



# Clinical Pattern and Spectrum of Atypical Endometriosis: A Series of 5 Cases

Nadia Shirazi \*<sup>1</sup>, Ruchira Nautiyal <sup>2</sup>, Rashmi Jindal <sup>3</sup>

<sup>1</sup>Professor, Department of Pathology, Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Jolly Grant, Dehradun, Uttarakhand, India.

<sup>2</sup>Professor, Department of Obstetrics & Gynaecology, Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Jolly Grant, Dehradun, Uttarakhand, India.

<sup>3</sup>Professor, Department of Dermatology, Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Jolly Grant, Dehradun, Uttarakhand, India.

\*Corresponding Author: Dr. Nadia Shirazi; [shirazinadia@gmail.com](mailto:shirazinadia@gmail.com)

Received 28 February 2023;

Accepted 13 March 2023;

Published 19 March 2023

## Abstract

Endometriosis refers to the extrauterine presence of hormonally active endometrial glands and stroma. This ectopic endometrial tissue exhibits cyclic bleeding, inflammation, fibrosis and leads to formation of adhesions. Endometriosis affects about 10% to 15% of women between 15 to 45 years of age. Clinical presentations vary from infertility, dysmenorrhoea, chronic pelvic pain, deep dyspareunia and even bleeding at external sites like the umbilicus. Besides involving fallopian tubes, bowel, liver, thorax, pericardium, pleura etc, the most commonly affected areas in the gastrointestinal tract are the descending colon, rectosigmoid, appendix, and ileo-caecum in descending order of frequency. This case series highlights some unusual presentations of endometriosis along with co-existence of other ovarian pathologies which are not frequently encountered in clinical practice. This series also highlights the role of preoperative radiology for an adequate clinical diagnosis and complete surgical excision.

**Keywords:** *Endometrial gland, stroma, extrapelvic, bladder, caecum, decidualised.*

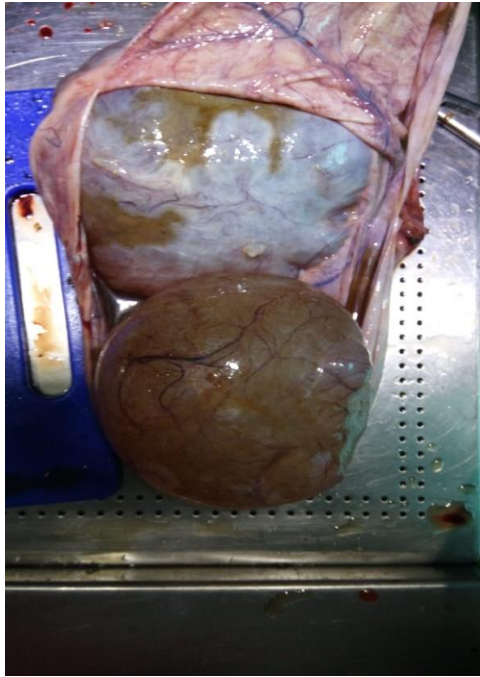
## Background

Endometriosis is a relatively frequently encountered condition affecting 10 to 15% of women of reproductive age <sup>[1]</sup>. Extrapelvic endometriosis (EPE) is infrequently reported and constitutes <12% cases of all endometriosis. The usual extrapelvic locations include the gut, bladder, ureters, lungs, under surface of diaphragm and even extremities. Endometriosis in surgical scars, within and around umbilicus, inguinal canal, arms and legs, skin and even in central nervous system have also been documented <sup>[2]</sup>. Since one of the pathophysiology involves retrograde menstruation theory, the chances of finding endometriosis get lesser as we move farther from the uterus. The clinical manifestations are varied and often lead to a mistaken diagnosis of malignancy, Crohns disease, Tuberculosis etc <sup>[3]</sup>. A strong clinical suspicion is required which is confirmed histopathologically. Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) offer higher diagnostic accuracy as compared to Ultrasonography (USG). Management involves complete surgical excision of endometriotic nodules however the condition can also be successfully treated medically by progesterone and danazol therapy.

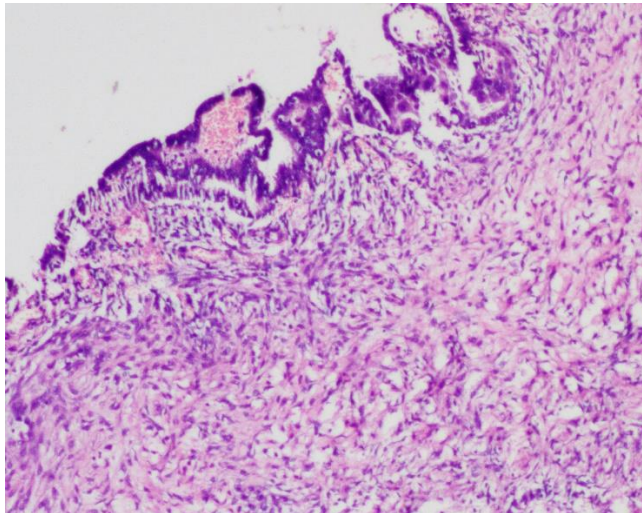
We present here a spectrum of 5 cases of endometriosis with atypical presentations after taking institutional ethical clearance as well as informed consent from the patients.

## Case 1

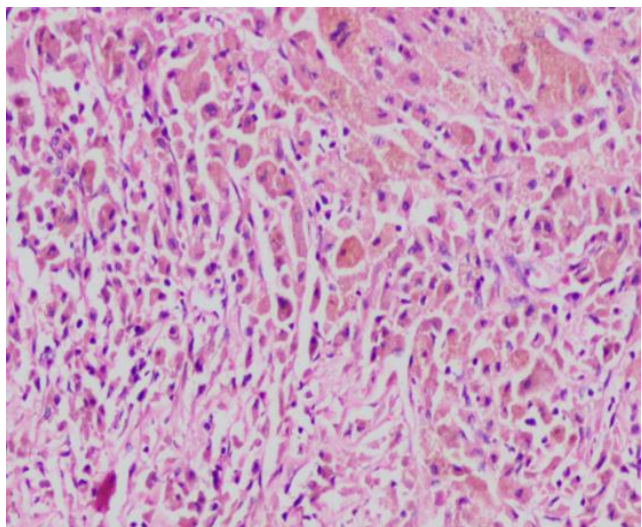
A 25-year-old female presented to the Gynecology OPD with complaints of pain in abdomen and fever off and on since 1 month. Her CA 19-9 & CA-125 levels were elevated. Ultrasound revealed a 17x10 cm sized multiloculated cystic lesion in the right ovary along with multiple smaller lesions (manifesting as internal echoes) in the adjacent areas. A probable clinical diagnosis of ovarian carcinoma was made. Frozen section of ovarian mass was reported benign cystadenoma and omental nodule showed only hemosiderin laden macrophages. Bilateral salpingo-oophorectomy was performed with nodal dissection and omental nodule excision. On gross examination, the ovary was multiloculated and filled with chocolate coloured fluid. (**Figure 1**) Histopathology demonstrated presence of nuclear stratification with complex papillary fronds sans stromal invasion. (**Photomicrograph 1**) Residual ovary showed few endometrial glands and stroma with numerous hemosiderin laden macrophages (**Photomicrograph 2**). A diagnosis of borderline mucinous cystadenoma with co-existent endometriosis in ovaries, omentum and on serosal aspect of bladder was made. She was discharged on 3-month Danazol therapy to suppress the pain as well as limit the growth of endometrial implants elsewhere in the peritoneum. She is doing well and is coming up for follow ups regularly.



**Figure 1: Enlarged multiloculated ovarian cyst filled with chocolate coloured fluid**



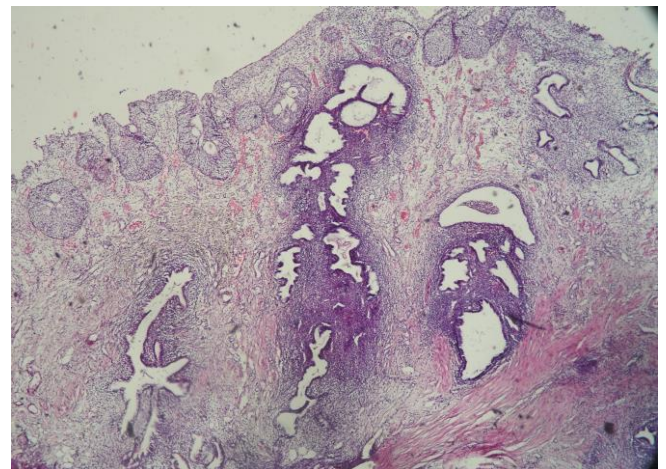
**Photomicrograph 1: Complex papillary fronds lined by columnar epithelium with regular nuclei (H&E: 10x10X)**



**Photomicrograph 2: Sheets of hemosiderin laden macrophages in surrounding parenchyma (H&E: 10x10X)**

### Case 2:

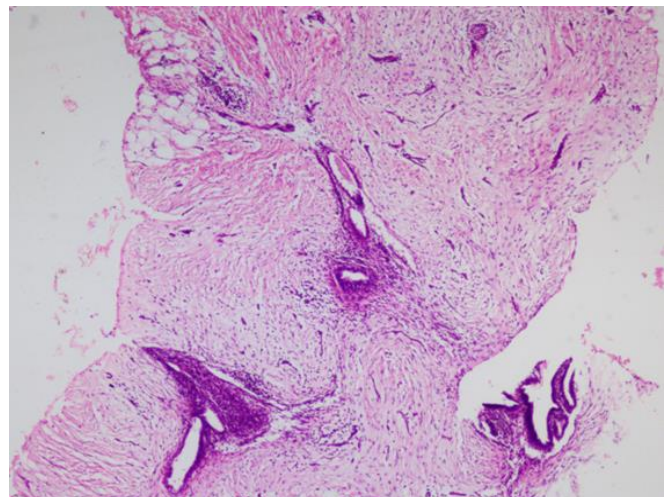
A 38-years old female presented to the urology OPD with complaints of burning during micturition, pelvic and low back pain since 3 months. She reported an episode of hematuria a week prior to presentation. Past history of surgery, especially caesarean section, was absent. The general and systemic examination was unremarkable. Urine culture was sterile and ultrasonography of genito-urinary tract revealed an irregular nodule simulating bladder tumor, measuring 1.5 cm in size. Intravenous urography confirmed irregularity in posterior wall of urinary bladder with sparing of ureters. A provisional diagnosis of urothelial carcinoma was made and the bladder growth was resected transurethrally. On gross examination, there were multiple tissue bits together measuring 4x2x2cm. On microscopic examination, all these bits showed sub-urothelial clustering of endometrial glands with dense intervening stroma and many hemosiderin laden macrophages. **(Photomicrograph 3)** There was no evidence of carcinoma and the patient was diagnosed as vesical endometriosis. She was discharged on Gonadotropin releasing hormone (GnRH) analogues and is currently asymptomatic.



**Photomicrograph 3: Submucosal endometrial glands and stroma in the urinary bladder (H&E: 10x10X)**

### Case 3:

A 38-year female who underwent vaginal delivery 6 months back presented with a nodule over the episiotomy scar. She also complained of cyclical pain over the region. The nodule was excised and sent for histopathological examination which revealed randomly scattered endometrial glands surrounded by compact stroma. A diagnosis of scar endometriosis was made. **(Photomicrograph 4)** Patient was discharged on medical management with GnRH analogues.

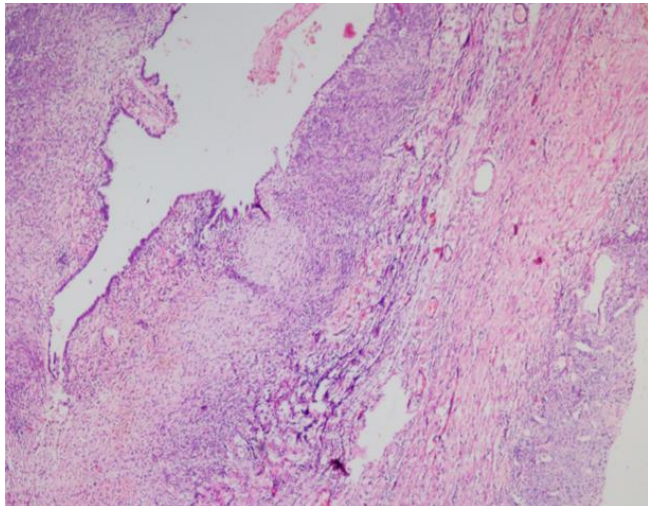


**Photomicrograph 4: Episiotomy scar seen infiltrated by endometrial glands and stroma (H&E: 10x10X)**



#### Case 4:

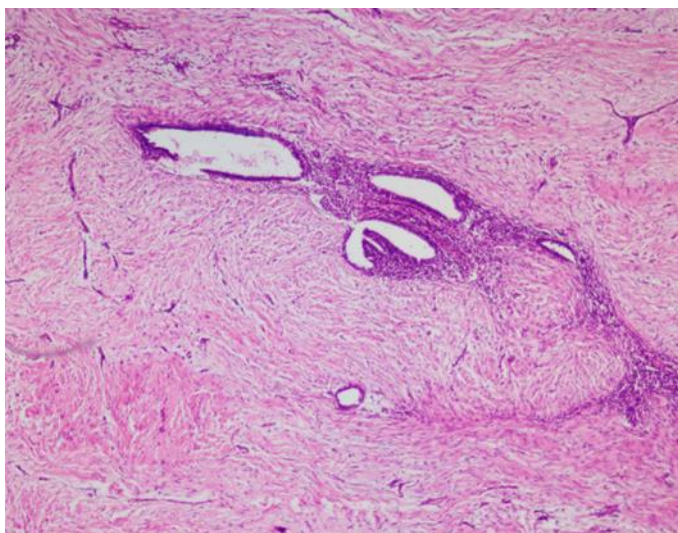
A 56-year female complained of a palpable mass in right iliac fossa since 6 months and presented with signs of acute bowel obstruction. Contrast Enhanced Computerized Tomography (CECT) abdomen revealed a 4.5x 2cm thickened mass in ileocaecal region. A provisional diagnosis of caecal carcinoma was made and limited right hemicolectomy was performed. Grossly, no definite growth was identified however the caecal wall was thickened to form a firm mass measuring 4 x2 x1.6 cm with adherent appendix. Microscopic examination revealed numerous scattered endometrial glands and stroma with fair number of macrophages in the ileocaecal region and in walls of appendix. **(Photomicrograph 5)** There was no evidence of epithelioid granuloma or malignancy. A diagnosis of extrapelvic ileocaecal endometriosis was made.



**Photomicrograph 5: Caecal wall showing endometriosis and fibrosis (H&E: 10x10X)**

#### Case 5:

A 41-year-old female presented with ruptured ectopic tubal pregnancy. Left sided salpingectomy with left oophorectomy was done and sent for histopathological examination. Grossly, the tube was ruptured and received in multiple bits admixed with blood clots. The ovary was mildly enlarged measuring 3.8x3 x1.2 cm. Few small cysts filled with chocolate colored fluid were identified. Microscopic examination demonstrated densely decidualized ovarian parenchyma along with few randomly scattered endometrial glands and stroma. **(Photomicrograph 6)** A diagnosis of decidualized endometrioma with co-existent ectopic tubal pregnancy was made.



#### Photomicrograph 6: Ovarian parenchyma exhibiting decidualisation and endometriosis (H&E: 10x10X)

#### Discussion

Endometriosis has been seen incidentally in upto 4% of women during laparoscopic ligation of fallopian tubes. However the exact prevalence is difficult to determine with precision and needs laparoscopy/surgery along with histopathology for confirmation [4]. There is no definite biomarker to diagnose endometriosis however CA-125 is seen to rise but doesn't show any correlation with therapeutic response [5]. Immunohistochemistry with Cytokeratin (CK) of different molecular weights like CK7 and CK 20 are claimed to be useful in the diagnosis of endometriosis externa [6].

Endometriosis although being multi-factorial, is largely estrogen dependent hence affects women in the reproductive years. The most accepted is the "retrograde menstruation theory" which suggests that cells of endometrium eject out of the fimbrial ends of fallopian tubes and get stuck on the peritoneum of pelvis and abdomen [7]. This theory likely explains the existence of gastrointestinal, pelvic and bladder endometriosis besides accounting for decreasing incidence of extrapelvic endometriosis at distances farther away from the uterus. The "coelomic metaplasia theory" states that any cell which is derived from the primitive coelom can convert into Mullerian epithelium thus forming endometrial stroma [8]. "Lymphatic or haematogenous spread" would explain the finding of endometriosis at distant sites. More recent studies have suggested an "immunological etiology" with an alteration of peritoneal factors that predispose some women to endometriosis. Endometriosis at sites of surgical incision is secondary to iatrogenic redistribution of endometrial stroma and glands during surgery. A proper preoperative clinic-radiological work up is necessary to ensure correct diagnosis and adequate surgical excision.

All our cases presented as tumors with unusual clinical associations and tumor like presentations. The first case, a 25-year female, presented with bilateral ovarian masses and multiple nodules in the peritoneum which were suspected to be malignant on basis of raised CA-125 and radiology. She underwent bilateral oophorectomy with regional nodal dissection. There were multiple peritoneal deposits of endometriosis throughout her peritoneum as well as on bladder surface which led to danazol prescription. In almost all our patients the symptoms were non-cyclic and presented with mass effects (eg. in ileocaecal region and bladder) or as multiple peritoneal nodules (associated with borderline mucinous cystadenoma).

Endometriosis involving the urinary tract is rare with a reported incidence of 1%, mostly, the urinary bladder. The frequency of urinary bladder being involved by endometriosis is 8 times more than ureter, the bladder-to-ureter -to-renal involvement ratio being 40:5:1 [9]. Endometriosis usually starts from the serosal aspect of bladder dome and subsequently invades the bladder transmurally and presents as a mass mimicking bladder neoplasm clinically and radiologically. The patient usually presents with haematuria and cystoscopy reveals nodular growth or fibrosis. Malignant transformation to clear cell adenocarcinoma is the most dreaded complication reported in upto 1% cases [10].

Five to fifteen percent of infertile women with or without pelvic pain suffer from extrapelvic endometriosis [11]. Intestinal endometriosis affects the rectum and sigmoid in up to 95 % cases followed by appendix (20%) and terminal ileum (5%) [11]. Endometriosis of the gastro-intestinal tract is usually superficial with unusual mucosal involvement. The patient may present with pain, distension of abdomen, altered bowel movement and/or bleeding from rectum. Advanced cases may show features of intestinal obstruction due to fibrosis and/or perforation specially in the ileocaecal and rectosigmoid areas. Initially the symptoms correlate with the menstrual cycle but with chronicity of the disease, such an

association can rarely be seen. Symptoms are often non-specific in nature, hence leading to a delay in diagnosis or a mistaken diagnosis of irritable bowel syndrome, Crohn's disease or malignancy. Colonoscopy is not usually diagnostic since these lesions are generally extramural.

The decidualized endometrioma associated with ruptured tubal ectopic pregnancy was a rapidly growing mass thereby leading to a clinical suspicion of malignancy. This rapid growth may be attributed to the hormonal environment in a gravid patient leading to excessive and sudden decidualisation and increased vasculature in pre-existing asymptomatic ovarian endometriosis [12]. This condition needs to be kept in mind as sometimes a clinical suspicion of malignancy may lead to an early termination of pregnancy.

Scar endometriosis is seen in upto 2% cases following hysterotomy and 0.03 to 0.4% cases after caesarean section [13]. The higher incidence following hysterotomy is noticed because the early decidua has more pluripotent capabilities leading to cellular replication and hence producing endometriosis. To prevent scar endometriosis, it is suggested that every surgery involving uterus and fallopian tubes should be concluded by thorough cleaning and vigorous irrigation by high jet solution before abdominal closure [14].

Since endometriosis is a multifocal disease, a thorough evaluation of all pelvic structures including the bowel, the bladder and ureters is always recommended. Transvaginal USG followed by MRI is essential especially if deeply infiltrating endometriosis is suspected. The management of endometriosis depends on the extent and location of endometriosis and severity of the symptoms. While no treatment is needed if patient is asymptomatic or has mild symptoms, medical treatment with continuous oral contraceptive pills, medroxyprogesterone, GnRH agonists and danazol have been used successfully. These agents tend to decrease the vascularity and volume of the disease however the chances of recurrence and relapse remain high following medical management [14].

## Conclusion

Endometriosis has varied clinical presentations along with unusual associations like decidualized ovarian stroma and borderline mucinous cystadenoma. The presentations also vary from case to case but the most common clinical feature in our series was lump and internal bleeding. The clinician should be aware of a diagnosis of endometriosis in extrapelvic sites like caecum and urinary bladder particularly in young to middle aged females. Management depends on the bulk of endometriosis, presentation and the site of involvement. It varies from simple observation, to medical and/or surgical treatment. Regular follow up is needed as recurrence can be seen in 28% of patients at 18 months after surgery and in 40% by 9 years [15]. These patients would require re-excision in most of these cases, however a possibility of malignancy should be kept in mind in case of repeated recurrences.

## Conflict of Interest of all authors:

None

## Financial Support

Nil

## References

- [1] Sonavane SK, Kantawala KP, Menias CO. Beyond the boundaries-endometriosis: typical and atypical locations. *Curr Probl Diagn Radiol* 2011;40(6):219-32

- [2] Machairiotis N, Stylianaki A, Dryllis G, et al. Extrapelvic endometriosis: a rare entity or an under diagnosed condition? *Diagnostic Pathology*. 2013;8:194.
- [3] Jubanyik KJ, Comite F. Extrapelvic endometriosis. *Obstet Gynaecol Clin North Am* 1997; 24: 411-40.
- [4] Choudhary S, Fasih N, Papdatos D, Surabhi VR. Unusual imaging appearances of endometriosis. *Am J Roentgenol* 2009;192(6):1632-44
- [5] May KE, Conduit-Hulbert SA, Villar J, Kirtley S, Kennedy SH, Becker CM. Peripheral biomarkers of endometriosis: a systematic review. *Hum Reprod Update* 2010;8:651-674
- [6] Takahashi K, Yamane Y, Kijima S. CA-125 antigen is an effective diagnostic for external endometriosis. *Gynecol and Obstet Invest* 1987;23:257-60
- [7] Sampson JA. Peritoneal endometriosis due to menstrual dissemination of endometrial tissue into the peritoneal cavity. *Am J Obstet Gynecol* 1972;14:422-69
- [8] Olive DL, Schwartz LB. Endometriosis. *N Engl J Med* 1993;328:1759-69.
- [9] Pastor-Navarro H, Giménez-Bachs JM, Donate-Moreno MJ et al. Update on the diagnosis and treatment of bladder endometriosis. *Int Urogynecol J Pelvic Floor Dysfunct*. 2007;18(8):949-54.
- [10] Nezhat FR, Pejovic T, Reis FM, Guo SW. The link between endometriosis and ovarian cancer. *Int J Gynecol Cancer* 2014;24:623-628
- [11] Patel BS, Tripathi JB, Patel FB, Rawal SA, Patel S, Gupta M. Extrapelvic Endometriosis: A study of 17 cases. *J South Asian Feder Obst Gynae* 2012;4(1):32-34
- [12] Fruscella E, Testa, AC, Ferrandina G. Sonographic features of decidualized ovarian endometriosis suspicious for malignancy. *Ultrasound Obstet Gynecol*. 2004;24:578-580
- [13] Wasfie T, Gomez E, Seon S, Zado B. Abdominal wall endometrioma after caesarean section. A preventable complication. *Int Surg* 2002;87:175-177
- [14] Wellbery C. Diagnosis and treatment of endometriosis. *Am Fam Physician* 1999;60:1753-68.
- [15] Selcuk I, Bozdogan G. Recurrence of endometriosis; risk factors, mechanisms and biomarkers. *J Turk Ger Gynecol Assoc*. 2013;14(2):98-103.



**Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The images or other third-party material in this article are included in the article's Creative Commons license, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons license and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this license, visit <https://creativecommons.org/licenses/by/4.0/>.

© The Author(s) 2023