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Case Report

Primary umbilical endometrioma: Analyzing the pathogenesis of endometriosis from an unusual localization

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ABSTRACT

Objective: This report presents a rare case of symptomatic primary umbilical endometriosis and reviews the literature on the topic with the aim to clarify some questions on the origin of endometriosis.
Case report: A 33-year-old woman with cyclic umbilical bleeding was found to have umbilical endometriosis. She had no history of pelvic or abdominal surgery. There was no past history of endometriosis or endometriosis-associated symptoms. An omphalectomy was performed after explorative laparoscopy to carefully inspect the abdominopelvic cavity and assess any coexisting pelvic endometriotic lesions. Histological examination confirmed the diagnosis of umbilical endometriosis.
Conclusion: Umbilical endometriosis is a rare but under-recognized phenomenon. Primary lesions are difficult to recognize, but probably represent an independent nosological entity. The possibility of endometriosis must be considered during the evaluation of an umbilical mass despite the absence of previous surgery. Complete excision and successive histology are highly recommended.

Introduction

Endometriosis is an elusive chronic disease caused by the growth of functional endometrial-like tissue outside the uterus, which in turn causes infertility and pelvic pain, and affects up to 10% of women of reproductive age [1]. Most commonly, the condition affects pelvic organs, however, among all diagnosed endometriosis, 12% are encountered at extragenital sites, such as the lungs, diaphragm, or umbilicus [2,3]. Umbilical endometriosis is a rare entity, first described in 1886; since then, approximately 100 cases have been reported in the medical literature [4]. It has an estimated incidence of 0.5–1% of all patients with extragenital endometriosis [5], and this percentage includes both secondary scar-related and spontaneous primary forms. The former, usually associated with pelvic endometriosis, is most often found in old surgical scars with direct seeding after laparotomy or laparoscopy, which has been proposed as the pathogenesis. By contrast, the spontaneous primary umbilical variety, considered much less common than the iatrogenic form, is not associated with previous abdominal or uterine surgery, and, to date, has an unclear origin [6].

We present an uncommon case of spontaneous umbilical endometriosis without peritoneal involvement, treated with laparoscopy-assisted radical surgery. In addition, a review of the literature on the topic is offered.

Case report

A 33-year-old woman presented with a 6-month history of spontaneous catamenial bleeding from the umbilicus. The patient had no history of abdominal or uterine surgery or trauma to her umbilicus, and had a spontaneous vaginal delivery. There was no past history of endometriosis or other endometriosis-associated symptoms. She did not use any oral contraception and had a regular menstrual cycle. On physical examination, conducted in the premenstrual period, there was a 1-cm solid, painful, reddish nodule at the surface of her umbilicus (Fig. 1A). There were no signs of infection. Preoperative workup included a transvaginal

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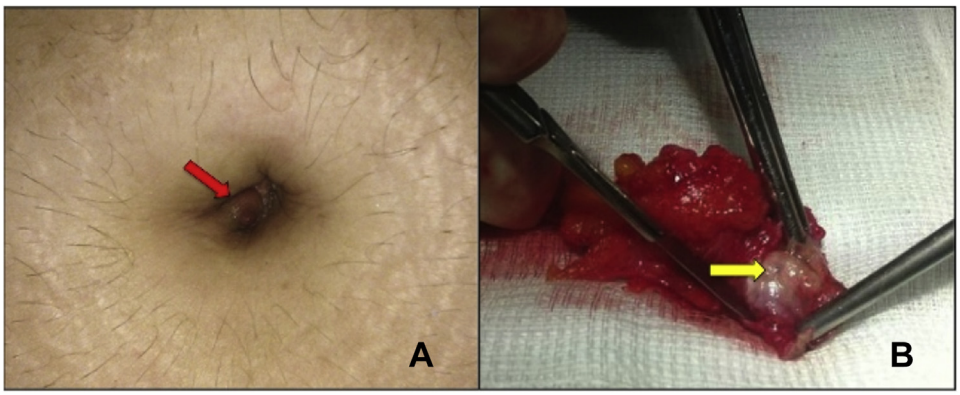

Fig. 1. Endometriosis of the umbilicus: (A) preoperative appearance of the umbilical endometriotic nodule (red arrow) and (B) excised tissue; yellow arrow shows a focal pigmented area.

ultrasound scan (US), and abdominopelvic and abdominal wall magnetic resonance imaging (MRI). At transvaginal US, the uterus and both ovaries appeared normal. Transcutaneous US showed a 0.8-cm well-defined, oval-shaped hypoechogenic area, apparently not involving the entire umbilicus but extending 2 mm below the skin surface. An initial differential diagnosis included umbilical granuloma, simple inclusion cyst, or benign or malignant neoplasm of the umbilicus. MRI confirmed the normality of the genital tract and abdominal organs, and revealed a small, poorly defined hypervascular umbilical nodule, in both T1- and T2-weighted sequences. Tumor marker cancer antigen 125 was negative. A lesion biopsy confirmed the suspected diagnosis of umbilical endometriosis. Therefore, it was decided to perform surgical excision after explorative laparoscopy, to carefully inspect the abdominopelvic cavity, and assess and treat any coexisting pelvic endometriotic lesions. The patient consented to surgical resection of the umbilical endometriosis after being fully informed of the associated risks and complications.

Surgical technique

A Veress needle was inserted along the left midclavicular line, and adequate pneumoperitoneum was obtained. A 5-mm trocar was inserted in the same site and, with a 5-mm optics, the pelvis and the upper abdomen were examined. No suspicious lesions, endometriotic or otherwise, were identified. Following the laparoscopic procedure, an omphalectomy was performed; the navel was excised *en bloc* including the nodule, fascia, and peritoneum (Fig. 1B). The peritoneum and fascia were then sutured, prior to fixation of the periumbilical skin to the latter. The skin was closed using interrupted absorbable sutures.

Histological examination confirmed the diagnosis of umbilical endometriosis. Microscopically, a typical area of endometriosis consisting of endometrial-type glands and stroma was seen. Additional immunohistological stains were performed (CK7+, CK20−, CD10+, ER+, and PR+) to support the histological finding of endometriosis (Figs. 2–4). Follow up consisted of assessment at 1 month and re-examination at 6 months. No relapses of the umbilical lesion have occurred, and, to date, the patient is asymptomatic with a normal umbilicus. Considering the risk of recurrence, she was invited to undergo periodic follow up.

Literature review

A review of the medical literature on spontaneous umbilical endometriosis from 1990 to 2013 was carried out. To this end, a PubMed electronic database search was initiated, using the following key words: endometriosis, umbilical nodule, umbilical endometriosis, primary umbilical endometriosis, and spontaneous umbilical endometriosis. All pertinent English-language articles

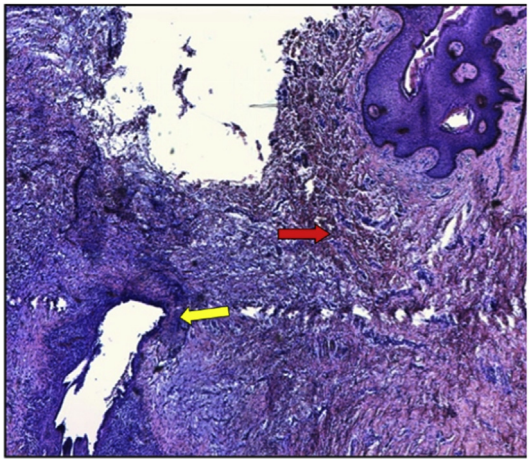

Fig. 2. Histological examination demonstrated endometrial gland surrounded by endometrial stroma (yellow arrow) beneath the squamous epithelium of the skin (red arrow) (hematoxylin and eosin, 4×).

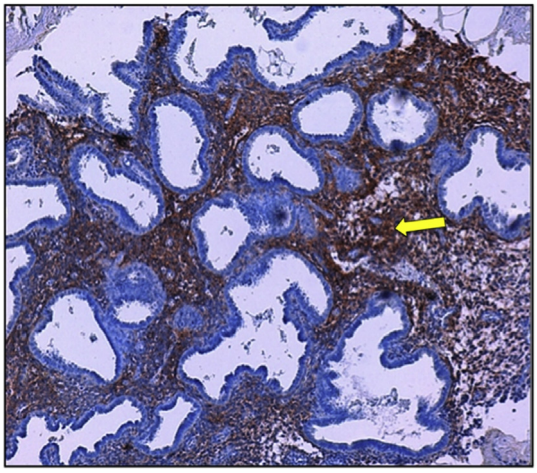

Fig. 3. Endometrial stroma diffusely positive for CD10 (yellow arrow) (immunohistochemical, 10×).

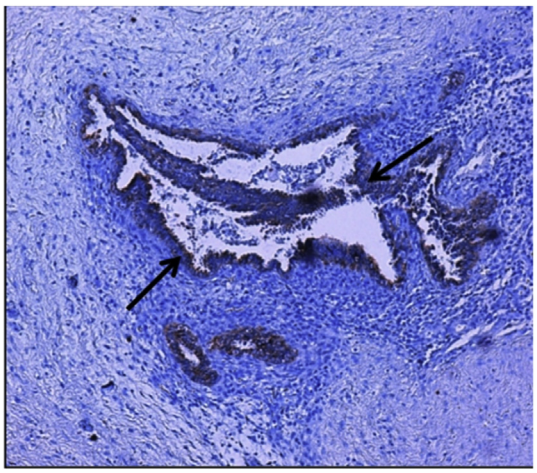

Fig. 4. Endometrial glands with positivity to CK7 (black arrows) (immunohistochemical, 10×).

were retrieved. Studies published prior to the year 1990 were excluded, as papers were sparse and often did not provide specific intraoperative and/or histological information. The following exclusion criteria were used: (1) previous abdominal surgery for caesarean section, gynecological disease, or general disease; (2) personal surgical history unspecified and therefore uncertain; and (3) lacking or nonspecific histological diagnosis. Seventeen articles were excluded (8 for previous abdominopelvic surgery, 2 for personal surgical history unspecified, and 7 for nonspecific histological diagnosis).

Our review identified and included 45 published studies [2,7–50]: 39 studies were single case reports, four articles referred two cases each, and only two articles reported on a case series of three women. The main results of these studies are shown in Table 1. In all considered cases, the authors found endometrial tissue compatible with benign endometriosis (histologically confirmed). The median size of the umbilical lesions was 18 mm. Based on all the cases (including those from our report), we found 47 (88.7%) symptomatic cases (95% CI, 78–95%); the most common symptoms were intermittent pain at the umbilical region (66.0%) and cyclic bleeding from the umbilical site (43.3%). The mean time between the appearance of symptoms and diagnosis was 28.8 months. In 11 cases (20.7%), there were pelvic and umbilical endometriotic lesions.

Discussion

Endometriosis is classically defined as an estrogen-dependent disorder, with the presence of endometrial tissue outside of the uterus in lesions of varying sizes and appearance. However, it is much more complicated than this, and because of this complexity, there are still many controversial aspects to be clarified [1,51,52].

The etiology of endometriosis is one such controversy. Several theories have been proposed, but none can explain the phenomenon adequately. The “hypothesis of migratory pathogenesis” is the most widely accepted theory; it postulates the spread of endometrial tissue by retrograde menstruation and implantation of endometrial cells into the peritoneal surface of pelvic organs [53]. Following this thought, authors suggest the use of hormonal therapy, thus decreasing or eliminating menstrual bleeding to reduce the probability of recurrence after surgery or peritoneal reimplantation [51,54]. Distinguishing between primary and secondary development of umbilical endometriosis may be relevant for understanding the pathophysiology.

The spread and subsequently proliferation of endometrial cells implanted in surgical scars after laparotomy or laparoscopic surgery or in episiotomy scars, represents the event causing the “iatrogenic form”; it is the major etiologic pathway leading to secondary umbilical endometriosis [6,13,55]. The primary umbilical localization obviously cannot be explained by this theory. This apparent discrepancy may be resolved by considering the existence of different forms of endometriosis originated through different pathogenic mechanisms, associated with the same histological appearance.

The hypothesis of origin of extragenital endometriosis by endometrial cells, which enter the uterine venous circulation and can then reach the brain, nasal mucosa, or spinal intradural [56–58], best explains distant sites of endometriosis. The theory of peritoneal mesothelial cells of coelomic origin, which undergo a metaplastic transformation into endometrial cells, would explain the exceptional formation of foci in the bladder and prostate of males [59]. With regard to primary umbilical endometriosis, in cases in which a simultaneous pelvic endometriosis is present (estimated from our review to be 20%), local inflammation surrounding the ectopic implants can favor the shedding of endometriotic cells, which may be transported to the umbilicus [18,23].

In cases of isolated umbilical endometriosis, the disease might arise from metaplastic changes of urachal remnants, as recently described by Mizutani et al [47]. Another possibility involves the funicular cord at birth: after delivery, the resected umbilical cord may easily be contaminated by endometrial cells freed during the stages of childbirth and in those immediately following, with a mechanism similar to that observed and reported in literature during cesarean sections, laparoscopy, and amniocentesis [60].

Primary umbilical endometriosis has a typical presentation: patients describe a firm, pigmented, or bluish nodule with pain and tenderness associated with cyclic bleeding or discharge from the umbilicus during menses [18,19,27]. However, all these pathognomonic symptoms are not usually present, and there are also totally asymptomatic cases. Investigation for the diagnosis of umbilical endometriosis is not a definite diagnostic tool. Reports have shown that transcutaneous US and MRI may reveal the relationship between the mass and the surrounding tissue, and are useful in the differential diagnosis with cysts, hernias, and hematomas [22]. Differential diagnosis of umbilical endometriosis may be difficult and should include hernia, urachal lesions, various granulomas, and more ominous entities such as metastatic carcinoma or melanoma [4,27]. Often, it is necessary to seek advice from a general surgeon.

Umbilical endometriosis may sometimes resemble a black or brown pigmented nodule assuming the characteristics of melanoma, and, in this case, epiluminescence microscopy (dermoscopy) can be helpful in improving the accuracy of diagnosis [34]. Finally, computed tomography characterization can confirm the lack of subfascial involvement. Additionally, CEA and CA125 tumor markers levels are often elevated, secondary to the presence of pelvic lesions. Histological analysis is the gold standard for diagnosis, and immunohistochemical stains of the estrogen and progesterone receptors can be used to resolve diagnostic dilemmas. Fine needle aspiration and percutaneous biopsy may be helpful if endometriosis is suspected, however, researchers report undiagnostic aspiration rates as high as 75% [27]. Excisional biopsy is more efficient [61].

The risk of malignancy from umbilical endometriosis is reassuringly low [61]. There is one reported case of an umbilical endometrioma with malignant transformation [62]; a second patient was noted to have endometriosis coexisting with endometrial adenocarcinoma that had metastasized to the umbilicus, a finding that was noted only at the time of surgery for the known endometrial malignancy [61].

Table 1
Review of the literature on primary umbilical endometriosis.

References	Cases	Presenting symptoms	Onset of symptoms (mo)	Umbilical treatment (associated surgery)	Lesion size (mm)	Endometriotic lesions associated
Igawa et al [7]	1	Periumbilical discomfort and pain during menses. Bloody discharge from the tumor simultaneous with menstrual period	12	Surgical excision of the nodule	18	None
Hill et al [8]	1	Umbilical swelling, intermittently painful	6	Excisional biopsy	NR	None
Albrecht et al [9]	1	Asymptomatic umbilical nodule	12	Excisional biopsy	10	NR
Carter et al [10]	1	Umbilical swelling, intermittently painful with no umbilical bleeding.	6	Surgical excision of the nodule	20	NR
Ichimiya et al [11]	1	Asymptomatic umbilical nodule	NR	Omphalectomy (hysterectomy with bilateral salpingoophorectomy and resection of the left inguinal mass)	25	Masses in the left ovary and in the left inguinal region
Khetan et al [12]	1	Umbilical pain and swelling	NR	Omphalectomy (dilatation and curettage, diagnostic laparoscopy)	NR	Cervical and pelvic endometriosis
Friedman and Rico [13]	1	Slowly growing, mildly painful nodule in the umbilicus	3	NR	8	NR
Ramsanahie et al [14]	1	Intermittent pain associated with lump in the umbilicus	24	Omphalectomy	20	None
Sidani et al [15]	1	Pain at the umbilical site, cyclic swelling and occasional drainage of brownish material	2	Surgical excision of the nodule	25	None
De Giorgi et al [16]	1	Asymptomatic umbilical nodule	NR	Surgical excision of the nodule	NR	None
Zollner et al [17]	1	Umbilical pain and cyclic bleeding from the umbilical region	6	NR	10	Implants in the anterior and posterior peritoneum of the uterus
Hussain et al [18]	1	Dark brown umbilical nodule on the umbilicus associated with cyclical pain and bleeding	7	Surgical excision of the nodule (laparoscopic tubal ligation)	NR	None
Frischknecht et al [19]	2	Recurrent, mildly painful nodule in the umbilicus; local tenderness and occasional bleeding	216	Surgical nodule excision (laparoscopic treatment of pelvic endometriosis rAFS III with diaphragmatic lesions)	20	Pelvic and diaphragmatic endometriosis lesions
		Bleeding discharges from painful growing umbilical nodule	NR	Surgical excision of the nodule	15	None
Razzi et al [20]	1	Intermittent pain and bleeding from the umbilicus	24	Nodule biopsy	10	None
Kerr et al [21]	1	Cyclical changes in nodule size and occasional pain	36	NR	8	NR
Techapongsatorn and Techapongsatorn [22]	1	Nodular cyclical bleeding	4	Surgical excision of the nodule	NR	None
Chiang and Teh [23]	1	Discharging, bleeding and painful nodule	8	Surgical excision of the nodule	20	NR
Teh et al [24]	2	Discharging, bleeding and painful nodule	8	Surgical excision of the nodule	20	None
		Intermittent, noncyclic pain and discharge at the umbilicus. Also reported swelling with erythema on three occasions	48	Omphalectomy	NR	None
Iovino et al [25]	1	Intense pain and umbilical bleeding during menstruation	12	Omphalectomy (wide hernia sac resection, hernia repair)	20	None
Ploteau et al [26]	1	Umbilical swelling, intermittently painful, with occasional bleeding	120	Surgical excision of the nodule (laparoscopic resection of pelvic nodule)	50	Cervical nodule
Kimball et al [27]	1	Painful umbilical mass	96	Omphalectomy (hysterectomy, bilateral salpingo-oophorectomy, abdominal colposuspension, culdoplasty, and midurethral sling)	50	None

(*continued on next page*)

Table 1 (*continued*)

References	Cases	Presenting symptoms	Onset of symptoms (mo)	Umbilical treatment (associated surgery)	Lesion size (mm)	Endometriotic lesions associated
Rosina et al [28]	1	Periodically bleeding nodule associated with severe abdominal pain	NR	Surgical excision of the nodule	10	Bilateral ovarian endometriosis
Elm et al [29]	1	Slightly painful umbilical nodule, tender to palpation	3	Surgical excision of the nodule	15	Elliptical mass posterior to the urethra
Wiegratz et al [30]	1	Umbilical increasing cyclic pain with cyclical discharge (first a cyclic clear-to-yellowish discharge and then umbilical bleeding)	24	Omphalectomy	Three lesions: 5, 10, and 15	None
Agarwal and Fong [31]	1	Dysmenorrhea and cyclical bleeding from the umbilicus	24	Omphalectomy	5	NR
Dessy et al [32]	3	Growing and cyclical bleeding nodule	NR	Omphalectomy	20	NR
		Abdominal swelling, sense of tension during premenstrual period	NR	Omphalectomy	10	NR
		Abdominal swelling, tension and pain during premenstrual period	NR	Omphalectomy	10	NR
Khaled et al [2]	1	Tender, painful, growing umbilical nodule	24	Surgical excision of the nodule	20	NR
Lee et al [33]	1	Tender umbilical mass that cyclically bleeds	4	NR	NR	NR
Chatzikokkinou et al [34]	1	Asymptomatic nodule	NR	Surgical excision of the nodule	15	None
Bagade and Guirguis [35]	1	Spontaneous and periodic bleeding from the umbilicus; pain and swelling in the umbilical area	4	Surgical excision of the nodule	15	NR
Malebranche and Bush [36]	1	Firm, cyclically swelling lesion developing in the periumbilical region	6	Omphalectomy	25	Endometriosis on the bladder, posterior uterus, ovaries, and sigma
Fukuda and Hideki [37]	1	Painful umbilical nodule	6	Omphalectomy	10	NR
Fedele et al [38]	2	Dysmenorrhea and chronic pelvic pain, cyclic umbilical bleeding, and local pain	NR	Omphalectomy (concomitant laparoscopic approach)	NR	Bilateral ovarian endometriomas
		Cyclic umbilical bleeding and local pain	NR		NR	None
Dadhwal et al [39]	1	Growing painful nodule	5	Omphalectomy	15	None
Kyamidis et al [40]	1	Growing and tender umbilical nodule with occasional bleeding during menses	120	Surgical excision of the nodule	NR	NR
Fernandes et al [41]	1	Cyclic periumbilical pain during menstruation	36	Surgical excision of the nodule (abdominal hysterectomy)	20	None
Richard et al [42]	2	Umbilical pain	48	Omphalectomy	30	None
		Abdominal pain and bleeding from the navel with menstruation	NR		NR	NR
Möhrenschlager et al [43]	1	Asymptomatic umbilical nodule	48	Surgical excision of the nodule	NR	NR
Kesici et al [44]	1	Umbilical discharging mass	10	Omphalectomy	25	None
Efremidou et al [45]	1	Cyclic painful umbilical lesion	72	Surgical excision of the nodule	30	None
Minaidou et al [46]	1	Umbilical painful nodule	12	Surgical excision of the nodule	30	None
Mizutani et al [47]	1	Asymptomatic umbilical nodule	36	Surgical resection of the nodule	20	NR
Singh et al [48]	1	Umbilical pain	18	Omphalectomy	NR	NR
Jaffernhoy et al [49]	1	Cyclical umbilical discharge, occasional dysmenorrhea, and menorrhagia	36	NR	NR	NR
Saito et al [50]	3 (out of 7)	Painful umbilical nodule	2	Biopsy	5	None
		Umbilical cyclical pain	8	Biopsy	10	Bilateral ovarian endometriomas and adenomyosis
		Cyclical umbilical pain and bleeding	7	Biopsy	NR	Bilateral ovarian endometriomas and adenomyosis
Present case	1	Catamenial umbilical bleeding	6	Omphalectomy	8	None

NR = not reported.

Surgical management is the treatment of choice, as suggested by literature results. Gonadotrophin-releasing hormone analog preoperatively may lead to incomplete excision and partial recurrence [31]. We recommend a complete selective excision of the lesion when the umbilicus is not involved *en bloc*; otherwise, it is necessary to perform an omphalectomy with umbilical reconstruction, to reduce the risk of recurrence. Furthermore, it is important to conduct an explorative laparoscopy in order to simultaneously identify possible pelvic lesions and investigate potential peritoneal involvement. Umbilical endometriosis is a rare but underrecognized phenomenon. Most cases are secondary, associated with previous surgery. Primary lesions, especially those not associated with concomitant pelvic lesions, are more difficult to understand, but probably represent an independent nosological entity, whose pathogenesis is different from that of the other forms.

There are often diagnostic challenges. The possibility of endometriosis must be considered during the evaluation of an umbilical mass despite the absence of previous surgery, paying special attention to menstrual symptoms or bloody discharge. Gynecologists can benefit from working with a multidisciplinary team that includes general surgery, radiology, and dermatology colleagues. Complete excision with the help of laparoscopic evaluation and successive histology are highly recommended for obtaining a definitive diagnosis and optimal treatment.

Conflicts of interest

The authors have no conflicts of interest relevant to this article.

References

[1] Gentilini D, Perino A, Viganò P, Chiodo I, Cucinella G, Vignali M, et al. Gene expression profiling of peripheral blood mononuclear cells in endometriosis identifies genes altered in non-gynaecologic chronic inflammatory diseases. Hum Reprod 2011;26:3109–17.
[2] Khaled A, Hammami H, Fazaa B, Zermani R, Ben Jilani S, Kamoun MR. Primary umbilical endometriosis: a rare variant of extragenital endometriosis. Pathologica 2008;100:473–5.
[3] Cucinella G, Granese R, Calagna G, Candiani M, Perino A. Laparoscopic treatment of diaphragmatic endometriosis causing chronic shoulder and arm pain. Acta Obstet Gynecol Scand 2009;88:1418–9.
[4] Latcher JM. Endometriosis of the umbilicus. Am J Obstet Gynecol 1953;66:161–8.
[5] Krumbholz A, Frank U, Norgauer J, Ziemer M. Umbilical endometriosis. J Dtsch Dermatol Ges 2006;4:239–41 [In German, English abstract].
[6] Mechsner S, Bartley J, Infanger M, Loddenkemper C, Herbel J, Ebert AD. Clinical management and immunohistochemical analysis of umbilical endometriosis. Arch Gynecol Obstet 2009;280:235–42.
[7] Igawa HH, Ohura T, Sugihara T, Hosokawa M, Kawamura K, Kaneko Y. Umbilical endometriosis. Ann Plast Surg 1992;29:266–8.
[8] Hill AD, Banwell PE, Sangwan Y, Darzi A, Menzies-Gow N. Endometriosis and umbilical swelling. Clin Exp Obstet Gynecol 1994;21:28–9.
[9] Albrecht LE, Tron V, Rivers JK. Cutaneous endometriosis. Int J Dermatol 1995;34:261–2.
[10] Carter S, Davidson T, Hussain N, McLaughlin J. A case of spontaneous endometriosis. J Obstet Gynaecol 1998;18:490–1.
[11] Ichimiya M, Hirota T, Muto M. Intralymphatic embolic cells with cutaneous endometriosis in the umbilicus. J Dermatol 1998;25:333–6.
[12] Khetan N, Torkington J, Watkin A, Jamison MH, Humphreys WV. Endometriosis: presentation to general surgeons. Ann R Coll Surg Engl 1999;81:255–9.
[13] Friedman PM, Rico MJ. Cutaneous endometriosis. Dermatol Online J 2000;6:8.
[14] Ramsanahie A, Giri SK, Velusamy S, Nessim GT. Endometriosis in a scarless abdominal wall with underlying umbilical hernia. Ir J Med Sci 2000;169:67.
[15] Sidani MS, Khalil AM, Tawil AN, El-Hajj MI, Seoud MA. Primary umbilical endometriosis. Clin Exp Obstet Gynecol 2002;29:40–1.
[16] De Giorgi V, Massi D, Mannone F, Stante M, Carli P. Cutaneous endometriosis: non-invasive analysis by epiluminescence microscopy. Clin Exp Dermatol 2003;28:315–7.
[17] Zollner U, Girschick G, Steck T, Dietl J. Umbilical endometriosis without previous pelvic surgery: a case report. Arch Gynecol Obstet 2003;267:258–60.
[18] Hussain M, Noorani K. Primary umbilical endometriosis—a rare variant of cutaneous endometriosis. J Coll Physicians Surg Pak 2003;13:164–5.
[19] Frischknecht F, Raio L, Fleischmann A, Dreher E, Luscher KP, Mueller MD. Umbilical endometriosis. Surg Endosc 2004;18:347.
[20] Razzi S, Rubegni P, Sartini A, De Simone S, Fava A, Cobellis L, et al. Umbilical endometriosis in pregnancy: a case report. Gynecol Endocrinol 2004;18:114–6.
[21] Kerr OA, Mowbray M, Tidman MJ. An umbilical nodule due to endometriosis. Acta Derm Venereol 2006;86:277–8.
[22] Techapongsatorn S, Techapongsatorn S. Primary umbilical endometriosis. J Med Assoc Thai 2006;89:1753–5.
[23] Chiang DT, Teh WT. Cutaneous endometriosis—surgical presentations of gynaecological condition. Aust Fam Physician 2006;35:887–8.
[24] Teh WT, Vollenhoven B, Harris PI. Umbilical endometriosis, a pathology that a gynecologist may encounter when inserting the Veres needle. Fertil Steril 2006;86:1764.e1–2.
[25] Iovino F, Ruggiero R, Irlandese E, Gili E, Lo Schiavo F. Umbilical endometriosis associated with umbilical hernia. Management of a rare occurrence. Chir Ital 2007;59:895–9.
[26] Ploteau S, Malvaux V, Draguet AP. Primary umbilical adenomyotic lesion presenting as cyclical periumbilical swelling. Fertil Steril 2007;88:1674–5.
[27] Kimball KJ, Gerten KA, Conner MG, Richter HE. Diffuse endometriosis in the setting of umbilical endometriosis: a case report. J Reprod Med 2008;53:49–51.
[28] Rosina P, Pugliarello S, Colato C, Girolomoni G. Endometriosis of umbilical cicatrix: case report and review of the literature. Acta Dermatovenerol Croat 2008;16:218–21.
[29] Elm MK, Twede JV, Turiansky GW. Primary cutaneous endometriosis of the umbilicus: a case report. Cutis 2008;81:124–6.
[30] Wiegratz I, Kissler S, Engels K, Strey C, Kaufmann M. Umbilical endometriosis in pregnancy without previous surgery. Fertil Steril 2008;90:199.e17–20.
[31] Agarwal A, Fong YF. Cutaneous endometriosis. Singapore Med J 2008;49:704–9.
[32] Dessy LA, Buccheri EM, Chiummariello S, Gagliardi DN, Onesti MG. Umbilical endometriosis, our experience. In Vivo 2008;22:811–5.
[33] Lee A, Tran HT, Walters RF, Yee H, Rosenman K, Sanchez MR. Cutaneous endometriosis. Dermatol Online J 2008;14:23.
[34] Chatzikokkinou P, Thorfinn J, Angelidis IK, Papa G, Trevisan G. Spontaneous endometriosis in an umbilical skin lesion. Acta Dermatovenerol Alp Panonica Adriat 2009;18:126–30.
[35] Bagade PV, Guirguis MM. Menstruating from the umbilicus as a rare case of primary umbilical endometriosis: a case report. J Med Case Rep 2009;10:9326.
[36] Malebranche AD, Bush K. Umbilical endometriosis: a rare diagnosis in plastic and reconstructive surgery. Can J Plast Surg 2010;18:147–8.
[37] Fukuda H, Hideki M. Cutaneous endometriosis in the umbilical region: the usefulness of CD10 in identifying the interstitium of ectopic endometriosis. J Dermatol 2010;37:545–9.
[38] Fedele L, Frontino G, Bianchi S, Borruto F, Ciappina N. Umbilical endometriosis: a radical excision with laparoscopic assistance. Int J Surg 2010;8:109–11.
[39] Dadhwal V, Gupta B, Dasgupta C, Shende U, Deka D. Primary umbilical endometriosis: a rare entity. Arch Gynecol Obstet 2011;283:119–20.
[40] Kyamidis K, Lora V, Kanitakis J. Spontaneous cutaneous umbilical endometriosis: report of a new case with immunohistochemical study and literature review. Dermatol Online J 2011;17:5.
[41] Fernandes H, Marla NJ, Pailoor K, Kini R. Primary umbilical endometriosis—diagnosis by fine needle aspiration. J Cytol 2011;28:214–6.
[42] Richard F, Collins J, Britt LD. Spontaneous umbilical endometriosis: a rare but clinically important entity. Am Surg 2011;77:E246–7.
[43] Möhrenschlager M, Arbogast HP, Henkel V. An umbilical nodule with cyclical changes. BMJ 2011;343:d5855.
[44] Kesici U, Yenisolak A, Kesici S, Siviloglu C. Primary cutaneous umbilical endometriosis. Med Arch 2012;66:353–4.
[45] Efremidou EI, Kouklakis G, Mitrakas A, Liratzopoulos N, Polychronidis AC. Primary umbilical endometrioma: a rare case of spontaneous abdominal wall endometriosis. Int J Gen Med 2012;5:999–1002.
[46] Minaidou E, Polymeris A, Vassiliou J, Kondi-Paphiti A, Karoutsou E, Katafygiotis P. Primary umbilical endometriosis: case report and literature review. Clin Exp Obstet Gynecol 2012;39:562–4.
[47] Mizutani T, Sakamoto Y, Ochiai H, Maeshima A. Umbilical endometriosis with urachal remnant. Arch Dermatol 2012;148:1331–2.
[48] Singh N, Kumar P, Ghosh R, Kumar S. The painful black umbilicus. Eur J Obstet Gynecol Reprod Biol 2012;163:240–1.
[49] Jaffernhoy S, Symeonides P, Levy M, Shiwani MH. Chronic umbilical discharge: an unusual presentation of endometriosis. Sultan Qaboos Univ Med J 2013;13:143–6.
[50] Saito A, Koga K, Osuga Y, Harada M, Takemura Y, Yoshimura K, et al. Individualized management of umbilical endometriosis: a report of seven cases. J Obstet Gynaecol Res 2014;40:40–5.
[51] Cucinella G, Granese R, Calagna G, Svelato A, Saitta S, Tonni G, et al. Oral contraceptives in the prevention of endometrioma recurrence: does the different progestins used make a difference? Arch Gynecol Obstet 2013;288:821–7.
[52] Vercellini P, Crosignani PG, Somigliana E, Viganò P, Frattaruolo MP, Fedele L. 'Waiting for Godot': a commonsense approach to the medical treatment of endometriosis. Hum Reprod 2011;26:3–13.
[53] Seracchioli R, Mabrouk M, Manuzzi L, Vicenzi C, Frascà C, Elmakky A, et al. Post-operative use of oral contraceptive pills for prevention of anatomical relapse or symptom recurrence after conservative surgery for endometriosis. Hum Reprod 2009;24:2729–35.

[54] Sepilian V, Della Badia C. Iatrogenic endometriosis caused by uterine morcellation during a supracervical hysterectomy. Obstet Gynecol 2003;102:1125–7.
[55] Ichida M, Gomi A, Hiranouchi N, Fujimoto K, Suzuki K, Yoshida M, et al. A case of cerebral endometriosis causing catamenial epilepsy. Neurology 1993;43:2708–9.
[56] Laghzaoui O, Laghzaoui M. Nasal endometriosis: apropos of 1 case. J Gynecol Obstet Biol Reprod 2001;30:786–8 [In French, English abstract].
[57] Barresi V, Cerasoli S, Vitarelli E, Donati R. Spinal intradural mullerianosis: a case report. Histol Histopathol 2006;21:1111–4.
[58] Laganà AS, Sturlese E, Retto G, Sofo V, Triolo O. Interplay between misplaced Müllerian-derived stem cells and peritoneal immune dysregulation in the pathogenesis of endometriosis. Obstet Gynecol Int 2013;2013:527041.
[59] Marranci M, Dianda D, Gattai R, Nesi S, Bandettini L. Umbilical endometriosis: report of a case and review of the literature. Ann Ital Chir 2000;71:389–92 [In Italian, English abstract].
[60] Victory R, Diamond MP, Johns DA. Villar's nodule: a case report and systematic literature review of endometriosis externa of the umbilicus. J Minim Invasive Gynecol 2007;14:23–32.
[61] Lauslahti K. Malignant external endometriosis: a case of adenocarcinoma of umbilical endometriosis. Acta Pathol Microbiol Scand Suppl 1972;233:98–102.