

Retrospective Histopathological Analysis of Endometriosis: An Elusive Disease with Different Presentation

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Abstract

Background: Endometriosis is an important benign gynecologic pathology defined by presence of a tissue similar to uterine endometrium, which is located endometrial glands and stroma out side of the uterus associated with pelvic pain. The most common site is ovaries followed by posterior broad ligament, fallopian tubes, colon and round ligaments. **Objective:** To evaluate the endometriosis cases through pathologic analysis of histological features, age, site, and clinical presentation of endometriosis. **Materials & Methods:** Retrospective study was undertaken for a period of 2years from May 2015 to May 2017 in department of pathology, Narayana Medical College & Hospital, Nellore, and Andhra Pradesh, India. **Results:** 20 Cases of endometriosis recorded in the department of pathology in 2 years (May 2015-May 2017). Of all endometriosis cases, majority were found in 30-40 years age group. Most common site was ovary 11 cases (55%), and least common site was abdominal wall (scar) 1 case (5%), sigmoid colon 1 case (5%). Most common presentation was pelvic pain 7 cases (35%) and dysmenorrhea 5 cases (25%), menorrhagia 4 cases (20%), constipation 1 case (5%) and abdominal lump 1 case (5%). Common associated pelvic pathology was leiomyoma of uterus. **Conclusion:** Endometriosis has no pathognomonic signs or symptoms and it is difficult to diagnose clinically. Histopathology is gold standard test for confirmation of the diagnosis.

Keywords: Endometriosis; Histogenesis; Histopathology; Ovaries.

Introduction

Endometriosis is a benign condition characterized by the presence of endometrial glands and stroma found outside of the uterus both at pelvic and extra pelvic sites. It is a hormonally dependent condition and associated with both pelvic pain and infertility [1]. The most commonly affected sites of endometriosis are the ovaries followed by the pouch of douglas, utero sacral ligaments, vesicouterine pouch, serosal surface of uterus, fallopian tubes, round ligament, and rectovaginal septum. Endometriosis can also be located inside the genital tract and can spread in to the cervix and vagina, especially the posterior vaginal

wall, which is related to frequently affected rectovaginal septum. Extra pelvic endometriosis can be found in unusual places like in the urinary tract, thorax, and nervous system, gastro intestinal tract (appendix, rectum, and sigmoid colon) and in cutaneous sites and like most frequent location is the abdominal wall [2]. Malignant change of endometriosis may occur in up to 1% of women, with most common site being the ovary [3]. The main causes of extra pelvic implants are gynecological procedures such of caesarian section, hysterectomy and it can even occur after laparoscopic surgery [4]. An endometriosis in the ovary may be defined as an area of endometriosis, usually in the ovary, that as enlarged sufficiently to be classified as a tumor. Endometrioma of ovary is also called chocolate when it is filled with old blood resembling tar or chocolate syrup [5]. Endometriosis grossly variable in appearance from a few minimal lesions on intact pelvic organs to massive ovarian endometriotic cysts that distort tube ovarian

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anatomy and extensive adhesions often involving the bowel, bladder and ureter [6]. Different mechanisms have been proposed for endometriosis including retrograde menstruation and implantation coelomic metaplasia, direct transplantation and vascular dissemination but no particular mechanism explain all cases and each may contribute at least to some extent [7]. Because of atypical presentation, extra pelvic sites endometriosis are often confused with granuloma, hematoma, keloid, incisional hernia, vascular formation, sebaceous cysts, lipoma or tumor [8]. The purpose of this study is to pathognomic histological features of the disease and there by facilitate pathological diagnosis.

Materials and Method

The present study comprises of 2 years retrospective study done from April 2015 to April 2017 conducted in department of pathology, Narayana Medical College, Nellore, Andhra Pradesh. A total number of 20 endometriosis were diagnosed in department of pathology. Detailed clinical data including age, site of lesion clinical features, gross features, microscopic appearance and associated other pelvic pathological

lesions were taken from histopathology record books. We included the cases which showed only endometrial stroma without glands in the foci of endometriosis. In our study we excluded the cases which showed adenomyosis with out endometriosis.

Results

Among 20 cases of endometriosis, most commonly affected age group was 30-40 years and least commonly affected age group were < 30 years and 51-60 years (Table 1). The average age of patients with endometriosis was 34.6 years. The young patient was 20 years and oldest 60 years. The most common site of endometriosis was ovary 11 cases (55%) followed by tube 7 cases (35%), abdominal wall 1 case (5%), and sigmoid colon 1 case (5%) (Table 2). The most common presentation was pelvic pain 7 cases (35%), dysmenorrhea 5 cases (25%), menorrhagia 4 cases (20%) constipation 1 case (5%) and abdominal lump 1 case (5%) (Table 3). Asymptomatic cases were noted in 2 (10%) cases. (Table 3). Endometriosis associated with other pelvic diseases shown in Table 4. Most common associated pelvic pathology was leiomyoma of uterus 11 cases

Table 1: Distribution of endometriosis cases based on Age

Age(years)	Cases	Percentage
<30	3	15
30-40	10	50
41-50	4	20
51-60	3	20

Table 2: Distribution of endometriosis cases based on sites

Site	No	Percentage
Ovaries	11	55
Tube	7	35
Abdominal wall	1	5
Sigmoid colon	1	5

Table 3: Distribution of endometriosis cases based on clinical symptoms

Clinical symptoms	No	Percentage
Pelvic pain	7	35
Dysmenorrhea	5	25
Menorrhagia	4	20
Constipation	1	5
Abdominal lump	1	5
No com complaints	2	10

Table 4: Associated Pelvic pathologies in endometriosis cases

Associated pathological findings	No	Percentage
Leiomyoma	11	55
Adenomyosis	2	10
Adenomatous polyp	1	5
Salpingitis	1	5
No Association	5	25

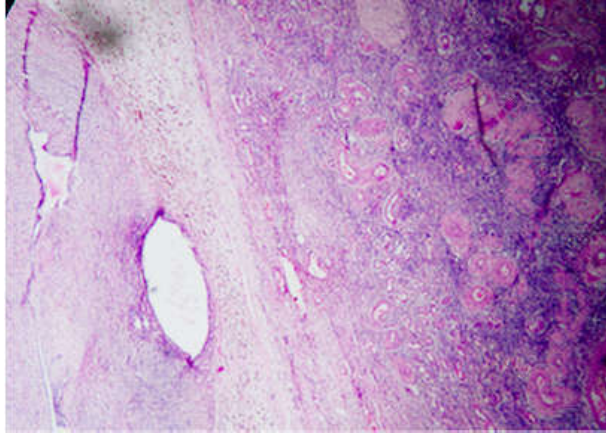


Fig. 1: Microscopic examination(100x), (H&E Stain) shows ovarian tissue consisting of corpus albicans, cortical cysts and endometrial glands, stroma and hemosiderin laden macrophages

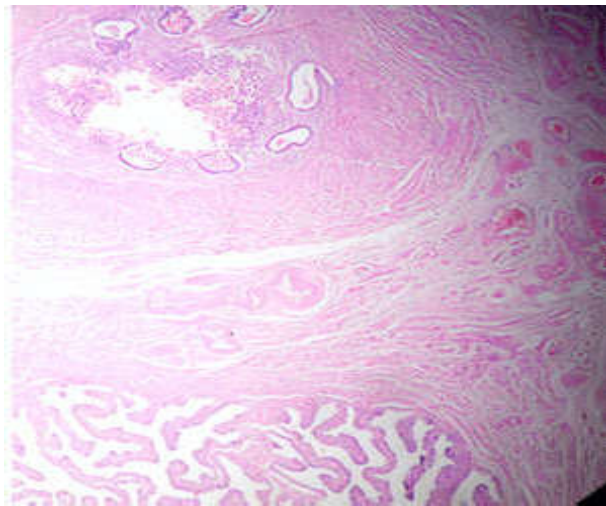


Fig. 2: Microscopic examination(100x), (H&E Stain) shows structure of tube and tubal wall having endometrial glands, stroma and hemosiderin laden macrophages

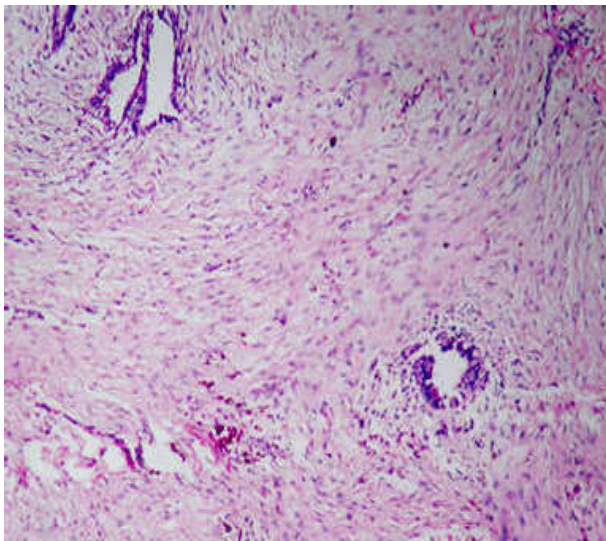


Fig. 3: Microscopic examination(100x), (H&E Stain) shows fibromuscular tissue with endometrial glands, hemosiderin laden macrophages and hemorrhages

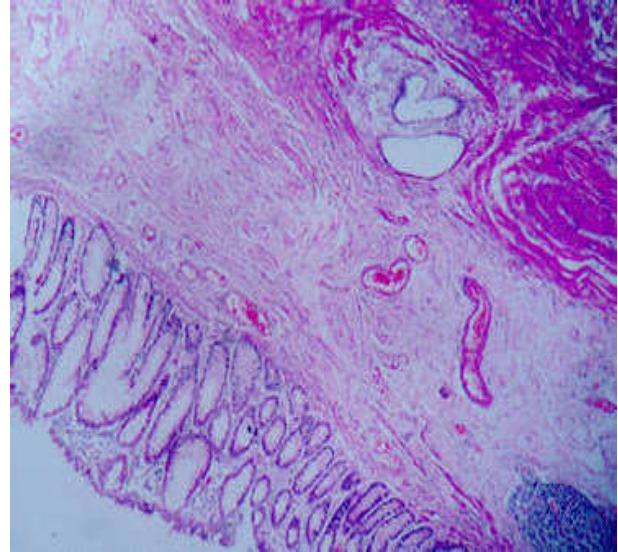


Fig. 4: Microscopic examination(100x), (H&E Stain) shows mucosal glands and submucosa muscularis shows endometrial glands decidualized endometrial stroma

(55%), followed by Adenomyosis 2 cases(10%), adenomatous polyp 1 case (5%), and salpingitis 1 case (5%). Endometriosis without significant associated diseases were found in 5 (25%) cases (Table 4).

Discussion

Endometriosis is estrogen dependent inflammatory condition accounting 8-10% of the women in reproductive age associated with primary or secondary infertility [9]. Endometriosis usually ends when menopause occurs because of the decrease in estrogen level during menopause. Endometriosis can reactivate in some postmenopausal women when iatrogenic or endogenous hormones are present. It is described by the presence of endometrial tissue outside the uterine cavity mainly on the ovaries and is the common cause of chronic pelvic pain, dysmenorrhoea and infertility [10]. Pathogenesis of the disease is still poorly understood. Different literature data have shown that estrogen is the most important factor that stimulates the growth of endometriosis and its production and metabolism is altered in disease process state [6]. Estrogen in women with endometriosis derives from three major sources. Secreted by the ovary into the circulation and produced in adipose tissue and skin via conversion of circulating androgens and synthesized locally in endometriotic tissue, which expresses complete steroidogenic enzymes including aromatase [11]. Both PGE₂ and PGF₂ alpha are produced in the uterus and endometriotic tissue of women with endometriosis

[12] . PGE2 is the most potent known physiological stimulator of estrogen biosynthesis in endometriosis. Endometriosis is some times described as two forms 1) external 2) internal. The internal form is synonymous with adenomyosis. In this condition a direct continuity is explained to exist between endometrium lining uterus and aberrant endometrium in the uterine wall. Adenomyosis is often classified with endometriosis but adenomyosis is described as different disease. External endometriosis is simply when the endometrial ectopic foci are located anywhere within the pelvis (ovary, pouch of Douglas, utero sacral ligaments, recto vaginal septum and vesico uterine pouch), abdominal cavity (bowel, omentum), outside (lungs, brain). Both diseases are of unknown cause and it is impossible to settle the question as to whether these are the same or different. Endometrium exists as a foreign tissue, it excites pathological tissue responses like hemorrhage and rective fibrous tissue. The sequelae of hemorrhage are in turn abnormal hemosiderin laden macrophages with focal calcification. Its first description as a pathology was given three centuries ago and recognition as a clinical entity by Sampson since 1918-192 [13]. The theories that were initially proposed for endometriosis were reviewed by Ridley [14] and grouped into (1) transplantation (2) coelomic metaplasia (3) metaplasia induced by factors released into peritoneal cavity. Sampson transplantation and implantation theory also called the theory of retrograde menstruation is the most widely accepted theory for formation of ectopic endometrium in endometriosis. This theory suggested that the origin of endometriosis is due to the propagation and attachment of ectopic endometriotic cells outside the uterus, in a continuous manner (adenomyosis) or by lymphatic, hematogenous mechanical dissemination (perineum or laparotomic scars).

In our study 20 cases of endometriosis were recorded in department of pathology in last 2 years (May 2015-May 2017). In the present study endometriosis commonly affected age group was 30-40 years with average age was 34.6 years. This finding was correlated with study carried out by Dominic A [15]. In our study the commonest site of endometriosis was ovary 11 cases (55%), followed fallopian tube 7 cases (35%), abdominal wall 1 case (5%) and sigmoid colon 1 case (5%). These findings were correlated with study carried out by Dominic A [15]. Our study most common clinical presentation was pelvic pain 7 cases (50%), followed by dysmenorrhea 5 cases (25%) and menorrhagia 4 cases (25%), constipation 1 case (5%) and abdominal lump 1 case (5%). In present study most common associated pelvic pathology was leiomyoma of uterus (55%) followed by adenomyosis 2 cases (10%), adenomatous

polyp 1 case (5%), and salpingitis 1 case (5%). Dominic A [15] study also shows leiomyoma of uterus is a common associated pelvic pathology with endometriosis. The significance of the association cannot be documented at this time. Infertility is a cause as well as a result of endometriosis, and the incidence of other pelvic diseases should be higher among women who have endometriosis than among those who do not [15].

Endometriosis presents a wide range of macroscopic variability. Endometriosis grossly variable in appearance from a few minimal lesions on intact pelvic organs to massive ovarian endometriotic cysts that distort tube ovarian anatomy and extensive adhesions often involving the bowel, bladder and ureter [6]. Endometriosis is microscopically diagnosed as the presence of glands and stroma. Diagnosis requires the presence of two or more of these histological features: endometrial epithelium, endometrial glands, endometrial stroma and hemosiderin laden macrophages. This ectopic tissue may present cyclical changes in which the glands show a minimal proliferative activity or an inadequate secretory transformation. This activity occurs because endometriotic lesions express estrogen and progesterone-specific receptors [16].

In most cases, the ovary is the primary site of external endometriosis. In the ovary, endometriosis exists in two forms 1) as the endometrial cyst 2) as the endometrial implant. Endometrial or chocolate cysts vary in size from 1 cm to 20 cm in diameter. They are bilateral in majority of the cases and rupture during removal. The content varies from a fresh hemorrhagic liquid to a thick chocolate colored fluid. The focal endometrial implant is a small blue puckered lesion, or dark brown or nodule with a few millimeters in diameter and indistinguishable small hemorrhagic follicles. The endometrial implant represents an early stage of the cyst. The microscopic features of endometrial implant of ovary shows corpus albicans and endometrial glands (Figure 1). Stroma shows hemosiderin laden macrophages and hemorrhages. The microscopic features chocolate cyst (endometriosis) shows cyst wall lined by endometrial epithelium, beneath which there is a characteristic endometrial stroma. The stroma contains large, oval, rounded to polygonal cells (siderophages) contain coarse granular or foamy with pale yellow brown pigment and endometrial glands. Adjacent area shows ovarian parenchyma.

Endometriosis of tube mainly due to the propagation and attachment of ectopic endometrial cells (endometrium) outside uterus, in a continuous manner through the fallopian tube (pelvic

endometriosis), mechanical dissemination (laparotomy scars). Microscopic features of tubal endometriosis reveals structure of tube and tubal wall having endometrial glands, hemosiderin laden macrophages and areas of hemorrhages (Figure 2).

Endometriosis of the anterior abdominal wall in or the umbilicus is always manifestation of external endometriosis. Scar endometriosis is commonly seen following surgical procedures on uterus and fallopian tubes and the incidence has been estimated to be only 0.03 to 0.15% of all cases of endometriosis [17]. The incidence of endometriosis abdominal wall is differ with literature due to small sample size of total cases in our study. In our study one case has been reported endometriosis of abdominal wall (5%) which is seen after the operation of caesarean section. The term scar endometriosis is used for well marked fibrous tissue with thick chocolate like liquid areas and is located anywhere in the surgical scar [18]. One study has reported scar endometriosis at surgical site it most commonly seen after the operation of caesarean section followed by episiotomy, hysterectomy, hysterotomy and laparotomy [19s]. Direct mechanical implantation seen to be the most plausible theory for explaining scar endometriosis. During caesarean section, endometrial tissue might be seeded into the wound and under estrogen influence these cell proliferates. In our study one abdominal wall endometriosis case reported which was presented with abdominal lump and clinically diagnosed as desmoid tumor. Grossly it shows fibrofatty mass measuring 4.5x4x3cm. cut section shows tiny cystic areas filled with thick jelly like material. Identified a small grey white nodule in adjacent fat. Microscopic features of abdominal wall endometriosis shows adipose tissue, fibromuscular tissue with endometrial glands lined by low columnar epithelium (Figure 3). Some of them are cystically dilated showing hemosiderin laden macrophages in the lumen (Figure 3). Adajacent stroma shows congested blood vessels and chronic inflammatory cells.

Endometriosis of the sigmoid colon is present in many late cases and indicates advanced disease. The involvement is commonly extrinsic. In our study one case reported presented with sigmoid colon with stricture. Grossly shows segment of intestine measuring 20 cm. cut section of intestine segment shows stricture identified measuring 3 cm ,which is 2 cm away from nearest resected margin. Distal part of intestine is dilated. Microscopic examination of stricture site of colon reveal mucosa lined by columnar epithelium, lamina propria shows chronic mononuclear inflammatory cell collection. Submucosa and muscularis shows endometrial glands with

decidualized endometrial stromal tissue noticed, transmural collections of chronic mononuclear cells and congested blood vessels (Figure 4).

This study probably do not indicate the exact incidence of the disease in the female population because of it is small sample size and representative of endometriosis cases which are recorded in histopathology records of department of pathology in our institute.

Conclusion

Today knowledge of the disease existence has increased. Because of its enigmatic etiopathogenesis, different individual presentations, the disease is recognized only after examination of pathological material. Histology is the hallmark of diagnosis

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