

Hepatic endometrioma: a case report and review of the literature: report of a case

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Abstract Hepatic endometriosis has an extremely rare occurrence characterized by the presence of ectopic endometrium in the liver. A diagnosis of hepatic endometriosis is established after surgery. A 51-year-old multiparous female was referred to our unit for investigation of a liver tumor. The patient reported a 6-month history of epigastric pain and vomiting. She had undergone conservative hysterectomy for uterine leiomyomas several years earlier. The results of liver function tests and the levels of tumor markers (CA 19.9, CEA, CA125, α FP) were normal. Radiological imaging (USS, CT and MRI) suggested the presence of liver cystadenoma, liver cystadenocarcinoma or cystic metastasis of the liver in the left liver lobe extending to the diaphragm with left hepatic vein compression. Laparotomy was performed. The intraoperative frozen sections suggested a diagnosis of endometriosis. Anatomical resection was performed, including left lobectomy with diaphragm resection. The final histology confirmed the presence of hepatic endometrioma without malignant transformation. Fourteen cases of hepatic endometrioma have been described in the medical literature. We herein report the 15th case. Making a

preoperative diagnosis of hepatic endometriosis is very difficult, despite conducting a complete investigation, in the absence of clinical and radiological characteristics. The diagnosis is made according to a histological examination of the whole surgical sample.

Keywords Endometriosis · Cyst · Hepatic endometrioma

Introduction

Endometriosis is a common, benign, estrogen-dependent, chronic gynecological disorder associated with pelvic pain and infertility. It is characterized by the presence of ectopic endometrial tissue [1]. Endometriosis is usually confined to the pelvis and reproductive organs. However, endometriotic lesions have also been described to occur in several remote sites, including the omentum, gastrointestinal tract, umbilicus, lungs, kidneys, pancreas and liver [2–6]. Hepatic endometriosis has an extremely rare occurrence characterized by the presence of ectopic endometrium in the liver. An extensive review of the literature showed that only 14 cases of hepatic endometriosis have been previously reported. We herein report the 15th case of intraparenchymal endometriosis of the liver in a postmenopausal female who presented with epigastric pain and vomiting. Making a preoperative diagnosis of hepatic endometriosis remains difficult, despite performing a complete investigation, due to the absence of specific clinical and radiological characteristics. A diagnosis of hepatic endometriosis is established after surgery.

Case report

A 51-year-old multiparous female was referred to our unit for investigation of a liver tumor. The patient reported a

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6-month history of epigastric pain and vomiting. She had undergone conservative hysterectomy for uterine leiomyomas several years earlier. Her ovaries were normal and left in place. Laparotomic and histological examinations did not find any endometriotic lesions. The patient was not currently undergoing menopause. The symptoms were not related to menses.

A physical exam revealed epigastric pain without any palpable masses. There were no other symptoms. Serological tests for hepatitis B and C were negative. The results of liver function tests and the levels of tumor markers (CA 19.9, CEA, CA125, α FP) were normal. An abdominal ultrasound scan revealed the presence of an 80 × 75 mm intraparenchymal hepatic necrotic tumor, while Doppler did not show any intratumoral vascularization. A computed tomography scan (Fig. 1) showed one well-limited, hypovascularized, cystic mass in the left liver lobe extending to the diaphragm with left hepatic vein compression and hemorrhagic contents in the lumen. No septation was observed. Magnetic resonance imaging (Fig. 2) showed a cystic mass in segments II and III of the liver with a high T1 signal and a heterogeneous T2 signal. Biopsies revealed necrotic tissue without malignant cells. The preoperative diagnosis included liver cystadenoma, liver cystadenocarcinoma or cystic metastasis of the liver.

A laparotomy was performed, which revealed a large cystic tumor in segments II and III with diaphragmatic infiltration. An abdominal cavity exploration revealed no other pathologic events. The intraoperative frozen sections suggested a diagnosis of endometriosis. Anatomical resection was performed, including left lobectomy with diaphragm resection. The patient's postoperative course was uneventful. After 6 months of follow-up, the patient was asymptomatic.



Fig. 1 Hepatic CT scan showing a cystic mass, hypovascularized, in the left liver lobe with a left hepatic vein compression, extending to the diaphragm

Macroscopy revealed a unilocular, encapsulated, cystic mass measuring 8 × 4.5 × 4 cm with an irregular border and hemorrhagic contents (Fig. 3).

On microscopic examination, we observed a thick fibrous capsule with residual hepatocytes and a ductular reaction. A cystic component was observed lined by cylindrical epithelium without atypia. The hemorrhagic-like contents corresponded to endometrial tissue with irregularly dispersed, occasionally cystic endometrial glands with

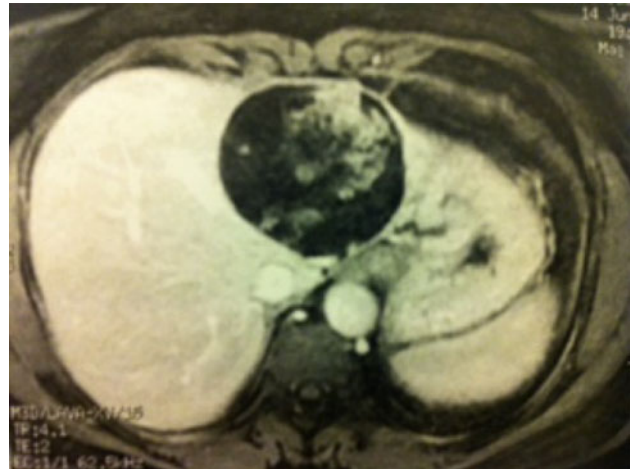


Fig. 2 Magnetic Resonance Magnetic (MRI) showing a cystic mass in segments II and III of the liver with hemorrhagic contents in the lumen



Fig. 3 Macroscopic examination of the liver tumor: under the liver capsule was observed an 8 × 4 × 4.5 cm cystic mass with a hemorrhagic content and an irregular fibrous capsule

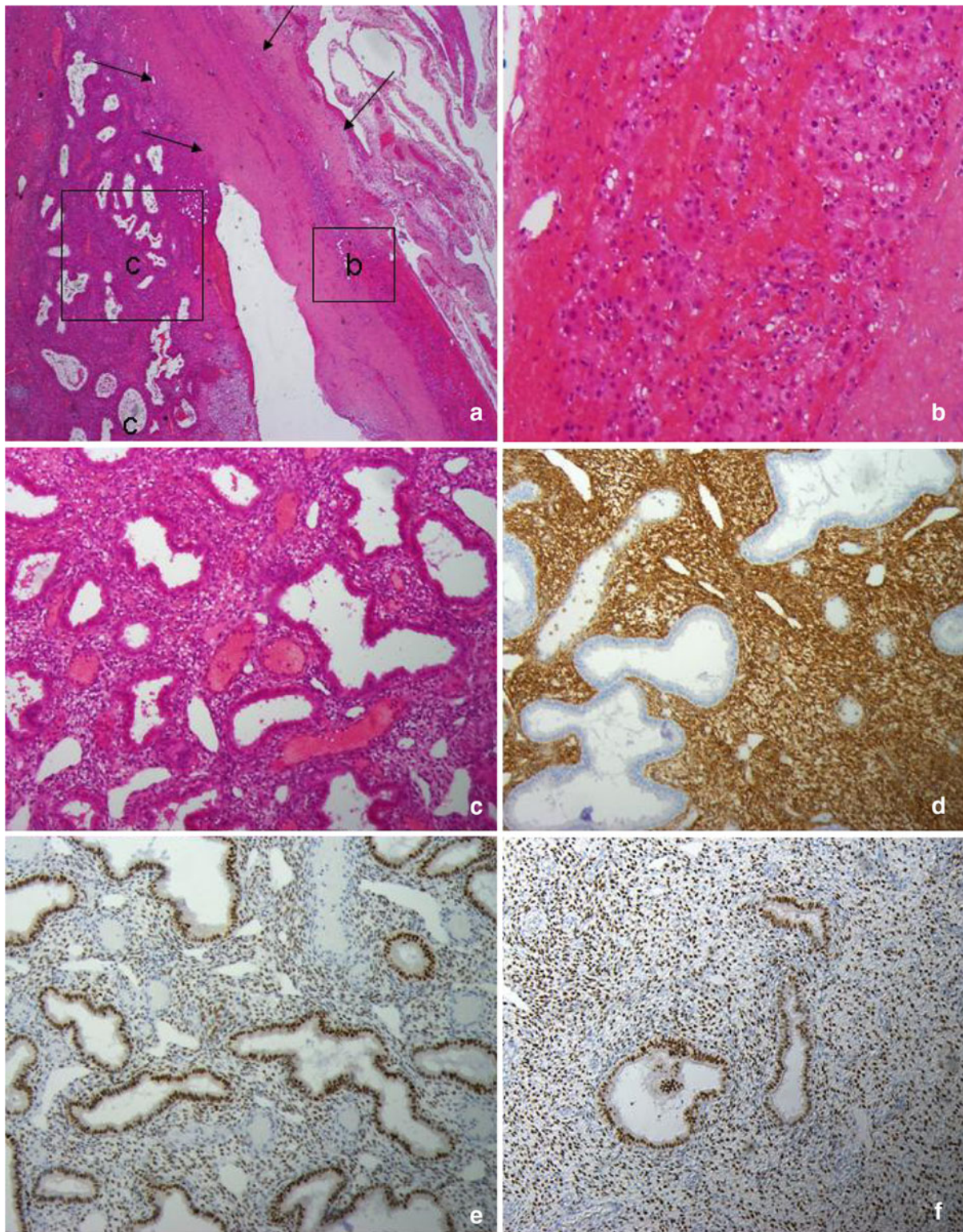


Fig. 4 Microscopic examination of the endometriosis cyst of the liver: at microscopic examination, we observe a fibrous capsule (**a**, *arrows*) with a ductular reaction, residual hepatocytes (**b**) and minimal lymphocyte infiltration. The solid hemorrhagic content of the cyst corresponded to endometrial tissue with irregularly dispersed

endometrial glands (**c**) and characteristic stroma positive for CD10 immunostaining (**d**). Moreover, endometrial and stromal cells expressed both estrogen receptors (**e**) and progesterone receptors (**f**). No hyperplasia no atypia was observed in epithelial or stromal component

Table 1 Feature of reported cases of hepatic endometriosis in literature

References Author/year	Age (year)	Localisation	Appearance	Tumour size (mm)	Symptoms	Endometrial history and treatment	Treatment
Finkel et al. [10]	21	Left lobe	Solitary cystic mass	130	Epigastric pain, RUQ pain	Yes, removal fallopian tube cyst	Cyst enucleation
Grabb et al. [5]	21	Left lobe	Solitary unilocular cystic mass	135	Epigastric pain, nausea, vomiting, hepatomegaly with right subcostal mass	No	Deroofing + danazol
Case 3 (1990)	37	Left lobe	Solitary multilocular cystic mass	100	Epigastric pain and mass	Yes, but no treatment	Left lateral segmentectomy + danazol
Case 4 (1996)	34	Right lobe	Solitary mass	120	Acute abdominal pain	No	Hemihepatectomy
Case 5 (1996)	62	Left lobe	Solitary cystic mass	120	Rightsided epigastric pain	No	Excision
Case 6 (1998)	60	Right lobe, falciform ligament	Two cystic masses	31 x 20 28 x 28	RUQ tenderness	Yes, HBSO	Left hepatectomy, excision
Case 7 (1998)	40	Left lobe	Cystic mass	64	Asymptomatic	Yes, ovarian cystectomy	Segmentectomy
Case 8 (2000)	25	Right lobe	Cystic mass with septations (CT scan)	50	Pelvic pain	Yes, medical treatment	Danazol
Case 9 (2002)	56	Left lobe	Solitary multilocular cystic mass (CT scan)	90 x 60	Epigastric pain, tender right upper abdominal mass	Yes, HBSO	Left hepatectomy
Case 10 (2002)	59	Right lobe	Large mass lesion (CT scan)	100 x 90	RUQ pain + hepatomegaly	Yes, removal of ruptured cyst, HBSO	Right hepatectomy
Case 11 (2002)	31	Bilobar	Multi-lobular mass lesions (CT scan)	100 x 50	Malaise, jaundice, abdominal distension	Yes, HBSO + HRT	En bloc removal of right lobe
Case 12 (2009)	48	Left lobe	Cystic mass, complex spetae (CT scan)	111 x 130	Chronic RUQ pain and tenderness	Yes, HBSO	Non anatomical resection
Case 13 (2011)	25	Right lobe	Irregular rounded hemorrhagic area (laparocopy)	60 x 50	RUQ pain and slight tenderness	No	Danazol
Case 14 (2011)	39	Right lobe + right basal lobe of the lung	Inhomogeneous mass (CT scan + MRI)	68 x 23	RUQ pain and chest pain, cough and biliary sputum	No	Segmentectomy and pulmonary wedge resection
Rivkine et al./2011 present case	41	Left lobe	Heterogeneous solitary cystic mass (CT scan)	80	Epigastric and shoulders pain	No	Left lobectomy + decapeptyl

RUQ right upper quadrant, *HRT* hormone replacement therapy, *HBSO* hysterectomy and bilateral salpingo-oophorectomy

characteristic endometrial stroma immunostained with CD10 (Fig. 4). The stromal and epithelial cells expressed estrogen and progesterone receptors. The epithelial cells were positive for CK7 and negative for CK20. No epithelial hyperplasia, atypia or invasive carcinoma was observed in the numerous examined tumor samples. The upper part of the capsule was adherent to the diaphragm.

We concluded the diagnosis to be hepatic endometrioma without malignant transformation.

Discussion

Endometriosis is an estrogen-dependent disease that affects 5–10 % females of reproductive age in the United States [1]. Its defining feature is the presence of ectopic endometrial tissue. The histological features include the presence of endometrial glands and stroma with frequent inflammatory reactions and intramacrophagic iron deposits [7].

Endometriosis has been reported to be more likely to occur in the pelvic organs (ovaries, fallopian tubes, uterosacral ligaments, Pouch of Douglas). The gold standard for diagnosing pelvic disease is surgical assessment, and a scoring system has been developed to assess the extent of disease. Endometriosis has been described as occurring in every part of the body (heart, lungs, kidneys, gastrointestinal tract, diaphragm, legs, bones, incisional scars, umbilicus, liver), [8, 9] except the spleen [3]. The first case of intraparenchymal endometriosis of the liver was reported by Finkel [10].

The pathogenesis of endometriosis remains unknown. Different theories have been proposed, including retrograde menstruation, coelomic metaplasia, altered cellular immunity, metastasis, a genetic basis, an environmental basis, and a multifactorial mode of inheritance with interactions between specific genes and the environment [11, 12]. Retrograde menstruation causing transcoelomic spread and consequent invasion within the pelvis could explain most observed lesions, especially those in the pelvis. However, this theory cannot explain distant or intraparenchymal liver lesions. Therefore, another theory has been raised involving venous and lymphatic dissemination of endometrial tissue to distant sites of implantation and the formation of intraparenchymal lesions. A third theory implicates iatrogenic injury after pelvic surgery for endometriosis followed by secondary dissemination [13–15]. A fourth theory, that of coelomic metaplasia, suggests that endometriosis develops from secondary Müllerian systems that result from metaplasia of the embryologic coelomic epithelium [16, 17].

The increased cell survival, inflammation and deficient differentiation that occur in endometriosis have been linked

to a stromal cell defect involving excessive formation of estrogen and prostaglandin in addition to progesterone resistance, all of which originate from two distinct epigenetic changes that affect the transcription factor SF1 and estrogen receptor β [6]. A working model is clinically relevant because targeting aromatase, COX-2, estrogen receptor β and progesterone receptors reduces pelvic pain and ablates visible endometriotic tissue [7, 18]. Serdar et al. [7] speculate that a genetic predisposition or exposure to environmental toxins by fetal progenitor cells destined to form adult female pelvic organs may result in epigenetic events, including promoter hypomethylation and the overexpression of SF1 and estrogen receptor β , which can play critical roles in the pathogenesis of endometriosis.

The first case of intraparenchymal endometriosis of the liver was reported by Finkel [10]. The patient was a 21-year-old female who complained of epigastric pain, nausea and vomiting. She was found to have an endometrial cyst measuring 13 cm in the left lobe of the liver. Since then, 13 cases have been described in the medical literature. We herein report the 15th case. In our case, the patient did not have a past of endometriosis; however, she had undergone hysterectomy for uterine leiomyomas several years previously and presented with a cystic mass measuring 8 cm in the left lobe of the liver. In this context, the most probable pathogenesis of endometriosis is a multifactorial mode of inheritance with interactions between specific genes and the environment with diffusion of endometrial cells. All cases of hepatic endometrioma are listed in Table 1. An analysis of this series reveals that hepatic endometriomas present with symptoms (93.33 %) corresponding to a cystic mass in all patients (100 %), unclear (86.67 %), measuring more than 5 cm (93.33 %) or more than 10 cm (53.33 %), often localized in the left lobe of the liver (53.33 %).

Consequently, we propose the following description of hepatic endometrioma: a symptomatic tumor occurring in young females that is a voluminous, cystic mass of the liver that must be considered in the differential diagnosis of cystic liver masses, particularly in patients with known endometriosis.

Hepatic endometrioma is an extremely rare lesion. Making a preoperative diagnosis of hepatic endometriosis is very difficult, despite conducting a complete investigation, in the absence of clinical and radiological characteristics. A diagnosis of hepatic endometriosis is established after surgery. The diagnosis is made according to a histological examination of the whole surgical sample.

This is the 15th case of hepatic endometrioma reported in the literature. The pathogenesis of the disease is unclear and requires elucidation with further clinical and experimental investigations. The clinical, biological and morphological characteristics of the disease need to be reported

in the literature to allow for the creation of a better diagnostic approach. We propose the systematic use of intraoperative frozen sections to avoid radical hepatectomy in order to decrease morbidity and mortality.

A diagnosis of endometriosis must be considered in the differential diagnosis of cystic liver masses, particularly in patients with known endometriosis.

Conflict of interest The authors declare that they have no conflicts of interest to report.

References

- Giudice LC, Kao LC. Endometriosis. *Lancet*. 2004;364:1789–99.
- Bergquist A. Extragenital endometriosis, a review. *Eur J Sci*. 1992;158:7–12.
- Markham SM, Carpenter SE, Rock JA. Extrapelvic endometriosis. *Obstet Gynecol Clin Am*. 1989;16:193.
- Marchevsky AM, Zimmerman MJ, Aufses AH Jr, et al. Endometrial cyst of the pancreas. *Gastroenterology*. 1984;86:1589–91.
- Grabb A, Carr L, Goodman JD, et al. Hepatic endometrioma. *J Clin Ultrasound*. 1986;14:478–80.
- Khan AW, Craig M, Jarmulowicz M, Davidson BR. Liver tumours due to endometriosis and endometrial stromal sarcoma. *HPB*. 2002;4(1):43–5.
- Serdar E, Bulun MD. Endometriosis. *N Engl J Med*. 2009;360:268–79.
- Saleh N, Daw E. Endometriosis in non-gynecological sites. *Practitioner*. 1980;244:1189–95.
- Sataloff DM, La Vorgna KA, McRarland MM. Extrapelvic endometriosis presenting as a hernia: clinical reports and review of the literature. *Surgery*. 1989;105:109–12.
- Finkel L, Marchevsky A, Cohen B. Endometrial cyst of the liver. *Am J Gastroenterol*. 1986;81:576–8.
- Sampson JA. Ovarian hematomas of endometrial type (perforating hemorrhagic cysts of the ovary) and implantation adenomas of endometrial type. *Boston Med Surg J*. 1922;186:445–73.
- Sampson JA. Peritoneal endometriosis due to menstrual dissemination of endometrial tissue into the peritoneal cavity. *Am J Obst Gynecol*. 1927;14:442–69.
- Marik JJ. Endometriosis etiology. *J Reprod Med*. 1997;19:301–2.
- Malick JE. The etiology of endometriosis. *J Am Osteopath Assoc*. 1982;81:407.
- Ridley JH. The histogenesis of endometriosis. *Obstet Gynecol Surv*. 1968;23:1.
- Suginami H. A reappraisal of the coelomic metaplasia theory by reviewing endometriosis occurring in unusual sites and instances. *Am J Obstet Gynecol*. 1991;165:214–8.
- Ferguson BR, Bennington JL, Haker SL. Histochemistry of mucosubstances and histology of mixed mullerian pelvic lymph node glandular inclusions: evidence for histogenesis by mullerian metaplasia of coelomic epithelium. *Obstet Gynecol*. 1969;33:617.
- Harris HA, Bruner-Tran KL, Zhang X, Osteen KG, Lyttle CR. A selective estrogen receptor-beta agonist causes lesion regression in an experimentally induced model of endometriosis. *Hum Reprod*. 2005;20:936–41.