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The ultrasound of subcutaneous extrapelvic endometriosis

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Keywords
extrapelvic endometriosis, cesarean section scar endometrioma, perineum endometrioma, umbilicus nodule

Abstract

Background: The presence of ectopic functional endometrial glands and struma anywhere except in the lining of the uterine cavity is considered as endometriosis. Extrapelvic endometriosis involving the abdominal wall cesarean section scar is uncommonly seen, and it rarely involves the perineum, umbilicus, pleura, kidneys, lungs and liver. **Objectives:** The purpose of the present study is to highlight rare ectopic sites, explain the pathogenesis of extrapelvic endometriosis, and evaluate the diagnostic significance of clinical findings, serum CA 125 level, and ultrasonography. **Materials and methods:** 24 female patients with extrapelvic endometriomas in whom the final diagnosis was based on the surgical results and histopathological reports of the excised specimens. The patients underwent a clinical examination, an ultrasound scan, and evaluation of the serum CA 125 level. They were also examined by transvaginal ultrasound to rule out ovarian endometriosis or uterine adenomyosis. They were further subjected to abdominal wall ultrasound in cases of cesarean section scar or umbilical region swellings, and transperineal ultrasound for perianal lesions. Transvaginal ultrasound was performed in patients with perineal endometrioma to assess the relation between the lesion and the external anal sphincter. **Results:** In 19 patients, abdominal wall cesarean section scar endometrioma was detected. Three patients had perianal endometriomas, and two patients – umbilical endometriomas. **Conclusion:** Ultrasound scanning was a useful diagnostic tool to evaluate extrapelvic endometriosis and its extension, especially in cases without typical clinical features that can be suggestive of endometrioma, low diagnostic sensitivity of serum CA 125, and low incidence of concomitant intrapelvic disease.

Introduction

The presence of ectopic functional endometrial glands and struma anywhere except in the lining of the uterine cavity is considered as endometriosis. The most common sites of endometriosis inside the pelvic cavity include the myometrium (adenomyosis), the ovaries, the uterine ligaments, and the pouch of Douglas. Extrapelvic endometriosis is seen involving the abdominal wall cesarean section (CS) scar, and rarely affects the perineum, umbilicus, pleura, kidneys, lungs, and liver[1].

The pathogenesis of endometriosis is based on many theories, for example implantation theory in which endometrial cells spread in a retrograde fashion through the fallopian tubes to the peritoneal cavity; metaplasia of mesothelial cells into endometrial glandular cells, endometrial emboli with altered immunological recognition of endometrial cells; and transplantation theory[2].

The clinical diagnosis of endometrioma depends on the presence of a palpable tender nodule in females during a childbearing period. The nodule undergoes cyclical changes, with an increase of pain intensity and size during menses. Perineal endometriosis usually occurs at the site of the episiotomy scar or healed perineal laceration after vaginal delivery, while abdominal wall endometriosis is usually seen at the site of cesarean section scar after the delivery by cesarean section[3–5].

Imaging modalities play an important role in the diagnosis of endometriosis, either at pelvic or extrapelvic sites, to reach an optimal preoperative surgical planning. Ultrasonography can help in detecting the site of ectopic

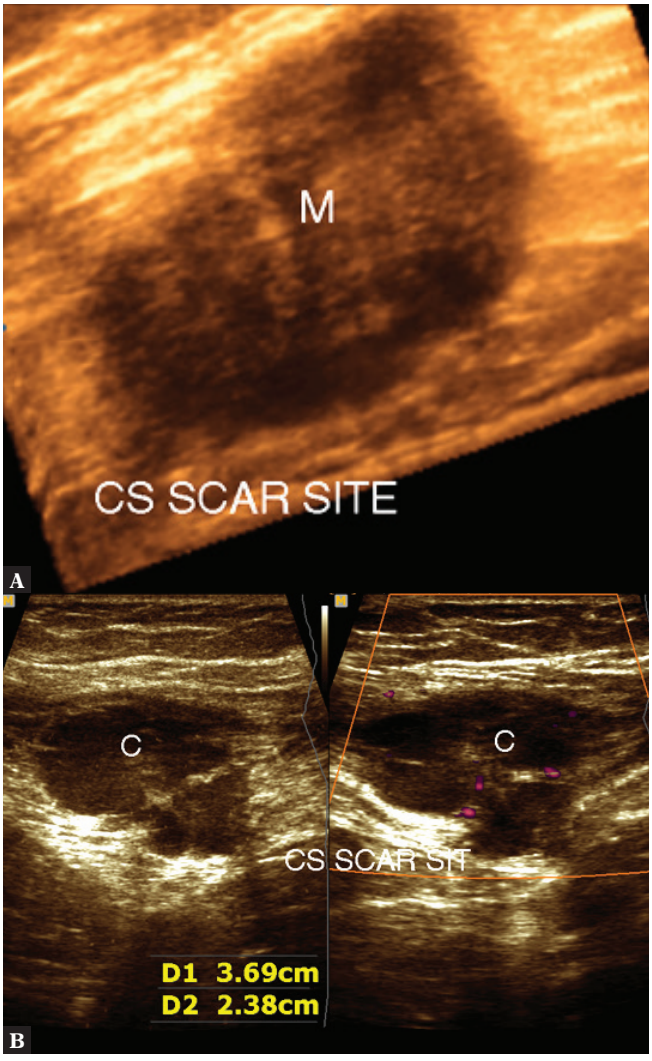

Fig. 1. A. *3D surface rendering of CS scar endometrioma (M) infiltrating the rectus abdominis muscle.* **B.** *2D B mode ultrasound of CS scar endometrioma of mixed cystic and solid pattern (c), seen involving the muscle planes*

endometrium and its anatomical relationship to the surrounding vital structures[2,3].

Objectives

The purpose of the present study is to highlight the rare ectopic sites and explain the pathogenesis of extrapelvic endometriosis. Another goal is to evaluate the diagnostic significance of clinical findings, serum CA 125 level, and ultrasound imaging.

Methodology

A retrospective study included 24 female patients with extrapelvic endometriomas in whom the final diagnosis was based on the surgical results and the histopathological reports of excised specimens revealing the presence of endometrial glands and stromal cells. The patients were admitted to the radiology department of our institute between February 2016 and March 2019. Their age ranged from 22 to 38 years. Among them, 19 patients complained of painful swelling at the site of their abdominal wall CS scar, and 3 patients with a history of vaginal delivery reported painful swelling at the perineal region anterior to the anal verge. Also, 2 patients complained of painful swelling at the region of the umbilicus.

Among the 19 patients with abdominal wall CS scar swelling, 15 patients showed no cyclical changes in the size of the swelling or pain intensity during the menstrual cycle, while 4 patients reported cyclical changes.

The 3 patients with perineal swelling showed no cyclical changes. The 2 patients with umbilical swelling had cyclical changes with an increment in the size of the swelling and pain intensity at the time of menstruation.

The onset of symptoms in all the patients ranged from 6 months to 12 years after the last vaginal or CS delivery. The average duration of symptoms was 11 months.

All the patients underwent a test to measure their serum CA 125 level, and transvaginal ultrasound to rule out ovarian endometriosis or uterine adenomyosis. They were further subjected to an abdominal wall ultrasound examination in cases of CS scar or umbilical region swellings, and transperineal ultrasound for the perineal lesions using linear multi-frequency ultrasound transducer (5–12 MHz) assisted by color Doppler and three dimensional capabilities. Transvaginal ultrasound was done in patients with perineal swelling to assess the relation between the lesion and the external anal sphincter using endocavitary multi-frequency (4–9 MHz) transducer, Sono ACE X8 ultrasound machine, Medison, Korea.

The B mode ultrasound exam was followed by Power Doppler evaluation of all lesions to assess the degree of lesion vascularity after optimizing the slow flow Doppler settings and three dimensional image reconstruction with multiplanar image analysis and volume rendering. All the results were recorded with a focus on the site, size, characteristic echo features of the nodule or cyst, and its relation to the surrounding structures.

All the patients were followed up, and the final diagnosis was achieved based on the surgical results and the histopathological reports.

Results

Extrapelvic endometriosis was detected in 24 patients. Among them, 19 patients were found to have abdominal wall CS scar endometrioma (Fig. 1), 3 patients – perineal endometriomas (Fig. 2, Fig. 3, Fig. 4), and 2 patients – umbilical endometriomas (Fig. 5, Fig. 6).

In the group of 19 patients with abdominal wall CS scar endometriosis, 17 patients had a single nodule, and

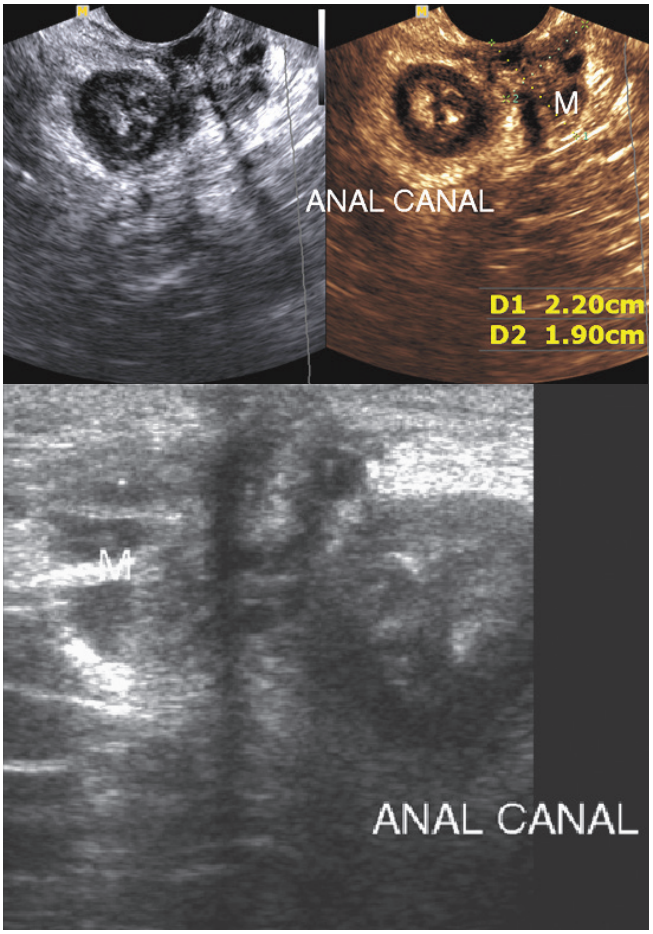

Fig. 2. *Transvaginal ultrasound of perianal endometrioma of mixed cystic and solid pattern (M), seen partially infiltrating the anal external sphincter*

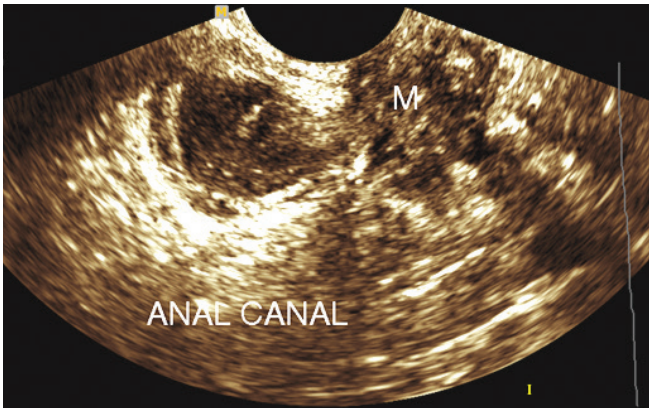

Fig. 3. *Transvaginal ultrasound of perianal endometrioma of solid pattern (M) seen infiltrating the external and internal anal sphincters of the anal canal*

2 patients had 2 nodules, with a total number of nodules equaling 21.

The site of the nodule was in the paramedian region in 7 lesions (33%), and in the lateral aspect (the corner) of the CS scar site in 14 lesions (67%). A total of 10 nodules

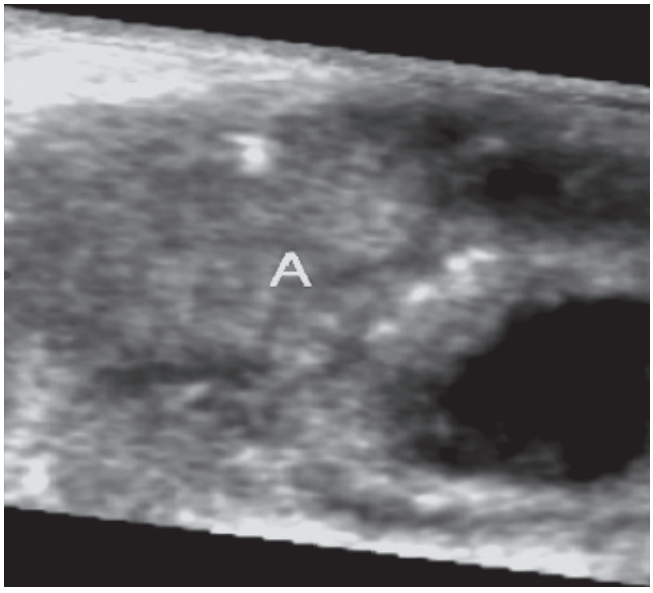

Fig. 4. *3D surface rendering of large perianal endometrioma showing solid pattern (A), with extensive infiltration of the external anal sphincter*

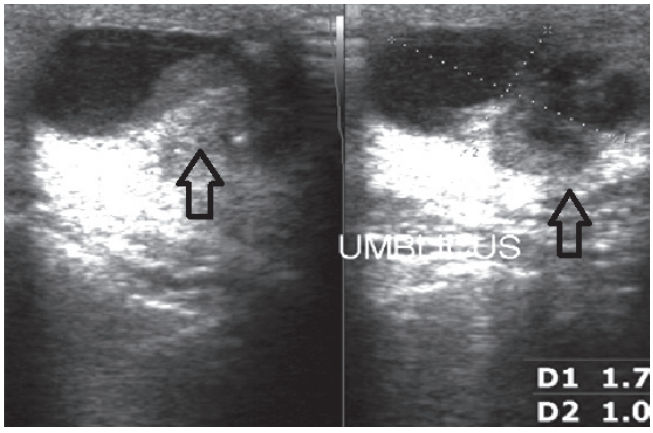

Fig. 5. *2D ultrasound of umbilical endometrioma of mixed cystic and solid pattern (arrows)*

were in a deep subcutaneous location (47.5%), 4 nodules (19%) were deep subcutaneous nodules extending to involve the fascia, 4 nodules (19%) were in a deep subcutaneous location infiltrating the underlying muscle planes, and 3 nodules (14.5%) were intramuscular nodules. The nodules were purely solid in 14 lesions (67%), mixed cystic and solid in 5 lesions (24%), and cystic with low-level internal echoes in 2 lesions (9%). All endometriomas with solid or mixed cystic and solid pattern showed heterogeneous echo pattern of the solid component and an irregular outline. Five endometriomas showed an increased vascularity inside, 14 nodules were hypovascular, and the 2 cystic endometriomas showed hypervascular walls.

The serum level of CA 125 was elevated in only 2 patients (9%). Concomitant pelvic endometriosis with ovarian endometriotic cyst was seen in 2 patients (9%), and uterine adenomyosis in 1 patient (4.5%).

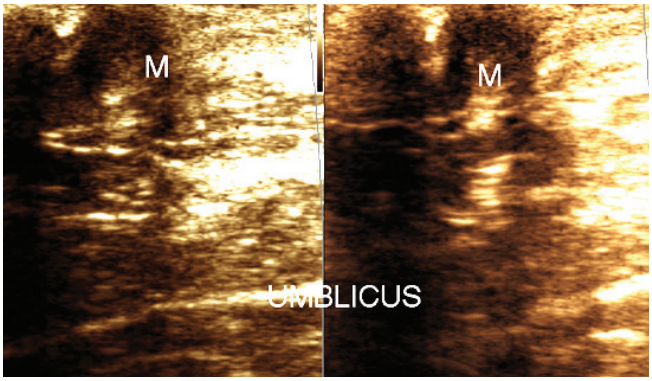

Fig. 6. *2D ultrasound of umbilical endometrioma of solid pattern (M)*

Three patients showed perineal endometriomas, and among them 2 patients had solid nodules, and 1 patient had a mixed cystic and solid nodule. All of them showed infiltration to the external anal sphincter: 1 nodule with mild infiltration of less than 1/3 of the circumference of the external sphincter, 1 nodule with infiltration less than ½ of the circumference, and the third nodule with extensive infiltration involving more than ½ of the circumference of the external anal sphincter.

Two patients with umbilical endometriomas showed a dark, tender nodule involving the umbilicus. One patient had no previous history of surgical intervention, and the nodule was associated with cyclical changes and bleeding from the umbilicus during menses.

The other patient was infertile, with no previous deliveries, but gave a history of hysterosalpingography performed 2 years previously, and reported a pigmented umbilical nodule that appeared 7 months earlier, which caused cyclical pain and was not associated with bleeding per umbilicus. One umbilical nodule was cystic with internal echoes, and the other was solid in nature.

Neither the case with perineal nor umbilical endometrioma showed an elevation in the serum CA 125 level, and only 1 case involved concomitant intrapelvic endometriosis.

Discussion

The pathogenesis of endometriosis is not fully understood. Common theories to explain the condition include implantation theory, celomic metaplasia, vascular and lymphatic spread, and an immunity-related disorder[2]. Another recently proposed theory suggests developmentally misplaced endometrial tissue to explain the presence of ectopic endometrium during fetal life[6].

No single theory can account for all the findings of the current study. In the authors' opinion, the only acceptable explanation for the presence of ectopic endometrium at the site of the surgical scar is iatrogenic implantation of endometrial cells at the time of surgery either during cesarean section for CS scar endometriosis or during vaginal delivery for perineal endometriosis, and the presence of ectopic endometrium at the site of umbilicus and the previously reported ectopic sites such as the liver and lungs can be explained by the vascular or lymphatic spread of endometrial cells, though iatrogenic implantation of ectopic endometrium through transperitoneal spread can also account for umbilical endometriosis. Consequently, ectopic endometrium cells can implant, grow, and invade the surrounding structures. For example, according to our findings they can grow in the deep subcutaneous region and infiltrate the underlying muscle planes, and metastasize in a way similar to malignant cells. Therefore, endometriosis can be considered as a benign inflammatory disorder with some malignant features. Chui *et al*. showed that ectopic endometrium had common features with malignancy as regards the capability to infiltrate and grow, and the possibility of angiogenesis, except that endometrioma had no surrounding desmoplastic reaction observed with malignancy[7]. Kao *et al*. reported that the stromal mesenchymal stem cells of the ectopic endometrium had the ability to implant in vivo and infiltrate, and were capable of angiogenesis with respect to the same cells of eutopic endometrium[8].

Endometriosis can be further regarded to behave in a similar way to hormone-dependent breast cancer in that it is able to grow, infiltrate, metastasize and be nourished with estrogen supplied from the ovaries, and subcutaneous fat. Both may regress with anti-estrogen therapy and aromatase inhibitors, and in cases of endometriosis, estrogen is formed by the ectopic endometrium itself, a finding that was presented in a study by Metzger *et al*. showing that the distribution of estrogen and progesterone receptors within the endometrial glands and stromal cells was homogenous and regular, and was of predictive response in the normal endometrium, and also markedly heterogeneous and of unpredictable response in the ectopic endometrium, which explains the lack of cyclical changes in ectopic endometrium and inadequate response to hormonal therapy in many patients[9].

The onset of symptoms was long and variable among our patients, which can be attributed to their immunity status, hormonal status, and the conception and contraception status.

According to the current study, the diagnosis of extrapelvic endometriosis should depend neither on the clinical features of tender, painful nodules with cyclical changes, nor the elevation of serum CA 125 levels, nor the presence of intrapelvic endometriosis in association with a painful scar nodule. Machairiotis *et al*., reported that serum CA 125 levels carry no diagnostic significance[2], and the current study showed similar results: the serum level of CA 125 was only elevated in 9.5% of our patients with CS scar endometrioma, and in no patients with perineal or umbilical endometriomas. Concomitant pelvic endometriosis was detected in 13.5% of cases with CS scar endometrioma, and in 20% of our cases with umbilical and perineal endometriomas. Therefore, the diagnosis should depend on the presence of a tender long-standing nodule at the site of surgical scar in a female during the childbearing period. The diagnosis is confirmed if the nodule shows common

ultrasound characteristics of endometrioma and undergoes cyclical changes.

The ultrasound features of endometrioma observed in the current study are solid hypoechoic nodule of an irregular outline, mixed cystic and solid nodule, and cystic nodule with thick walls showing low-level echoes inside.

Most solid nodules were hypovascular, with a few showing mild hypervascularity inside.

The most common nodule with late onset after cesarean section developing at or close to the site of the abdominal wall CS scar is endometrioma, and it should be evaluated first before considering other etiologies which are very uncommon.

Other masses which may appear at the site of the CS scar are desmoid tumors of the abdominal wall, CS scar incision hernia, and in the early postoperative period also subcutaneous cellulites or subcutaneous or intramuscular collections[5].

Patients with perineal endometrioma after vaginal delivery presenting with a nodule within the fat tissue of the episiotomy scar should undergo a meticulous ultrasound examination with transperineal, transvaginal and endoanal approaches to assess accurately the size and extension of the nodule, and the degree of involvement of anal sphincters.

Extensive involvement of anal sphincters renders surgical excision of the nodule difficult, and increases the risk of postoperative focal incontinence. Administration of gonadotropin-releasing hormone analogs did not give a satisfactory response, however, it was useful in the preoperative period to reduce the size of edema associated with the mass to make the edges of nodule well-defined in order to be easily resected during surgery. The surgical management of perianal endometrioma depends on a narrow excision with sphincteroplasty or an incomplete excision of large nodules with an extensive degree of anal sphincter infiltration[1].

Umbilical endometriosis could be primary or secondary. Patients with primary endometriosis had an unremarkable medical history of previous surgical interference[10].

One case with umbilical endometriosis in the current study was secondary with a previous history of hysterosalpingography, while the other case was primary with an unremarkable medical history of previous surgical interference.

The treatment of umbilical endometriosis is mainly surgical, through omphalectomy[11].

Conclusion

Ultrasound is a useful diagnostic tool to evaluate extrapelvic endometriosis and its extension, especially in cases without typical clinical features that can be suggestive of endometrioma, considering the low diagnostic sensitivity of serum CA 125 levels, and low incidence of concomitant intrapelvic disease.

Conflict of interest

Author does not report any financial or personal connections with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

Ethical statements

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national), and with the Helsinki Declaration of 1964 and later versions.

Informed consent

Informed consent was obtained from all patients for including them in the study.

Source of funding

Not present.

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