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A RARE CASE OF SEROUS CARCINOMA OF THE UTERINE CORPUS THAT ARISES IN POLYP

Ana Kocevska[1,3], Emil Bajalski[1], Dimitar Georgiev[1], Bashkim Ismaili[1], Kristina Skeparovska[1,3], Shenol Tahir[2,3], Aleksandar Nakov[1]

[1] Specialized Hospital for Gynecology and Obstetrics "Mother Teresa" – Skopje, R.North Macedonia

[2] University Clinic for Surgical Diseases "St. Naum Ohridski" – Skopje, R.North Macedonia

[3] Faculty of Medicine, "Ss. Cyril and Methodius" University in Skopje, R.North Macedonia

Abstract

Endometrial polyps (EPs) are common pathological findings and their prevalence range is between 16% to 34% depending on characteristics of the examined population and detecting methods. Clinically, these lesions cause thickening of the endometrium and abnormal uterine bleeding. Asymptomatic EPs can be detected by routine ultrasound examination or infertility investigations. Most EPs are benign.

Their malignant potential is highest in postmenopausal women with uterine bleeding (2.3%). Serous carcinoma is the prototype of type-II endometrial cancer (nonendometrioid) and accounts for <10% of all endometrial carcinomas.

It is a very aggressive tumor, unrelated to estrogen stimulation, arising occasionally in endometrial polyps or from precancerous lesions developing in atrophic endometrium that mainly occur in older women.

We present a case of 72-years-old patient with uterine bleeding, with thick and heterogenous endometrium detected on ultrasound. Fractionated explorative curretage was performed and serous carcinoma that arises in polyp was diagnosed. After operative treatment, histopathological analysis of the operative material showed stage II of the disease.

Keywords: endometrial polyps, abnormal uterine bleeding, serous carcinoma, endometrial thickening.

Introduction

Endometrial polyps are benign proliferations of the endometrium that contain various amounts of glandular tissue, connective tissue and blood vessels. The morphological diversity of EPs is a reflection of the type of endometrium which they originate from, so they can range from atrophic to hyperplastic and carcinomatous [1].

Endometrial polyps are common pathological findings and their prevalence range is between 16% to 34% depending on characteristics of the examined population and detecting methods [2].

Clinically, these lesions cause thickening of the endometrium and abnormal uterine bleeding. Asymptomatic EPs can be detected by routine ultrasound examination or infertility investigations [2]. Most EPs are benign. In a meta-analysis of their malignant potential, the risk was found to be highest in postmenopausal women with uterine bleeding (2.3%) [3].

Endometrial cancer (EC) is the fourth most commonly diagnosed malignancy and the seventh most common cause of cancer death in women in the United States. In the Republic of North Macedonia, in 2020, there were 369 new cases of cancer of the uterine body, which was 10.9% of all new cases of malignancies and was the third most common in women, after breast cancer and colorectal cancer [4].

There are two different pathogenetic types of endometrial carcinoma:

- The most common type, type I (endometrial adenocarcinoma, 80%) occurs in women with a history of chronic exposure to estrogen action that was not opposed by progestogens.

These are estrogen dependent neoplasms. Such tumors usually begin as atypical endometrial hyperplasia that progresses to cancer. The first pathogenetic type of the disease arises in women with obesity, hyperlipidemia, anovulatory menstrual cycles, infertility, late onset of menopause.

This tumors tend to be well differentiated (endometrioid type) with a low nuclear grade and usually have a more favorable prognosis [5].

- Type II ((nonendometrioid, 20%) endometrial carcinomas are estrogen independent neoplasms, which occurrence is not associated with unopposed estrogen action and endometrial hyperplasia.

These tumors occur on the basis of atrophic endometrium and/or polyps, have a high nuclear grade and serous or clear-cell histology. Many of these tumors are associated with a mutation of the p53 tumor suppressor gene [5].

Serous carcinoma is the prototype of type II endometrial cancer and accounts for <10% of all endometrial carcinomas [6]. It is a very aggressive tumor, unrelated to estrogen stimulation, arising occasionally in endometrial polyps or from precancerous lesions developing in atrophic endometrium that mainly occur in older women [7]

In the meta-analysis of Megane Clarke et al., they analyzed 129 studies with 4079 patients and found that postmenopausal bleeding occurs in 90% of patients with endometrial carcinoma, but only in 9% of those who have postmenopausal bleeding, endometrial carcinoma is diagnosed [8].

Case report

We present a case of 72-years-old patient with serous carcinoma of the uterine corpus that arises on polyp. She was 20 years postmenopausal and had 3 pregnancies with 3 spontaneous deliveries. She was taking antihypertensive therapy and denied personal and family history of malignant diseases.

The value of the Body Mass Index was 28 (pre-obesity). On bimanual vaginal examination, the uterus was slightly enlarged and mobile. Postmenopausal bleeding was present. Hematological and biochemical parameters were within reference ranges.

The transvaginal ultrasound examination showed that heterogeneous and irregular endometrial thickening was present [image 1].

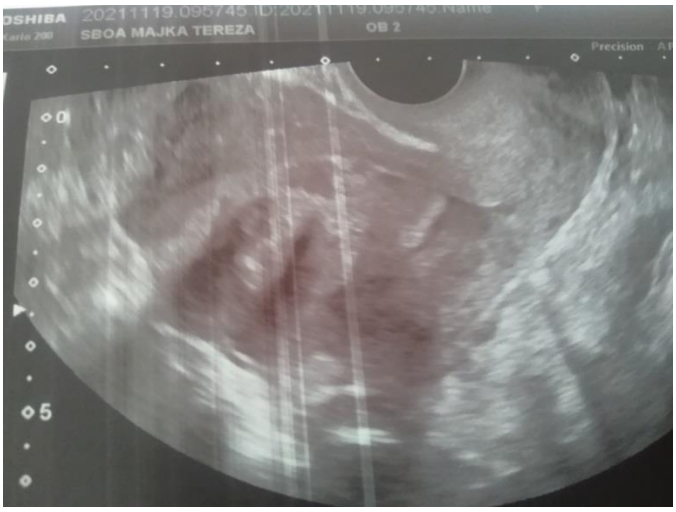

Image 1. Ultrasound image that shows heterogeneous and irregular endometrial thickening

We performed fractionated explorative curettage. The histopathological report showed presence of parts of an endometrial polyp made of fibrotic endometrial stroma and cystic dilated endometrial glands.

The surface of the polyp is covered with atrophic endometrium and in some parts it is covered with malignantly altered endometrium. The morphology of serous endometrial carcinoma with complex papillary and glandular architecture is present. It is also present in some of the glands of the polyp. Fragments of neoplastic tissue are also present in the material.

Tumor cells have a sparse cytoplasm, polymorphic nuclei and pronounced nuclear atypia with visible nucleoli. Pathological mitoses have been verified. Tumor cells are arranged in papillary and pseudoglandular structures, in sections with a micropapillary architecture.

No lymphovascular invasion or infiltration of the cervical stroma was found. Immunohistochemical analysis showed the following results: p53 (+), CK AE1 / AE3 (+), CK7 (+), ER (+), PR (+/- partial), WT1 (+/- partial) and CK20 (-).

Two months after the curettage, the patient underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy. Pelvic lymphadenectomy and omentectomy were not performed. Histopathological analysis of the operative material showed the absence of lymphovascular infiltration but presence of myometrial and infiltration in the cervical stroma (pTNM = pT2 pNx pMx R0 L0 V0 Stage II).

Cytological analysis of the peritoneal fluid showed presence of benign cells. The patient was referred for further treatment to an oncologist, where chemoradiotherapy was performed.

Discussion

In the study of Milosevic et al, 32.7% of 961 postmenopausal patients were found to have an endometrial polyp [9]. Menopause is considered as a risk factor for endometrial neoplasia arrising in a polyp. Fernandez-Parra et al. examined 653 patients and found that prevalence of carcinomatous polyps was 1.5% and they were diagnosed only in symptomatic postmenopausal women (with bleeding) but not in asymptomatic and premenopausal women [10].

In one multicenter italian study of 1152 asymptomatic and 770 symptomatic postmenopausal women with hysteroscopic polypectomy, Ferrazzi et al detected only 1 case (0.1%) of a carcinomatous polyp present in an asymptomatic patient.

This prevalence was 10-fold lower than in symptomatic patients ($p < 0.0001$). The prevalence of polyps with atypical hyperplasia was 1.2% in asymptomatic women and 2.2% in symptomatic women ($p < 0.005$). Polyp diameter was the only variable significantly associated with abnormal histology (cancer, atypical hyperplasia) in asymptomatic women (OR for mid-diameter polyps> 18 mm, 6.9; CI, 2.2-21.4) [11].

A study by Antunes Jr et al, performed on 475 patients aged > 40 years, found that 13.47% had a polyp with endometrial hyperplasia without atypia, 1.05% had a polyp with atypical endometrial hyperplasia, and 2.74% had carcinomatous polyps. Premalignant and malignant lesions were associated with age and postmenopausal bleeding

In this study, the recommendation is to remove polyps in all older women and whenever postmenopausal bleeding is present. In women without risk factors, routine polypectomy may be delayed to reduce surgical risks and costs [12].

Endometrial serous carcinoma is an uncommon variant of endometrial carcinoma and constitutes approximately 10% of all endometrial glandular tumors. It occurs in postmenopausal elderly women and arises in a background of atrophic endometrium from a precursor known as endometrial intraepithelial carcinoma. It is estrogen independent and negative for estrogen receptor.

In contrast, endometrioid adenocarcinoma is associated with hyperestrogenism and estrogen receptor positivity [13].

The serous type of uterine carcinomas are 3–10% of all cases [14] but despite the small percentage of women carrying this histological subtype, a disproportionate number of them will succumb compared to the endometrioid type group. More specifically, approximately 40% of uterine cancer-related deaths are attributed to the serous variant [15].

This is an extremely aggressive cancer and has a high risk for recurrence, metastasis and death. Therefore, it has been suggested that even patients with stage IA disease might be treated with adjuvant chemotherapy [16]. However, it has been also reported that the clinical outcome is excellent when the tumor is confined to endometrial polyp or endometrium [17].

It's aggressive biological behavior could elucidate its distinct clinical course; it is usually diagnosed at a more advanced stage, and it is associated more frequently with extra-pelvic recurrence [18,19].

Consequently, 5-year survival rates do not exceed 45% [20,21] and even in the best performing stage I patients, the 5-year survival rate is about 70%, which is considerably worse than in patients with the endometrioid type [22].

In our study, a mutation in the p53 tumor suppressor gene was detected, positive estrogen receptors were present, as well as partially positive progesterone receptors. p53 mutations were found in a subset of approximately 10–20% of endometrioid carcinomas, which were mostly grade 3 [23]. But in serous carcinomas, this mutation is present in 90% of the cases [24].

The cancer was in stage II so it has spread from the body of the uterus into the connective tissue of the cervix (cervical stroma). Pelvic lymphadenectomy was not performed, so we have no information if there is involvement of the regional lymph nodes.

Lymphadenectomy is required for the optimal staging of uterine carcinomas and is correlated with survival benefit in several studies [25,26]. However, these results have been criticized, and more studies are now in progress to further evaluate the clinical significance of lymphadenectomy in endometrial cancer [27].

Conclusion

Endometrial carcinoma is the most common gynecological malignant neoplasm, but the disease is associated with a favorable survival rate because most of the cases are symptomatic and diagnosed in an early stage.

Postmenopausal bleeding occurs in approximately 90% of patients with endometrial cancer, but only 9% of women with postmenopausal bleeding have endometrial cancer.

We have described a case of endometrial serous carcinoma arising in the endometrial polyp, in stage II of the disease. This is an extremely aggressive cancer and has a high risk for recurrence, metastasis and death.

They are 3–10% of all cases but approximately 40% of uterine cancer-related deaths are attributed to the serous variant. Because this cancer usually presents with symptoms in the early stages (postmenopausal bleeding), timely diagnosis and appropriate therapy are most important.

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