

Metastasis from breast cancer to an endometrial polyp; treatment options and follow-up. Report of a case and review of the literature

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Summary

Introduction: The female genital tract is rarely involved by metastatic tumors. The most common anatomic locations are the ovaries and the vagina. A case is presented of metastatic breast carcinoma to the vulva and endometrial polyp, both exceptional. **Case Report:** We report the case of an 83-year-old female who presented with vaginal bleeding. Lobular breast carcinoma was diagnosed earlier and during follow-up vulvar metastasis was detected. Hysteroscopic examination because of postmenopausal bleeding revealed an endometrial polyp which was resected. The morphology and immunohistochemistry of the polyp were consistent with lobular breast cancer: metastatic breast cancer to an endometrial polyp. After reviewing the literature 15 cases of metastatic breast carcinoma to endometrial polyps have been reported. The clinical presentation and course, risk factors, treatment and follow-up are discussed. **Conclusion:** Metastasis of a breast carcinoma to the vulva and an endometrial polyp are extremely rare, but clinicians should be aware of both phenomena.

Key words: Breast cancer; Uterine metastasis; Endometrial polyp; Treatment; Follow-up.

Introduction

Metastases to the endometrium from extra-genital tumors are rare. The most common anatomic location for metastases to the female genital tract are the ovaries and the vagina. The primary tumor is most frequently located in the breast followed by the gastrointestinal tract, lung, kidney and skin (melanoma) [1, 2]. When an extra-genital tumor metastasizes to the uterus it is predominantly located in the myometrium, in a minority of cases the metastases is confined to the endometrium [1, 2]. We present a case of metastatic breast carcinoma to the vulva and endometrial polyp, and review the literature.

Case Report

An 83-year-old nulliparous female presented with postmenopausal uterine bleeding. She had been diagnosed with invasive lobular breast carcinoma five years before presentation. The breast cancer had been disseminated to the pleural and peritoneal cavity and was hormone receptor-positive and Her2/neu negative. She was then treated with first-line hormonal therapy with letrozol. During routine follow-up vulvar metastasis was detected which was surgically excised. The tumor of the vulva had identical histological, immunohistochemical and hormonal receptor status compatible with the primary lobular breast cancer. Because of progressive pleural metastases letrozol was replaced by tamoxifen. One year before presentation to our department, the patient presented with nausea and vomiting which was caused by metastasis to her stomach. Third-line hormonal therapy with fulvestrant was started.

Because of her postmenopausal bleeding transvaginal ultrasonography was performed and showed thickening of the endometrium and a polypoid lesion with mixed echo refringence.

Endometrial curettage revealed insufficient non-diagnostic material. Hysteroscopy showed an atrophic uterine cavity with an endometrial polyp which was resected diathermically.

Macroscopic examination showed a polyp with a diameter of 3.5 cm. Histologically the polyp consisted of cystic dilated glands lined by columnar epithelium without atypia, surrounded by a fibrovascular stroma. Focally the glands showed mucinous metaplasia and in some areas there was periglandular stroma condensation. Within the stroma there were several foci of monotonous epithelial cells arranged in small nests and cords (Figure 1). These cells were immunohistochemically positive for cytokeratin (AE1/3) and estrogen receptor (Figure 2). Morphology and immunohistochemistry were consistent with metastatic lobular breast carcinoma to an endometrial polyp. The features of the polyp itself were characteristic, though not pathognomic, for a tamoxifen-associated endometrial polyp. After one year of follow-up the patient is in a good condition. There is no evidence of progressive disease.

Discussion

This is the first case of a metastatic breast cancer to the vulva and to an endometrial polyp in the same patient. Uterine metastases of extra-genital malignant tumors are rare. Breast cancers, especially lobular carcinomas are the most common primary tumor. The vulva is one of the more unusual sites of metastases from a breast carcinoma. Perrone *et al.* found only 16 cases in 72 years after reviewing the literature. For an accurate diagnosis and treatment, a differentiation should be made between primary and metastatic breast cancer of the vulva.

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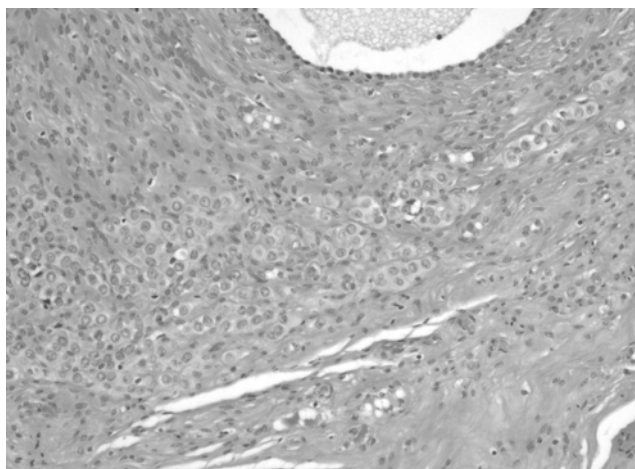


Fig. 1

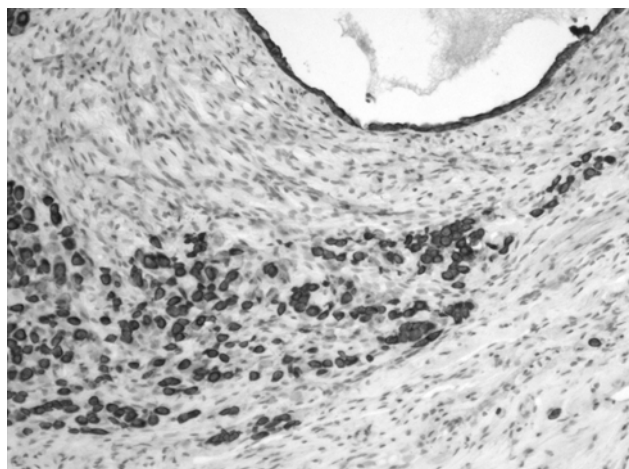


Fig. 2

Figure 1. — Nests and cords of monotonous epithelial cells in the stroma of the polyp (and part of a cystically dilated gland).
 Figure 2. — Immunostain with AE1/3 showing positivity of the epithelial cells (and glandular epithelium).

Primary breast cancer of the vulva originates from ectopic breast tissue in the vulva, which develops along the mammary ridges [3]. In our case metastases from a primary breast cancer to the vulva was obvious because of the similarity in histological, immunohistochemical and receptor status. Furthermore, the diagnosis was supported by the absence of normal breast tissue in the specimen and a history of breast cancer.

Endometrial metastasis from a breast carcinoma is also uncommon. Kumar *et al.* found two of 63 cases (3.8%) with metastases to the endometrium, Mazur *et al.* seven cases in 149 patients (4.7%) [1, 2]. Polyps are the most common benign lesion in the endometrium, and metastasis to a polyp is exceptional. Because little is known about presentation, risk factors, clinical course, treatment and follow-up of metastasis to endometrial polyps we reviewed the literature.

A search was performed in May 2010 with the key words: breast carcinoma, metastasis and polyp. The search revealed 13 articles in which 15 patients with metastases from a breast carcinoma to an endometrial polyp are described [4-16]. The articles and patient characteristics, including our case, are described in Table 1. Eight patients had lobular breast cancer, seven had ductal adenocarcinoma and one patient an apocrine type. Ductal carcinoma accounts for approximately 70-75% of all breast cancers; lobular carcinoma for 5-20%. The breast cancer was primarily treated by surgery in 13 patients, and three patients were treated palliatively because of widespread dissemination (Manipadam *et al.*, Aydin *et al.*, and our case). Five patients received chemotherapy as adjuvant therapy, four radiotherapy and 12 patients (75%) hormonal therapy with tamoxifen. Tamoxifen, a nonsteroidal anti-estrogen, is used for adjuvant and palliative treatment and chemoprevention of breast cancer. Tamoxifen may also exert estrogenic effects on the endometrium and may result in a variety of proliferative lesions including primary or metastatic

carcinomas. A causal association between tamoxifen and uterine metastasis from breast cancer has not been established. Vaginal bleeding or discharge was the first manifestation in 11 patients which led to further examination and diagnosis of the endometrial metastasis. In the remaining five patients the metastasis was diagnosed during routine examination. The time between the primary diagnosis and metastasis ranged between eight months and six or more years. The maximal diameter of the polyp ranged between 1.5 and 11.5 cm. Eight patients, with no signs of widespread dissemination, received a total abdominal hysterectomy with bilateral salpingo-oophorectomy. During follow-up two patients died (9 months and 4 years after diagnosis) because of disease progression. Two patients had no evidence of disease 11 and 26 months after surgery. Of the remaining four patients the follow-up was unknown. In the four patients with signs of widespread dissemination two patients received palliative treatment. One patient did not receive any treatment and our patient received a polyp resection as part of her treatment. Three patients had signs of disease progression during follow-up and one patient died within one year. Our patient has no signs of progressive disease after one year follow-up. The remaining four patients were treated with a polyp resection but the follow-up is unknown.

Although the number of patients is small, the results of the literature search show that treatment of an endometrial metastasis from breast carcinoma is dependent on signs of widespread dissemination. Total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed in patients without further evidence of disease.

If additional investigations revealed other sites of metastases no treatment or palliative treatment was given. The presence of uterine metastases usually indicates an advanced stage, but does not always imply widespread dissemination.

Table 1. — Summary of reported cases in the literature.

Case	Age (yrs.)	Histologic type primary tumor	Lymph node metastasis	Adjuvant therapy	Clinical symptom	Time elapsed between primary tumor and metastasis (months)	Maximal diameter polyp (cm)	Treatment procedure
Sullivan <i>et al.</i> [4]	83	Ductal	Yes	No	No	72	11.5	TAH+BSO
Corely <i>et al.</i> [5]	58	Ductal	Yes	TAM	Vaginal bleeding	> 36	NM	TAH+BSO
Aranda <i>et al.</i> [6]	76	Lobular	No	No	No	36	9	TAH+BSO
Kennebeck <i>et al.</i> [7]	71	Ductal	Yes	TAM	No	30	NM	Palliative RT/CT ^b
Martinez <i>et al.</i> [8]	78	Lobular	Yes	TAM	Vaginal bleeding	24	3.3	TAH+BSO
Martinez <i>et al.</i> [8]	58	Ductal	Yes	RT, CT	Vaginal bleeding	≥ 36 ^c	NM	TAH+BSO
Lambot <i>et al.</i> [9]	70	Apocrine	Yes	TAM, RT	Vaginal bleeding	48	1.5	TAH+BSO
Horn <i>et al.</i> [10]	73	Ductal	No	TAM, CT	No	56	8	TAH+BSO
Alvarez <i>et al.</i> [11]	69	Lobular	Yes	TAM, RT, CT	Vaginal bleeding	48	1.5	None ^d
Houghton <i>et al.</i> [12]	62	Lobular	Yes	TAM	Vaginal bleeding	14	3	Polyp resection
Houghton <i>et al.</i> [12]	92	Lobular	Unknown	TAM	Vaginal bleeding	60	3	Polyp resection
Al-brahim <i>et al.</i> [13]	53	Lobular	Yes	TAM	Vaginal bleeding	48	7	Polyp resection
Acikalin <i>et al.</i> [14]	58	Ductal	Yes	TAM, CT	No	48	5	TAH+BSO
Manipadam <i>et al.</i> [15]	70	Lobular	Yes	CT	Vaginal bleeding	NM	3	Polyp resection
Aydin <i>et al.</i> [16]	60	Ductal	Unknown	TAM, RT	Vaginal bleeding	8	6.5	CT, ANA
Our Case	83	Lobular	Yes	LET, TAM, FUL	Vaginal bleeding	60	3.5	Polyp resection

ANA: anastrozole; BSO: bilateral salpingo-oophorectomy; CT: chemotherapy; FUL: fulvestran; LET: letrozole; NM: not mentioned; RT: radiotherapy; TAH: total abdominal hysterectomy; TAM: tamoxifen.

^a Therapy started before the metastases to the endometrium was diagnosed.

^b Palliative radiotherapy because of vaginal extension, unresectable. Because of disease progression palliative chemotherapy was started.

^c 22 years earlier breast cancer to the right mammary, 19 years earlier left-sided breast cancer. 3 years after the left-sided breast cancer the patient presented with vaginal bleeding.

^d No treatment was given because of widespread dissemination, with skull and spine metastasis.

Conclusion

Metastases from breast cancer to the genital tract are uncommon, with metastases to the vulva and endometrial polyp being very rare. Although metastasis to the endometrium is exceptional, it is clinically very important because it can be the first sign of widespread disease. Vaginal bleeding is often the first symptom, but patients can be asymptomatic. The relationship of metastases and tamoxifen treatment is unclear, but was found in 75% of the cases. Total hysterectomy with bilateral salpingo-oophorectomy is the treatment in patients without signs of widespread dissemination. Clinicians should be aware of the possibility of uterine metastatic involvement in women with uterine bleeding and a history of breast cancer.

References

- [1] Mazur M.T., Hsueh S., Gersell D.J.: "Metastases to the female genital tract. Analysis of 325 cases". *Cancer*, 1984, 53, 1978.
- [2] Kumar N.B., Hart W.R.: "Metastases to the uterine corpus from extragenital cancers. A clinopathological study of 63 cases". *Cancer*, 1982, 50, 2163.
- [3] Perrone G., Altomare V., Zagami M., Vulcano E., Muzii L., Battista C. *et al.*: "Breast-like vulvar lesion with concurrent breast cancer: a case report and critical literature review". *In Vivo*, 2009, 23, 629.
- [4] Sullivan L.G., Sullivan J.L., Fairey W.F.: "Breast carcinoma metastatic to endometrial polyp". *Gynecol. Oncol.*, 1990, 39, 96.
- [5] Corley D., Rowe J., Curtis M.T., Hogan W.M., Noumoff J.S., Livolsi V.A.: "Postmenopausal bleeding from unusual endometrial polyps in women on chronic tamoxifen therapy". *Obstet. Gynecol.*, 1992, 79, 111.
- [6] Aranda F.I., Laforga J.B., Martinez M.A.: "Metastasis from breast lobular carcinoma to an endometrial polyp. Report of a case with immunohistochemical study". *Acta Obstet. Gynecol. Scand.*, 1993, 72, 585.
- [7] Kennebeck C.H., Alagoz T.: "Signet ring breast carcinoma metastases limited to the endometrium and cervix". *Gynecol. Oncol.*, 1998, 71, 461.
- [8] Martinez-Montero I., Dominguez-Cunchillos F., Muruzabal J.C., Miguel de C., Recari E., Ezcurdia M.: "Uterine metastases from breast cancer". *Acta Obstet. Gynecol. Scand.*, 1999, 78, 165.
- [9] Lambot M.A., Eddafali B., Simon P., Fayt I., Noël J.C.: "Metastasis from apocrine carcinoma of the breast to an endometrial polyp". *Virchows Arch.*, 2001, 438, 517.
- [10] Horn L.C., Einkenkel J., Baier D.: "Endometrial metastasis from breast cancer in a patient receiving tamoxifen therapy". *Gynecol. Obstet. Invest.*, 2000, 50, 136.
- [11] Alvarez C., Ortiz-Rey J.A., Estévez F., de la Fuente A.: "Metastatic lobular breast carcinoma to an endometrial polyp diagnosed by hysteroscopic biopsy". *Obstet. Gynecol.*, 2003, 102, 1149.
- [12] Houghton J.P., Ioffe O.B., Silverberg S.G., McGrady B., McCluggage W.G.: "Metastatic breast lobular carcinoma involving tamoxifen-associated endometrial polyps: report of two cases and review of tamoxifen associated polypoid uterine lesions". *Mod. Pathol.*, 2003, 16, 395.
- [13] Al-brahim N., Elavathil L.J.: "Metastatic breast lobular carcinoma to tamoxifen-associated endometrial polyp: case report and literature review". *Ann. Diagn. Pathol.*, 2005, 9, 166.
- [14] Acikalin M.F., Oner U., Tekin B., Yakuz E., Cengiz O.: "Metastasis from breast carcinoma to a tamoxifen-related endometrial polyp". *Gynecol. Oncol.*, 2005, 97, 946.
- [15] Manipadam M.T., Walter N.M., Selvamani B.: "Lobular carcinoma metastasis to endometrial polyp unrelated to tamoxifen. Report of a case and review of the literature". *APMIS*, 2008, 116, 538.
- [16] Aydin O., Bagci P., Akyildiz E.U., Ozguroglu M., Ilvan S.: "Metastasis from breast carcinoma to endometrial polyp". *Eur. J. Gynaecol. Oncol.*, 2008, 29, 666.

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