoff A., Cooney J.V., Hunter R.E.: "An unusually large endometrioma simulating an ovarian malignancy". *Am. J. Roentgenol.,* 1988, *151,* 834.
[7] Moll U.M., Chumas J.C., Chalas E., Mann W.J.: "Ovarian carcinoma arising in atypical endometriosis". *Obstet. Gynecol.*, 1990, *75*, 537.
[8] Brosens I.A., Van Ballaer P., Puttemans P., Deprest J.: "Reconstruction of the ovary containing large endometriomas by an extraovarian endosurgical technique". *Fertil. Steril.,* 1996, *66,* 517.
[9] Donnez J., Nisolle M., Gillet N., Smets M., Bassil S., Casanas-Roux F.: "Large ovarian endometriomas". *Hum. Reprod.,* 1996, *11,* 641.
[10] Roth M.S., Goodner D.M.: "Large endometrioma occurring in an adolescent". *Obstet. Gynecol.,* 1977, *49,* 364.
[11] Bellina J.H., Schenck D.: "Large postmenopausal ovarian endometrioma". *Obstet. Gynecol.,* 2000, *96,* 846.

Address reprint requests to:
R.S. CHAMBERLAIN, M.D., M.P.A., F.A.C.S.
Chairman & Sureon-in-Chief
Surgery, Saint Barnabas Medical Center
Livingston, New Jersey 07039 (USA)
e-mail: rchamberlain@sbhcs.com