CASE REPORT

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Bilateral primary fallopian tube carcinoma: a case report

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Abstract

Primary cancer of the fallopian tube is a very rare tumor nowadays, accounting for approximately 0.14–0.3% of all tumors of the female genital tract. From these, bilateral primary cancer is found in less than 25% of all cases. We report here a case of bilateral primary cancer of the fallopian tube in a 48-year-old woman, associating uterine fibromatosis.

Keywords: fallopian tube cancer, adenocarcinoma, microinvasive carcinoma, cellular atypia, uterine fibromatosis.

Introduction

Primary cancer of the fallopian tube is a rarely diagnosed tumor, accounts for 0.3% of all cancers of the female genital tract [1–3] and almost all are adenocarcinomas [4]. Most reports consist of small and retrospective series.

In histological features and behavior, fallopian tube carcinoma is similar to ovarian cancer; thus, the evaluation and treatment are also essentially the same [5]. The vast majority (>95%) of fallopian tube cancers are papillary serous and adenocarcinomas [6]. More often, tumors can grow from smooth muscle fallopian tubes – sarcomas and from other cells of tube – transitional cell carcinomas. It is important to distinguish between primary malignant tumors of the fallopian tubes from other primary sites, most often the ovaries, endometrium, gastrointestinal tract, breast or in primary peritoneal carcinomatosis. Metastatic carcinomas are seen 10 times more often than primary tumors.

The most common primary cancer is the ipsilateral ovary, which has spread by direct invasion or from a contralateral ovary *via* transcoelomic spread.

The etiology of adenocarcinoma of the fallopian tube is uncertain. The risk factors are thought to be infertility, nulliparity or low parity, pelvic infection (chronic tubal inflammation), and a family history of ovarian cancer [7].

We report a very rare case of bilateral fallopian tube adenocarcinoma in a 48-year-old female with nonspecific symptoms, who also developed a concomitant uterine fibromatosis.

Patient, Methods and Results

Patient, age 48 years, was hospitalized for bleeding, and pelvi-abdominal pain. Pain and bleeding started several months ago, without any medical history and no significant hereditary medical history.

The general clinical examination revealed normostenic patient with normal cardiovascular parameters and normal weight.

Lung radiograph showed no changes with no pleuro-pulmonary symptomatology.

Gynecological examination reveals: normal cervix, the uterus in retroversion, with multiple fibroid nodules, the size of 10 weeks pregnancy; in the right part of the uterus, a tumoral adnexa about 10/8 cm, and in the left part, the left tumoral annex about 6/7 cm, both with preserved mobility.

Transvaginal ultrasound reveals enlarged uterus, with multiple fibroid nodules, latero-uterin bilateral cystic formations about 10 cm in the right side and 6 cm in the left side.

Laboratory tests show leukocytosis (10.54×10^3), the rest being normal. Tumor markers: CA125 normal.

Surgery was decided. Intraoperative findings: enlarged uterus as 10 weeks pregnancy, with multiple fibroid nodules, both ovaries were normal, both tubes were dilated, plied, closed thin wall and homogeneous consistency. It was practiced total hysterectomy with bilateral anexectomy and they were send for pathology exam. Both tubes were sent for extemporaneous pathology exam. The result was papillary proliferation with cellular atypia, pleomorphism, suggestive of adenocarcinoma.

For the histopathological study, we harvested fragments from the uterine annexes, which were fixed in neutral formalin and paraffin embedded. Histopathological exam in classic Hematoxylin–Eosin (HE) staining showed simple endometrial hyperplasia of the endometer as well as fibromatous nodules of the uterine wall. We found one well-differentiated adenocarcinoma on each fallopian tube (Figure 1), which completed invaded the salpingeal wall, including the serosa (Figure 2); we also found a micro-invasive carcinoma on the left parameter.

For the immunohistochemical study, we took 3-μm thick sections by using a microtome (Microm HM350) enhanced with a special transfer system for sections (Section Transfer System, STS). Histology cups were harvested on special slides covered in a layer of positively-charged amino acid residues, slides covered in poly-L-Lysine (Sigma) for enhancing the adherence of sections to the slides. After a quick drying period of 5–10 minutes on a plate heated at 40^0C, sections were transferred in an incubator at 50^0C and kept overnight. For the positive and differential diagnosis, we used the following markers (Table 1).

Table 1 – ***Antibodies used for the immunohistochemical study***

Antibody	Manufacturer	Clone	Host/Target/Clonality	Antigen retrieval	Dilution
Anti-p53	Dako	DO-7/IgG2bk	Ms/Hu/Monoclonal	EDTA, pH 9	1:50
Anti-PCNA	Dako	PC10/IgG2ak	Ms/Hu/Monoclonal	Sodium citrate, pH 6	1:50
Anti-Ki67	Dako	IgG1k/MIB-1	Ms/Hu/Monoclonal	Sodium citrate, pH 6	1:100
Anti-CK7	Dako	OV-TL 12/30	Ms/Hu/Monoclonal	Sodium citrate, pH 6	1:50
Anti-CK18	Dako	DC 10	Ms/Hu/Monoclonal	EDTA, pH 9	1:25
Anti-CK20	Dako	Ks20.8	Ms/Hu/Monoclonal	Sodium citrate, pH 6	1:25
Anti-ERα	Dako	1D5	Ms/Hu/Monoclonal	EDTA, pH 9	1:50
Anti-PR	Dako	PgR 636	Ms/Hu/Monoclonal	EDTA, pH 9	1:50

The immunohistochemical study revealed an intense reaction to anti-PCNA, more than 85% of tumor cell nuclei were moderately or strongly positive, aspect indicating particularly high mitotic potential of these cells (Figure 3). A very intense reaction was observed to anti-p53 antibodies, where more than 70% of tumor cell nuclei appeared positive (Figure 4). This immunohistochemistry aspect showed that in this case there was a profound disturbance of the genetic program, with the emergence of a mutant p53 gene, which encoded the occurrence of the pathological protein marked immunohistochemically. In contrast, the antibody response to Ki67 was moderately positive, only about 35% of the nuclei were positive (Figure 5). The response to estrogen and progesterone was very different; thus, the reaction was very low to estrogen, less than 1% of the nuclei being positive (Figure 6). Instead, the reaction was intensely positive to progesterone – over 95% of tumor cell nuclei being positive (Figure 7).

Of cytokeratins, we noted a positive focal intensely positive reaction to cytokeratin 7 (Figure 8), intensely positive cytokeratin 18 staining (Figure 9) and negative cytokeratin 20 reaction (Figure 10). Based on histopathological and immunohistochemical data, our diagnosis was well-differentiated primary bilateral tubal adenocarcinoma, with serous invasion, G1 stage; microinvasive carcinoma in the left parameter.

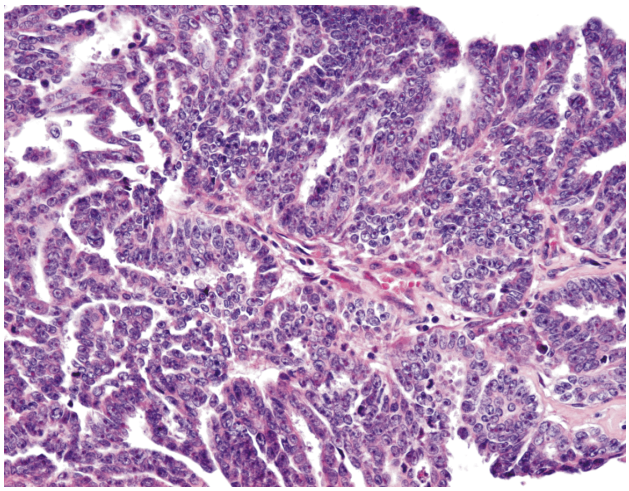

Figure 1 – ***Well-differentiated adenocarcinoma of the fallopian tube. HE staining, ×200.***

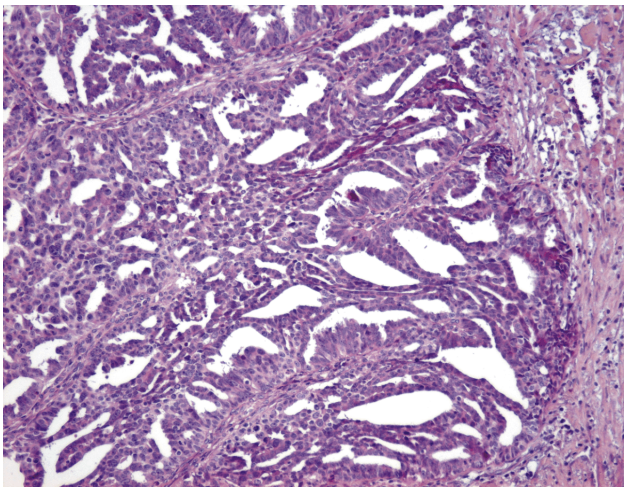

Figure 2 – ***Adenocarcinoma invading the muscular tunic of the uterine tube. HE staining, ×100.***

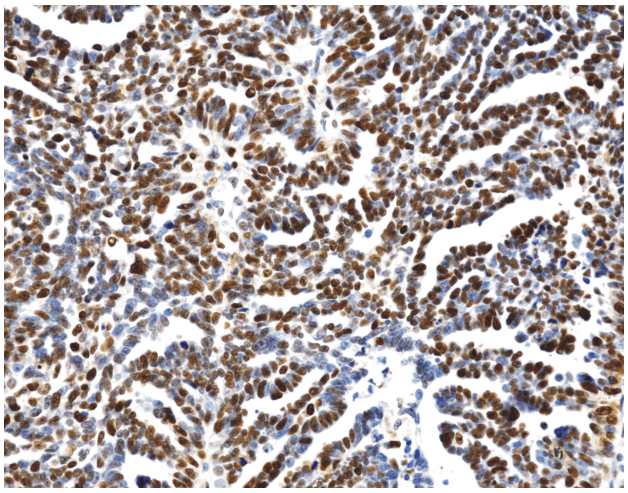

Figure 3 – ***Tumoral cells intensely positive for PCNA. Immunostaining with anti-PCNA antibodies, ×200.***

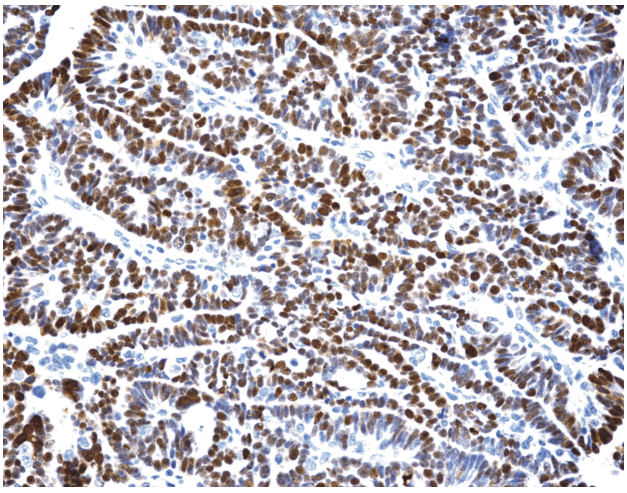

Figure 4 – ***Intensely positive reaction to p53. Immunostaining with anti-p53 antibodies, ×200.***

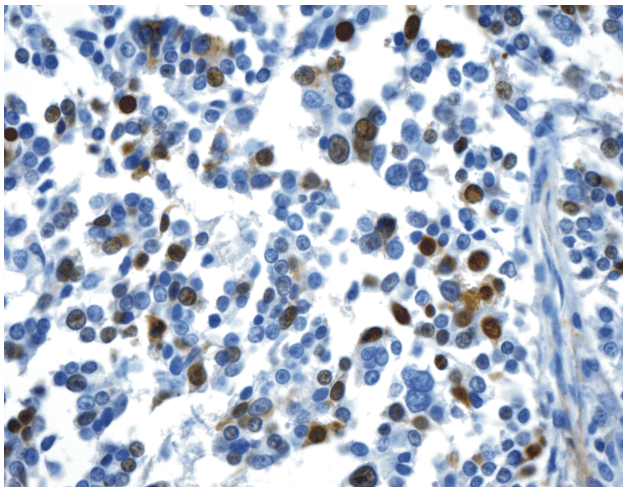

Figure 5 – ***Immunohistochemical image of a well-differentiated adenocarcinoma, in which we can observe the positivity to Ki67 of approximately 35% of the nuclei of tumor cells. Immunostaining with anti-Ki67 antibodies, ×400.***

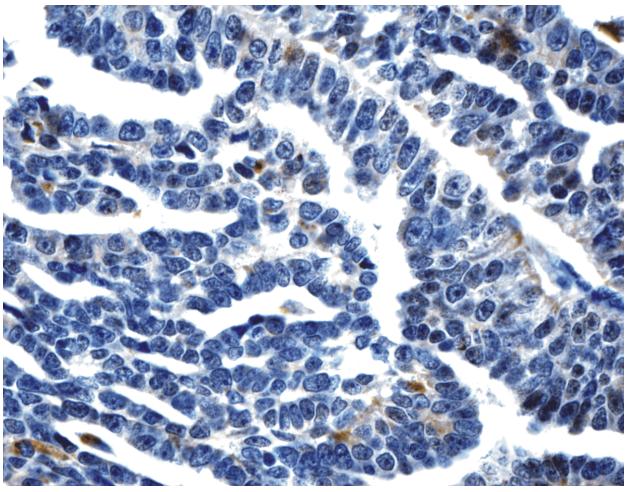

Figure 6 – ***Tubar adenocarcinoma with weak positive reaction to estrogen. Immunostaining with anti-estrogen antibodies, ×400.***

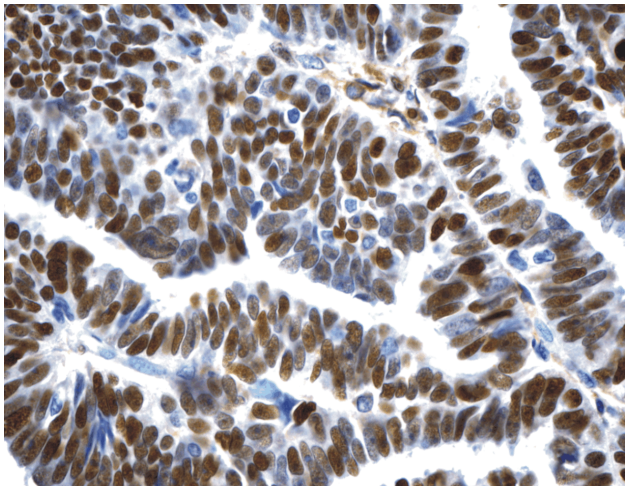

Figure 7 – ***Tumor cells with intensely positive reaction to progesterone. Immunostaining with anti-progesterone antibodies, ×400.***

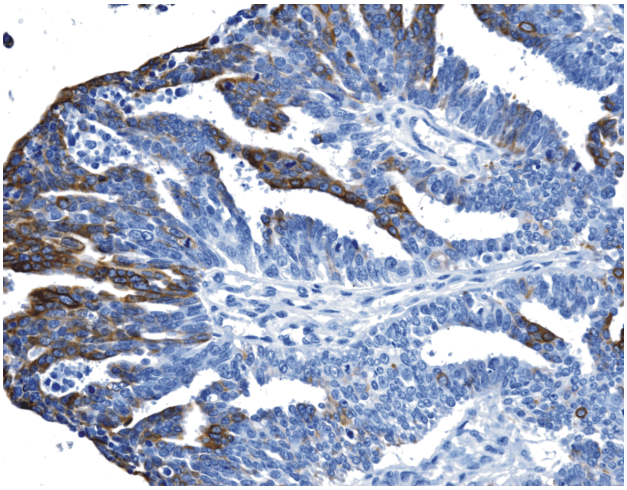

Figure 8 – ***Tubar adenocarcinoma with focal, inhomogeneous reaction to cytokeratin 7. Immunostaining with anti-CK7 antibodies, ×200.***

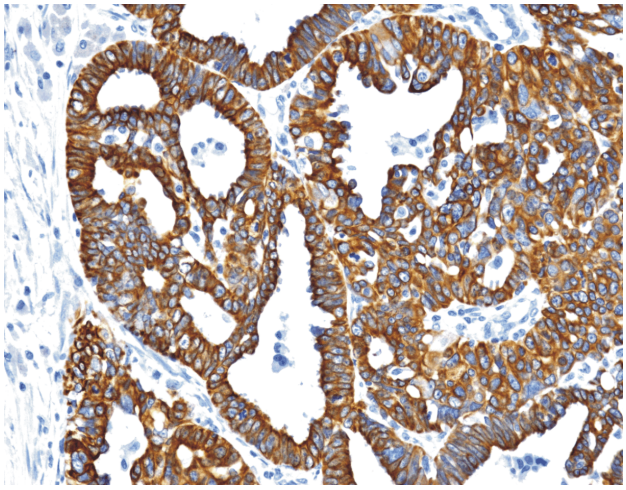

Figure 9 – ***Tubar adenocarcinoma with an intensely positive reaction to cytokeratin 18. Immunostaining with anti-CK18 antibodies, ×200.***

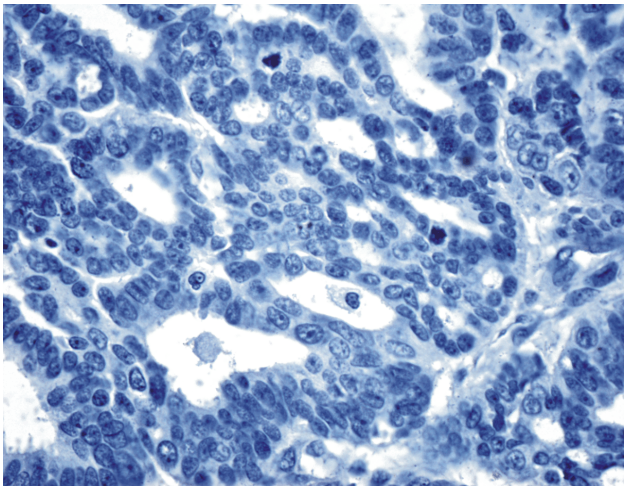

Figure 10 – ***Negative reaction of cells from a tubar adenocarcinoma to cytokeratin 20. Immunostaining with anti-CK20 antibodies, ×400.***

Discussion

According to some studies, primary carcinoma of the fallopian tube is a rare cancer, accounting for approximately 0.14–1.8% of the malignant genital tumors in women [7]. Based on data from nine cancer registries, it was estimated that in the United States the average annual incidence of primary fallopian tube carcinoma is 3.6 per million women [8]. Up to the present time, there have been reported about 2000 cases of primary fallopian tube cancer [9]. In these cases, bilateral primary fallopian tube cancer represents 20–25% [10, 11] and is therefore very rare.

According to some authors, the actual incidence of carcinomas of the tube would be much higher because a large proportion of serous carcinomas are diagnosed as ovarian cancers would develop in the fallopian tube and would then include the ovary [12–14].

Primary fallopian tube cancer occurs most often between the fourth and sixth decade of life [15], the average age of occurrence being 55 years. However, primary fallopian tube cancer has been reported in young girls aged 17–19 years [16].

These tumors are usually asymptomatic, and therefore the diagnosis is rarely made preoperatively. The most common reported symptom is abnormal vaginal bleeding, pelvic pain, abnormal vaginal discharge, and abdominal distention [5]. There is a syndrome called "hydrops tubae profluens", which consists in a pelvic mass, profuse watery or honey-colored vaginal discharge and pelvic pain that essentially goes away upon sudden disappearance of the mass. Less frequent symptoms include abdominal distension and urinary urgency. In many cases, symptoms are vague and nonspecific. The triad of pain, metrorrhagia and leucorrhea is considered pathognomonic for tubal carcinoma, but inconstantly occurs. Primary fallopian tube carcinomas often mistaken for benign pelvic disease or ovarian cancer [6].

In our case, the symptoms were scarce and unspecific. Maltroragia and abdominal pain did not suggest the existence of a lesion of the fallopian tube, but rather a sign determined by the uterine fibromatosis.

Generally, in perimenopausal and postmenopausal women with an unusual, unexplained or persistent vaginal discharge, even in the absence of bleeding, should be evaluated for an occult tubal cancer.

Fallopian tube cancers are often found incidentally in asymptomatic women at the time of abdominal hysterectomy and bilateral salpingo-oophorectomy.

Transvaginal sonography can be of assistance in evaluating abnormal adnexal masses and may aid in early diagnosis of fallopian tube cancer. If sonography demonstrates that an adnexal mass is solid or has both solid and cystic components, we should think to a neoplastic tumor, the size does not matter anymore. Visualizing the fallopian tubes by transvaginal ultrasonography for identifying incipient stages of salpingeal cancer is difficult and information is still inconclusive [17]. The fallopian tubes are usually not visualized during routine abdominal sonography because of the lack of an acoustic interface, but the outline of the fallopian tubes is possible if there is a sufficient quantity of fluid in the cul-de-sac. Because of the rarity of fallopian tube cancer, reports of the sonographic appearance are limited. However, the sonographic detection of a solid or cystic adnexal mass that is separate from the ovary, in a postmenopausal woman, should induce a suspicion for fallopian tube carcinoma. Sonographic evaluation of the fallopian tubes presents one of the greatest challenges for the sonographer. Presently, sonography is unable to diagnose fallopian tube cancer, but it may be a differential diagnosis when an adnexal mass is identified.

Serum levels of CA125 can be abnormally high in patients with gynecologic diseases, both cancer and non-cancer types (endometriosis, early pregnancy). Despite all this, many studies consider that serum level of CA125 is more useful in detecting serous cancers of the fallopian tube and ovary compared to abdominal or transvaginal ultrasound [18]. Although, CA125 is non-specific, assessing a preoperative level is recommended in a postmenopausal woman with a pelvic mass, for later comparison and assessment of response to therapy [19]. According to other studies, the serum level of CA125 is elevated in advanced stages of serous ovarian and tubal cancer [18], therefore not being useful for incipient stages of these types of cancer.

Histological diagnosis may be difficult because of the similarities of fallopian tube cancer and metaplastic processes associated with inflammation of the tubal epithelium found in pelvic inflammatory disease and other gynecologic cancers. Another complicating factor is multi-focal neoplasia, which can occur in tubar cancer, other genital organs and the peritoneal cavity [20]. Diagnostic criteria for the diagnosis of tubal cancer:

- The main tumor grossly should be in the tube;
- Histologically, the tubal mucosa should be involved with a papillary pattern;
- If the tubal wall is involved largely, transition from benign to malignant tubal epithelium should be identified.

When the ovaries are involved, differentiation between tubal and ovarian cancer should be tested. When ovarian cancer extends to the tube, serosal involvement is usually evident and the mucosa of the endosalpinx may not be involved. In tubal carcinoma, there is usually intraperitoneal involvement before the ovaries are affected, so the peritoneal cytology is important in this disease entity. When the muscularis is invaded or the cancer is located in the fimbria, the prognosis is worsens, even with disease limited o the tube. The tubal late stage simulates late stage ovarian cancer with intraperitoneal spread. The conclusion is that the fallopian tube cancer has a tendency for lymph node metastasis [21].

Conclusions

Fallopian tube cancer is rare and often an intraoperatory discovery, as early diagnostic methods developed until now remain ineffective. It is often mistaken with ovarian cancer before surgery.

Acknowledgments

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