Endometriosis: rare localizations in two cases

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Summary

Endometriosis is a disease in continuous evolution due to its various aspects and atypical localizations. Every year many women all over the world are affected by it.

In typical localizations the diagnosis is simple; the symptoms include pelvic pain and in most of cases sterility.

In rare localizations the symptoms are non-specific and the diagnosis is difficult. In particular an intestinal isolated localization is often asymptomatic or can cause non-specific pelvic pain, irregular intestinal activity and in such case, a subocclusive condition often with a diagnosis of inflammatory bowel disease.

Two cases of rare localizations of endometriosis are described in the intestinal wall and a cesarean section scar. An analysis of the etiopathogenesis and diagnostic approach in these rare localizations is presented.

Key words: Endometriosis; Heterotopy; Extragenital localizations; Pelvic pain.

Introduction

Despite important advances in the last few years, endometriosis is still a remarkable social disease considering the fact that in the USA about 7 million women suffer from it. According to a UN report, 150 million women in the world are afflicted by endometriosis [1].

Endometriosis is a pathological state resulting from the dissemination and growth of endometrial tissue in anomalous places or it occurs through a metaplastic process, outside the normal sites. This disease is considered to be heterotopic [2].

The pathology is seldom documented in the pre-menarche period or after menopause, but is often associated with women between 20 and 50 years old. Therefore, it is a typical disease of reproductive age [3, 4].

Endometriosis lesions are usually confined to the ovaries, uterine ligaments, recto-vaginal septum, pelvic peritoneum, vagina and vulva, but they can occur even in the intestinal tract, the omentum, the mesentery or the hepatic peritoneum.

Rarely are endometriosis lesions found on the cutis (surgical scars resulting from episiotomy and laparoscopy), in the lung, the pleura, the kidney or in the brain and limbs.

It is not easy to establish the exact prevalence of endometriosis because the final diagnosis must result not only from a clinical study but also from direct laparatomic or laparoscopic examination and from subsequent anatomical and pathological confirmation by microscopic examination.

Clinical manifestations are characterized by a wide range of symptoms, and none can be considered pathognomonic of endometriosis.

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Case 1

In October 2005, a 37-year-old woman came to the Department of Obstetrics and Gynecology of the University of L'Aquila for irregular intestinal activity and rectum hemorrhage associated with modest pelvic pain, especially during the menstrual period.

In March 2003 she delivered spontaneously after a normal pregnancy and in the anamnesis there were no important or remarkable gynecological data. In 1999 she had hyperthyroidism due to Graves-Basedow disease.

In 2002 she had undergone a rectoscopy and a pancolonoscopy for frequent rectum hemorrhaging. During the rectoscopy a polypoid formation with a knolled surface situated 10 cm from the anal sphincter was removed and many biopsies were performed. Microscopic evaluation showed epithelium of large intestine mucosa with hyperplastic aspects and modest signs of flogosy stratified one on top of the other. On the basis of this result and the associated symptoms, irritable bowel syndrome was diagnosed.

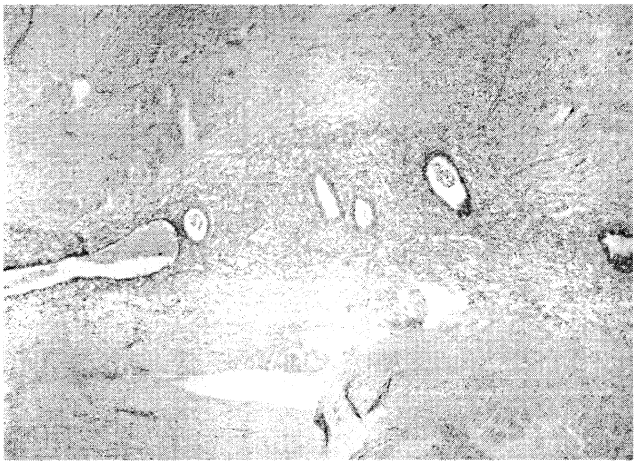
In March 2005 she repeated the colonoscopy in which an edematous mucosa emerged, 10 cm from the anal sphincter; the area was a hyperemic and granulated. A small polypus (3 mm) covered by apparently intact mucosa was found 30 cm from the anal sphincter which was completely removed by a biopsy. The intestine was thoroughly explored and seemed to stretch adequately, and was covered by apparently normal mucosa with a well represented underlying vascular mucosa. Microscopic evaluation of the colic mucosa was normal, except for a little fragment in which it was possible to observe a very small area with some gland fluid hyperacidity.

During her stay in our ward the patient underwent a pancolonoscopy. Macroscopic examination showed a slightly bluish area about 10 cm from the anus; many biopsies were performed revealing colic endometriosis with cytokeratin (20 positive) in the apical portion of every crypt and cytokeratin (7 positive) in a limited area of the fragment.

Transvaginal ultrasound was performed and CA125 checked but they both resulted negative.

Due to the risk of a pelvic localization of the endometriosis, the patient underwent laparoscopy. The absence of endometriosis foci in the pelvis let us conclude that the patient was affected by isolated intestinal endometriosis.

Fig. 1



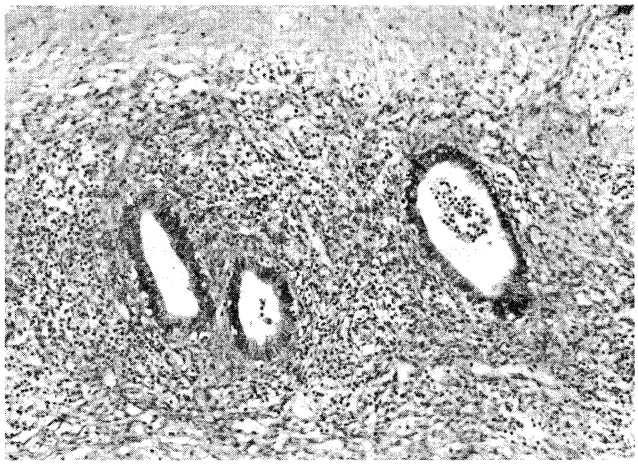


Fig. 2

Figure 1. — Hypodermal site showing endometrial glands covered by pseudostratified cylindrical epithelium. The glands are immersed in fusiform stromal cells (H&E x 4).
Figure 2. — Hypodermal endometriosis (H&E x 10).

Case 2

A 33-year-old woman reported that in the last few months a new formation came out of the surgical scar from a previous cesarean section three years before. In the anamnesis, she had undergone partial thyroidectomy for a nodule which caused hyperthyroidism: still today she is underging therapy with thyroid hormones and is affected by psoriasis.

The new formation was painful, especially during the menstrual period, and the same lesion was subjected to growth.

At the objective evaluation, the formation had well defined borders and was painful on palpation. The cutaneous formation was removed under local anesthesia.

Under macroscopic examination an oval formation 5 x 3 x 2.5 cm in diameter was seen with a cutaneous nodule (2 x 5 x 1 cm) with scarred and grey areas in a 1.5 mm section. The microscopic test showed sclerosing hypodermal endometriosis (Figgures 1 and 2).

The final diagnosis was iatrogenic hypodermal endometriosis

Discussion

Extragenital localizations of endometriosis are uncommon and without any specific symptoms. In most cases they are characterized by catamenial pain.

The disease has very singular characteristics, therefore it is important to distinguish it from inflammatory and neoplastic pathologies. Ectopic endometrium reacts, like normal uterine mucosa, to stimuli from ovarian hormones, especially estrogens, and it adopts proliferous and functional aspects (including flaking and bleeding during the menstrual period) very similar to the processes which happen in normal endometrium. Therefore it must be considered as a typical disease of reproductive age.

Although in recent decades a lot of data has been published about endometriosis, the etiopathogenetic mechanisms still remain unknown.

Many theories have attempted to define the possible pathogenic mechanism of endometriosis, but until now they have often lacked good scientific documentation, thus the etiopathogenesis of endometriosis is controversial [5, 6].

From an anatomic point of view, the origin of endometriosis has been discussed for a long time, with two main groups of theories emerging:

1) a "in situ" development of the pathology, through coelomic metaplasia;

2) endometrium dissemination in ectopic places by different mechanisms:

- retrograde menstruation
- lymphatic and/or vascular dissemination
- direct endometrial invasion.

According to the modern theory of induction, endometriosis could be the end result of local metaplasia induced by the presence of endometrium [7].

Most authors agree with the endometrial origin of ectopic epithelia rather than the mesothelial one.

Finally, surgical dissemination which is responsible for some localizations on laparotomic and episiotomic scars appears instead obvious.

The existence of very controversial theories and the lack of an univocal etiopathogenesis of endometriosis led us to ask if endometriosis is a single disease with various anatomopathological manifestations or if it represents a group of different diseases with an etiology and histological clinical aspects which are specific and independent.

With regards to isolated colic endometriosis without any pelvic involvement, the ethiopathogenesis could be explained by Beck's metaplasia where in ectopic locations, inclusion of isles of mesenchimal tissue would be assisted by which hormone stimulus could evolve into endometriosis.

Considering that the ovary and Muller's ducts derive from coelomic mesothelium, the supporters of this theory hypothesize that ovarian germinal epithelium can change into endometrial tissue. Generally, however, the potential of peritoneal mesothelium is considered a secondary Muller's system, so let us suppose that the possibility exists that also peritoneal endometriosis can be born from a process of mesothelial metaplasia. Actually, this theory is supported by a few cases of primitive endometriosis without any pelvic involvement [7]. For the diagnosis cytokeratin 7, a specific marker of some epithelia that derive from Muller's ducts, is useful.

Generally, ectopic endometrium adheres to the intestinal serous surface, but it can also invade the intestinal wall. Mucosal infiltration is rare, but can cause ulceration, hemorrhage, or perforation due to the influence of ovarian hormones causing congestion and obstruction.

Chronic inflammation can develop adherences which conceal the endometrial tissue and also stenosis or obstruction.

Clinical manifestations are characterized by various symptoms which are often atypical and cannot be considered pathognomonic. In particular, intestinal localizations, often asymptomatic, can non specifically bring about pelvic pain, irregular intestinal activity and, seldomly a subocclusive or occlusive condition. The severity of the intestinal symptoms, however, often does not correlate with the extension of the lesion.

In our opinion, for a correct diagnosis of intestinal endometriosis, it is very important to investigate any symptomatology which can only be determined from an accurate history. Therefore, precise diagnostic investigations such as rectoscopy and colonscopy can allow us to exclude or confirm possible diagnostic suppositions resulting from this kind of symptomatology, which include irritable bowel syndrome, Crohn's disease, diverticulitis and hemoperitoneum.

Normal instrumental investigations (colonoscopy, opaque enema, etc.) performed on patients with this kind of symptomatology due to the presence of endometriotic tissue revealed, in most cases, stenosis of the terminal ileum [8]. Thus these women had to undergo resection of the ileum for suspected Crohn's disease; however the follow-up histological examination showed chronic phlogosis of the mucosa, ulcerations and endometriosis isles of the muscular and subserous tissue.

The diagnostic value of opaque enema and colonoscopy is not very reliable because endometriosis rarely invades the intestinal mucosa [9].

Among the rare localizations, endometriosis of the abdominal wall is characterized from ectopic endometrium near a surgical scar, more frequently after cesarean section, although cases of endometriosis after laparotomic and laparoscopic surgery have been reported in the literature [10].

Moreover, there are many cases of endometriosis in areas corresponding to an episiotomy scar. This observation suggests that ectopic endometrium can be inducted iatrogenically through a mechanical implant. Also animal experiments have confirmed the possibility of transplanting vital endometrial tissue to ectopic locations [11].

Taking root is probably due to an alteration in the immune system, especially for the local cell component. The role of the immune system is an important consideration because through specific modifications it would permit the endometrial tissue to implant and grow vascularly by in ectopic locations.

There are numerous factors which are able to contrast the immune reaction such as transforming growth factor β (TGFβ), prostaglandin E2, placental protein 14 or glycodelin (PP14), and interleukin 10. These factors have been demonstrated to be higher in the peritoneal fluid and endometriotic tissue of affected women [12]. An environment rich in these factors involved non-specific suppression of the cell-mediated immunity, well correlated with the defected activity performed by natural killer cells (NK) at a local level in endometriosis [12]. In conclusion endometrial ectopic cells tend to use classical mechanisms to elude immune-overseeing.

Endometriosis of the abdominal wall can be easily diagnosed by its simple symptomatology and clinical objectivity. In fact, in abdominal wall localizations, the lesions appear as little nodules with different color, are painful during menstruation and, in most cases, the patients afflicted have a previous history of abdominal surgery, laparoscopy or cesarean section.

Conclusion

In rare localizations of endometriosis, the symptomatology is more frequently characterized by non-specific and subtle symptoms which are unlikely correlated with endometriosis, particularly in those isolated cases which do not have pelvic involvement that facilitates the diagnosis. The latter characteristic is very interesting because it shows the importance of knowledge of rare sites of endometriosis, allowing the opportunity of diagnostic suspicion when clinical data are apparently controversial, after obviously excluding, the most frequent causes of this symptomatology.

The role of laparoscopy in this pathology is remarkable from a diagnostic and therapeutic point of view.

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