

Extra-genitally located endometriosis

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Abstract

Endometriosis is defined by the presence of ectopic and endometrial islands outside the uterus. The significance of its finding is also outlined by its less frequent localizations (intestine, gall bladder, lungs) and by its differentiated symptoms complicating the differential diagnosis. The definitive diagnosis can only be reached through a histopathological examination as the detection of this affliction may lead to severe therapeutic errors (radical resection). The importance of an early diagnosis may help in preventing and delaying the effects of this affliction.

Keywords: ectopic endometriosis, histopathological examination, treatment errors.

Introduction

Endometriosis afflicts millions of women and adolescents throughout the world. At times, this disorder can entail devastating effects, rendering the woman or the adolescent incapable of caring about herself or her family, attending school, fulfilling social commitments, sustaining her career or private pursuits. Not only does endometriosis affect the patient alone but it may also have repercussions on all around [1].

Even though surveys signal heightened frequency of this disease in adolescents as well, the lesion is more likely to occur and become clinically significant in women, delaying pregnancy since prolonged ovarian function, uninterrupted by pregnancy, results continued stimulus of proliferating and expanding the disorder.

The incidence appears to be constantly soaring, it being related to current tendencies of delaying conception toward the fourth decade of life. It is likewise one of major causes of infertility [2].

Etiology, pathogenesis

The etiology of the disease has not yet been fully demonstrated. Of the many theories considered along the years, only two have remained valid.

The theory of celomic epithelium metaplasia sustains that endometriosis might originate in peritoneal endothelium metaplasia which, in its turn, derives from celomic epithelium, the same as genital organs do. The cause of such metaplasia might be hyperestrogenemia, in the presence of which mesenchymal elements, either covered or not by epithelium layer, would be likely to turn itself into endometrium or inflammation (embryonal

celomic cells are supposed to turn into endometrium under the impact of inflammatory phenomena).

The second is the theory of endometrial origin backed up by two hypotheses:

- The "back flow" theory (retrograde menstruation) upheld by John Sampson, 1921: endometrial fragments in menstrual blood are taken over, through the tubal pavilion, into the peritoneal cavity, where they get affixed.

- The theory of vascular metaplasia, ratified by Sampson and Halban, explains the other endometrial locations: the proliferation reaching myometrial interstices may penetrate blood and lymph vessels causing real endometrial embolism in any tissue or organ of the body [3, 4].

Considering the condition of tubal reflux during menstruation in 90% of women, certain authors recently maintain the theory of immunity according to which the development of the graft is the immune deficit.

The functional deficiency of peritoneal macrophages (manifested by low cytotoxicity and deficient stimulus of NK cells) might lead to a decrease in the defense power of peritoneum as against endometrial cells [5, 6].

Outer endometriosis proper is the result of the presence, growth and performance of endometrial tissue (glandular tissue and support stromal elements) elsewhere rather than inside the uterus.

Extragenital endometriosis localized due to various symptoms can complicate the differential diagnosis.

The effect of endometriosis on peritoneal medium may affect fertility. There is a raised level of peritoneal fluid while the amount and exercise of peritoneal macrophages (white scavenger cells) is increased.

Likewise, cytokines (chemical messengers) such as IL-1, IL-2, IL-6, INF-alpha, the interferon, C3, C4 are increased. All that may affect ovocyte-spermatozoa interaction. Furthermore, serum samples in women with endometriosis proved to be embryotoxic in mice embryonary cultures (78% of cases). Unmonitored estrogen therapy may lead to pre-malign or malign alteration of residual foci of endometriosis.

Endometriosis may play its part in the pathogenesis of certain earlier stages of malign ovarian epithelial neoplasms.

Detection, by various methods, and therapy of endometriosis may avert the patient's negative social impact, may solve chronic pelvic pains and help in preventing or delaying the effects of the disease.

☒ Sites of extra-genitally endometriosis

Gastrointestinal tract

The most frequent cases of extragenital endometriosis is found in the gastrointestinal tract with the predominance of the sigmoid colon and recto-sigmoid.

Patients suffering of endometriosis evidence inflammatory alterations and immunity system changes. CA-125 antigen does not seem to be a safe index in diagnosing the affliction. Dosing with CA-125 antigen may help in discriminating endometrial cysts from other cyst types (yellow body cysts). Injections with various germs play a significant part in modifying the immunologic medium of the endometrium. Positive results in combating both systems of chronic pelvic pains and low fertility problems can be derived by using DNA detecting methods such as genetic tests (gene probes) and the Papanicolau test.

Colon endometriosis

Symptomatology of colon endometriosis comprises clinical intestine disorders evidenced by sore defecation, rectal bleeding and even severe intestinal occlusion. When typical endometriosis is evident elsewhere in the pelvis, a diagnosis of colon endometriosis is obvious. Still, there are instances when clinical signs, the size and the features of substance matter lying between the intestinal walls or the obstruction degree render differentiation from carcinoma hard to make even in laparoscopy. It is uniquely through the anatomopathologic test that a safe diagnosis can be settled.

Endometriosis usually arises on serous surfaces of the intestine and, by a wider involvement, may trigger bleeding, healing to fibrosis, contraction and narrowing of the lumen in absence of ulceration or of mucosal lesion in contraction area.

Macroscopically, an anatomopathologic investigation reveals a blue non-capsulated mass with blurred limits at times shaped as diffuse, irregular inflammations extended mostly along the surface.

Microscopical inspection evidences that it reproduces uterine mucosa aspect, to a certain extent.

A persistent proliferative epithelium is occasionally evidenced even in the aspect of glandulo-cystic hypertrophy [7].

Small intestine endometriosis

Small intestine endometriosis is less often met, it being evident in 1–7% of patients diagnosed with digestive tract endometriosis, routinely affecting the appendix or the ileum under Meckel diverticulum.

Clinically, there is evidence of recurrent bouts of nausea, vomiting, abdominal pain, abdominal distention, premenstrually or else during menstruation. Although certain patients evidence intestinal obstruction, intestinal perforation is, however rare [8].

Obstructions are the result of four mechanisms:

- the intestine is tied up because of fibrous adhesences;
- fibrous reaction lying around endometriotic deposits are likely to cause stenotic rings;
- volvulus as a result of adhesences;
- intersusceptions can also appear.

In case of intestinal obstruction, volvulus, intestinal perforation, fibrous obstruction a surgical solution is obviously recommended.

The following gross aspects are notices intra-operatively:

- endometrial structure does not attempt to embrace the intestine as carcinoma does;
- tumor can be lifted the same as a button along the intestinal wall and moves easily without involving the whole intestinal segment;
- no enlarged lymph ganglia are perceived in the area.

Urinary tract

Symptomatology is quite varied and non-specific in endometriosis of urinary bladder and urethra. Cystalgia, cyclical hematuria, dysuria, the high frequency of maturation and of cystitis may be noticed where endometriosis is present in the urinary tract.

Bladder lesions are most often located anteriorly on the dome, further off from the trigon and it firstly affects serosa before it involves the muscular cover of the bladder.

The presence of bluish nodes (more distinguished during menstruation) is noticed cytoscopically. A urethral involvement was equally reported by intermittent obstruction with cyclical renal colic, in correlation with menstruation. The obstruction is generated by the scarred constrictive tissue near peritoneal endometriosis in a certain area of the pelvis, along the urethra.

Cyclic hematuria is evidenced clinically in case of urethral wall invasion.

Kidney endometriosis is rare. Only 20 cases have so far been reported. It is manifested by back and rib pain, permanent microscopic, macroscopic and less often cyclical hematuria.

When the cyclical aspect is present, it is correlated with the premenstrual stage. Intravenous pyelograms evidence clear but non-specific anomaly, it frequently suggesting renal carcinoma.

Respiratory tract

Thoracic endometriotic cases have also been reported to involve either the parenchyma or the pleura.

Thoracic lesions are likely to cause cyclic recurrent hemoptysis or spontaneous recurrent pneumothorax of which symptoms coincide with menstruation. Endometriotic areas trigger, in all locations, bleeding episodes termed “substitutive menstruation periods” by certain authors.

Epistaxis emerges in pulmonary location which is “substitutive nasal menstruation” secondary to typical vascular congestion and to nasal mucosa hyperemia induced through cyclical elevation of estrogen levels [9].

Nervous System

Rare cases of sciatic nerve involvement have been reported, that being embraced by endometrial zones extending deeply under ligaments, accompanied by cyclical sciatica linked to menstruation periods [10, 11].

Skin

Endometriosis of diverse cutaneous zones seems to have arisen as result of a direct implant but in certain cases lymphatic spreading or even metaplasia of adjacent epithelial celomic derivatives springs of itself in such remote areas. Macroscopically, lesions can take over a polypoid vesicular aspect with tar or even serous content, with or without adherential phenomena. The presence of glands and endometrial stroma is rendered evident macroscopically, with or without macrophages loaded with hemosiderin. Endometrial glands are not always apparent so that ectopic endometrial stroma is looked upon as sufficient in settling the diagnosis. Endometrial foci alternate with zones of fibrous reshuffling.

Female genital tract

Evolution of endometriosis is linked to ovarian function as ectopic foci of endometrial mucosa are sensitive to hormonal stimulation by the ovary. Therefore, as long as ovarian function persists, the volumetric growth of these foci also carries on. Incipient detection of the disease, the correct setting of differential diagnosis is feasible today by help of cytology, rectoscopy, irrigography or seric antigen CA-125 identification in the middle of the follicular stage, but a safe diagnosis can only be set by biopsy and histologic screening.

While considering the immunologic alterations in patients with endometriosis, immunologic factors such as endometrial etiology should not be overlooked.

The diminished reactivity of T-cells, the mediated cytotoxicity of autologous endometrial cells was reduced in Rhesus monkeys with spontaneous endometriosis and likewise in infertile women with endometriosis.

Several researchers reported the answering capacity of NK cells: low cytotoxicity of fluid NK cells in patients with K 562 endometriosis (a target cell lysed by NK cells *in vitro*) as well as on heterologous and autologous endometrium.

Certain increased levels in a variety of antibodies have also been reported in patients with endometriosis. A raised basal activation of peritoneal macrophages has likewise been noticed in patients with endometriosis by certain researchers [12].

Of all facts considered it can be highlighted that endometriosis is a systemic affection with associated symptoms which are not conspicuously gynecologic.

Such indices, taken alone, cannot signal the presence of endometriosis. Yet, assessed together, as a profile, alongside other indices comprising inflammation and immunity activation, they indeed are of help in settling the diagnosis.

Patients with endometriosis shows the elements found in inflammation, represented by: microcalcifications, histological fibrosis and destruction of the image. Patients with endometriosis supervised by us evidenced such characteristics as met in inflammation: microcalcifications, fibrosis and destruction of histological image.

CA-125 antigen does not seem to be an index of reliability in diagnosing endometriosis, due to its lowered sensitivity to the affection. The ectopic endometriotic tissue is hormone-dependent, being submitted to certain periodical alterations during the menstrual cycle. Dosage of CA-125 antigen may be of use in differential diagnosis of endometriotic cysts as against those belonging to other types.

Endometriosis may coexist with infectious diseases, either acute or chronic of feminine genital apparatus, the symptomatology of such affections partially overlapping. The identification of microbial flora, being the cause of infections and inflammations of feminine genital apparatus, is necessary with a view to assessing chronic pelvic pain or lowered fertility. In such a case, the treatment of infectious agent will contribute to both fighting chronic pelvic pain and fertility problems.

Microscopic examination of intestinal endometriosis evidences the aspect of uterine mucosa, yet, with slight differences. A proliferative-type epithelium usually arises, which, at times, takes on the appearance of cystic glandular hypertrophy or evidences fibrous alterations around the affected structure.

In urinary bladder and ureter endometriosis lesions firstly affect the serous and, at times, the very muscular coating of vesical wall.

In cases of cutaneous locations, the presence of glands and of endometrial stroma is evidenced microscopically, while endometriosis foci alternate with zones of fibrous recovery.

Precocious diagnosis of endometriosis is achieved by help of cytology, rectoscopy or by determining seric CA-125 antigen at the middle of follicular phase, but the precise diagnosis is established by puncture biopsy correlated with anatomopathological tests.

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