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A Case of Clear-Cell Endometrioid Adenocarcinoma Developed in an Endometrioid Cyst of the Ovary

M. Batinova, St. Djambazova, I. Hubavenska**

Department of Anatomy, Histology and Embryology, Medical University, Plovdiv
** Department of General and Clinical Pathology, Medical University, Plovdiv*

We present a case of a 33-year-old female with ovarian cyst verified clinically and ultrasonographically, which required surgical therapy. Cystadenoma was found on the gefrir examination. Right-sided adnexectomia was performed. The postoperative histological examination verified mixed clear-cell endometrioid adenocarcinoma originating in endometriotic cyst with atypia of the lining epithelium.

Key words: clear cell; endometrioid adenocarcinoma; ovarian cyst.

Introduction

Endometriosis is an ectopically situated endometrium – glands and stroma. In cases of localisation in the myometrium it is classified as internal endometriosis (adenomyosis); when localised in other sections of the genital tract it is classified as external genital or extragenital endometriosis.

Endometriosis is a relatively common condition, found in 29% of women undergoing laparotomy [3]. It is often found in the ovaries, and its origin is associated with metaplasia of the mesothelium of the ovary into a uterine-corporal type or with the implantation of endometrial cells retrogradely carried through the uterine tube [7]. Macroscopically it manifests as cysts of varying size, called endometrioid or "chocolate" cysts.

Endometriosis rarely gives rise to malignant tumours, but it is believed to play a major role in their development in the presence of an excess of exogenous (e.g. tamoxifen) and endogenous estrogens [4, 6]. S a m p s o n was the first to describe the malignant transformation of endometriosis in 1925 [5]. Later a multitude of authors have reported malignant changes in the endometriosis in genital and extragenital places. They often make note of ovarial carcinoma associated with the endometriosis – in particular clear-cell adenocarcinoma and endometrioid adenocarcinoma. Several authors have described atypical endometriosis and have classified it as precancerocis.

In this report we describe a case of mixed clear-cell/endometrioid adenocarcinoma which originated in a endometrioid cyst.

Case description

A thirty-three-year-old woman (S. R. B. No 1425-31/05) with two-week-long complaints of pain in the lower abdomen, stronger on the right side. A gynecologic examination revealed a tumoural formation in the region of the right ovary. An echography of the pelvis established a right-sided ovarial cyst. A laparotomy was performed. Gefrir examination showed the process in the right adnexes to be a cystadenoma. Per the diagnosis the only surgery undertaken was a right-sided adnexectomy.

A macroscopic inspection of the biopsy specimen established a monolocular cyst 10 cm in diameter, with thick, dense, and in some places fibrous yellowish-brown walls, its cavity filled with thick chocolate-like matter. A washout revealed a dense, solid knot filling more than a half of the cavity, on a wide base, with coarse imperfections and with a light-yellowish-gray sectional surface flecked with hemorrhages, necroses, and cavities with jelly-like contents. The tissue fragments of the biopsy specimen were processed and stained according to routine methodology with haematoxyllin and eosin.

During the histological examination of the sections along the wall of the cyst we discovered focal upholstery made of endometrioid epithelium – in places single-layered,

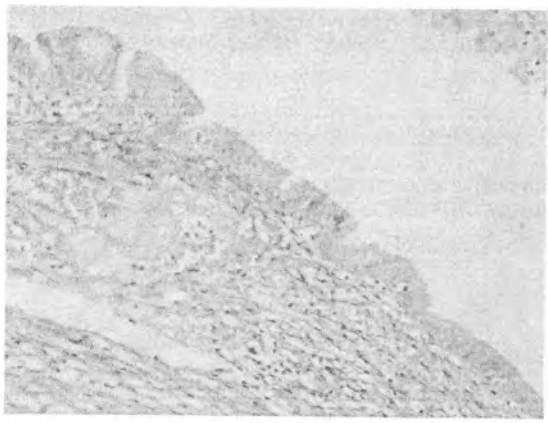

Fig. 1. Wall of endometrioid cyst lined with single-layered endometrioid epithelium and area lined with taller, stratified epithelium showing signs of cellular atypism. × 40

Fig. 2. Local clear cell metaplasia in the wall of endometrioid cyst. × 10

Fig. 3. Dense tumoural knot with fields of clear cell carcinoma and endometrioid adenocarcinoma. ×10

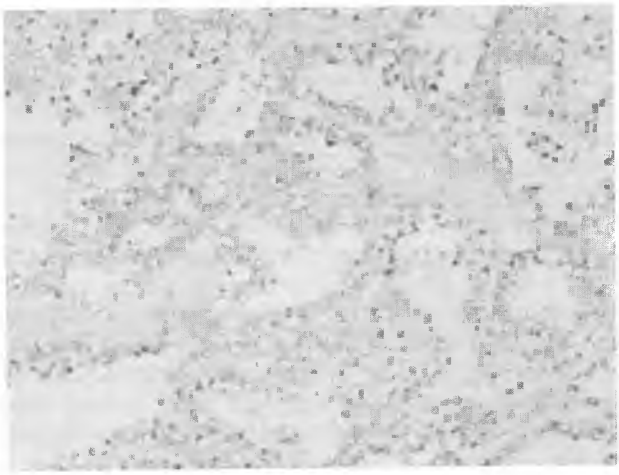

Fig. 4. Area of clear cell carcinoma. × 40

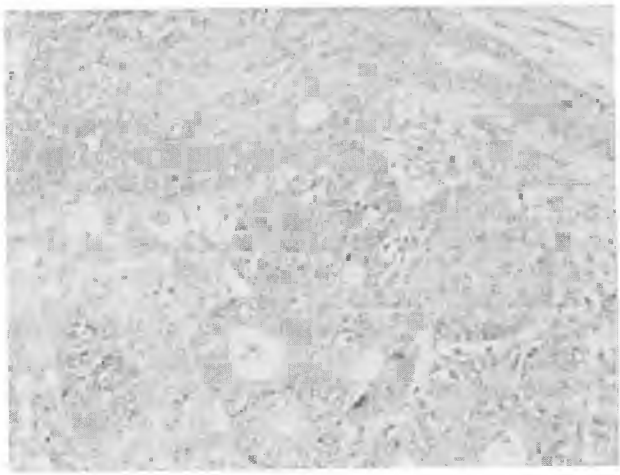

Fig. 5. Endometrioid adenocarcinoma with area of squamous cell metaplasia. Magnification x 40

in places multilayered, stacked higher and exhibiting signs of cellular atypism – hyperchromic nuclei, polymorphism, increased nucleus-to-cytoplasm ratio (Fig. 1). The endometrioid epithelial upholstery is absent in some places or is substituted by clear-cell ("thumbtack-like") epithelium, mucinous, eosinophilic epithelial metaplasia (Figs. 2, 3). In isolated short and narrow islets under the epithelium we found endometrioid stromal cells.

During the histological examination of the dense tissue knot we observed a mixing of fields with the characteristics of both clear-cell adenocarcinoma and endometrioid adenocarcinoma amidst considerable fibrous stroma. The endometrioid component has focal squamous cell metaplasia (Figs. 3, 4, 5). Biopsy verification of mixed clear-cell/ endometrioid adenocarcinoma in an endometrioid cyst with atypism of the upholstering epithelium required relaparotomy, hysterectomy with left-sided adnexectomy and omentectomy. No histological evidence for endometriosis or a malignant process was found in the material from the relaparotomy.

Discussion

Sampson was the first to note that malignant alterations can emerge from endometriosis and proposed the following criteria for detecting them: 1) there is clear evidence of endometriosis near the tumour; 2) the histological type of the tumour suggests endometriosis as the probable origin; and 3) there is no other primary site [3, 5]. In 1990, H e a p s et al. presented 195 prior cases of malignant tumours originating from foci of ovarial or extraovarial endometriosis and also discussed 10 of their own cases. Out of 205 cases, 165 (78%) involved ovarial endometriosis, 44 (21.3%) were extraovarial endometrioses, and 4 patients had endometriosis both inside and outside the adnex [5].

Other reports based on retrospective material show that ovarial endometriosis is most often combined with clear-cell adenocarcinoma and endometrioid adenocarcinoma. The cases of endometriosis with ovarial adenocarcinoma vary between 21-73.9% (mean 38.6%) for clear-cell adenocarcinoma and from 9.6-41.9% (mean 24.4%) for endometrioid adenocarcinoma [5]. According to another source, the most common ovarial tumours associated with endometriosis are the endometrioid tumors (70%). The predominant part (90%) of carcinomas connected to extraovarial endometriosis are also of the endometrioid type [2].

The number of tissue sections in a given case of endometriosis is a factor that influences the percentage differences in reported cases. The fewer the sections made, the fewer the cases involving endometriosis [5]. In addition, the tumour may completely invade the source tissue, eliminating all histological evidence of typical or atypical endometriosis [3].

Czernobilsky and Morris investigated 192 cases of endometriosis and first described atypical endometriosis [3]. Atypical endometriosis is characterised by abnormal but not malignant cells which exhibit hyperchromasia, light to moderate polymorphism, and increased nucleus-to-cytoplasm ratio. The epithelial cells are usually tall and layered. Czernobilsky and Morris also described inflammatory atypia in endometriosis, where cells are in one row, with minimal nucleic hyperchromasia, and are adjacent to noticeable stromal inflammation [3].

The age of patients with atypical endometriosis varies between 27 and 39 years (mean 35.3 years). The attending symptom is abdominal pain. Often, endometrioid cysts are described macroscopically. In reports, atypical endometriosis is present in only 1.7% of cases of endometriosis without neoplasm and is combined very often with malignant epithelial neoplasm /predominantly clear-cell or endometrioid carcinoma [3].

Andersen et al., Kaoru et al. report cases of atypia and metaplasia of the endometrioid epithelium – in cilliar, eosinophilic, mucinous, clear-cell „thumbtack-like", squamous epithelial cells. These authors both note that cilliar and eosinophilic metaplasia are the most common types of metaplasia of ovarial endometriosis combined with ovarial carcinoma.

Recently there has been research into the biological behavior and proliferative activity of typical and atypical endometriosis with ovarial carcinoma based on immunohistochemical analysis with KI-67 [5]. KI-67 reactions with nuclear nonhistone protein manifest in the nuclei of proliferative cells during the cell cycle, with the exception of G0 and early G1 phases. Several immunohistochemical studies with Anti KI-67 monoclonal antibodies have proven a close connection between the KI-67 index and biological behavior. These reports suggest that premalignant lesions and carcinoma *in situ* have proliferative activity lower than that of carcinoma but higher than that of normal and benign epithelium. They also suggest that KI-67 can provide prognostic information in some cases of carcinoma [5, 6].

In a study by B a l l o u k et al., DNA aneuploids have been observed in 3 out of 6 endometrioid cysts with severe atypia, while histologically normal epithelium is diploid [1,5].

We believe in the appropriateness of more thorough future research aimed at determining the biological significance of metaplastic changes in the endometriosis, and of the atypical endometriosis in carcinogenesis.

Conclusion

The case we have reported matches the criteria for malignant transformation in an endometrioid cyst indicated by Sampson; we have observed manifestations of atypism and metaplasia in the cyst epithelium; as a mixed clear-cell/endometrioid adenocarcinoma the case is especially interesting, as we could not locate other reports of mixed carcinoma in endometrioid cyst and endometriosis.

Note: The numbers in parenthesis correspond to the numbers of the microscope pictures on the disk.

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