Case Report

Endometrial carcinoma metastatic to the clitoris: A case report☆

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Article info

Article history:
Received 17 October 2013
Accepted 26 December 2013
Available online 2 January 2014

Keywords:
Endometrial carcinoma
Metastasis
Clitoris

Introduction

Metastatic skin lesions developing from a primary cancer are a relatively rare phenomenon; however, when found and identified, this discovery may lead to the diagnosis of an important internal malignant disease that is clinically silent [1]. An extensive meta-analysis carried out by Krathen et al. [2] in 2003 reported an overall incidence of skin metastases of 5.3%, with the breast being the most common primary site.

Skin metastasis from an endometrial carcinoma is a very rare finding considering the high frequency of this neoplasia. Krathen et al. [2] found one case of skin metastasis in 86 cases of endometrial cancer analyzed, corresponding to a rate of 1.1%. Furthermore, metastatic vulval tumors correspond to 5–8% of malignant skin neoplasias, with 9% of these originating from an endometrial carcinoma [3,4].

Metastasis may occur to adjacent organs by direct extension or in the form of distant metastasis (lungs, liver or bones) by lymphatic or hematogenous spread. Skin metastasis may also occur by direct extension, lymphatic dissemination or by implantation at the site of surgical scars [1,5].

The present study reports on the case of a postmenopausal patient with vaginal bleeding and a tumor on the clitoral hood, originating from an endometrial carcinoma.

Case report

A 65-year-old female was admitted to the Gynecology Department of this hospital on August 3, 2012 with abnormal lower genital tract bleeding that began in November 2011. Bleeding was moderate, intermittent, dark in color and odorless. One month after the onset of this complaint, a painless, slow-growing, hardened nodule appeared on her clitoris.

The patient also reported concomitant pelvic pain that began after the appearance of the nodule. She described this as a burning pain that irradiated to her thighs and became worse when she walked. She lost 10 kg in weight in 30 days. The patient had a clinical history of systemic arterial hypertension and dyslipidemia. Her menarche occurred at 11 years of age and her menstrual cycles were irregular. She was a virgin and had never used contraceptives, underwent menopause at 55 years of age and had never used hormone replacement therapy. She had never undergone gynecological examination and denied any family history of gynecological or bowel cancer.

Physical examination

The patient’s overall condition was fair, pale and dehydrated. According to medical records, Hgb = 9.2 and Hct = 28.1. The patient was sick in bed, showed atypical presentation of the abdomen, and felt pain at deep palpation of the hypogastrium. Presence of a hard, firm palpable mass involving the hypogastrium and extending as far as the umbilical scar was observed.

Gynecological examination

Atrophic vulva with a fibrous, ulcerated, nodular lesion affecting the clitoral region, friable and infiltrating and measuring approximately 4 cm was found. Specular examination was deferred to the operating room because the patient was a virgin and unable to tolerate the exam. She was not obese (BMI 17.2 kg/m2) and was aware about the clitoral mass, but felt constrained to talk about the case with her family, not allowing the examination by them. The mass was discovered by her family when medical care was necessary. The patient had no other risk factors for vulval metastasis, in addition to late diagnosis.

Laboratory tests showed anemia and CA 125 measurement of 137.56 U/mL. Complete abdominal ultrasound evaluation showed an increase in uterine volume, but provided no additional details. Chest
tomography showed multiple uncalcified, diffuse nodules and micro-
nodules in both lungs suggestive of secondary implants.

A second pelvic ultrasound carried out in the department showed a
uterine volume of 406 cm$^3$, with imprecise borders and a diffusely
heterogeneous myometrium. Complex masses extended to the left
and right adnexal regions. The mass on the left side had a volume of
468 cm$^3$ and consisted of a predominantly anechoic area, while the
mass on the right side had a volume of 137 cm$^3$ and consisted predomi-
nantly of a solid area that reached the retrouterine region (volume of
126 cm$^3$). Endometrium size of 1.3 cm with fluid in the uterine cavity
was observed. Ovaries were not visualized.

The lesion was resected from the clitoris and uterine curettage was
performed, with the removal of a moderate amount of blackened mate-
rial. No lesion was seen in the vaginal canal or in the cervix. Examination
also revealed stenosis of the upper third of the vagina and an atrophic,
flat cervix with a punctiform external orifice.

Histopathology of the clitoral lesion revealed an ulcerated invasive
carcinoma, with glandular and squamous differentiation and a clear-
cell pattern (Fig. 1). The fragments of the endometrium obtained
from the curettage were compatible with a grade II endometrioid ade-
nocarcinoma, which was infiltrating the myometrium in the specimen
analyzed (Fig. 2).

The material obtained from the clitoral lesion was submitted to
immunohistochemical analysis, revealing an estrogen-receptor positive
adenocarcinoma, suggesting metastasis to the skin of the clitoral region
that was positive (in some of the cells) for cytokeratin 7 and negative for
cytokeratin 20 and 5100 protein, with reactivity only in the nerve
filaments.

It was decided not to operate due to the patient’s debilitated state.
She was given palliative oncological care and died 6 months after diag-
nosis. The treatment consisted of only palliative relief on pain and no
cure, just a pelvic radiotherapy (300 cGy/day for 10 days) for antialgic
purpose was initiated. Chemotherapy was not started for the same
reason.

Discussion

Considering that endometrial carcinoma is the most common malign-
nant gynecological neoplasia in developed countries, this is divided into
two categories: type I or endometrioid (prevalent) and type II in accor-
dance with whether or not it is estrogen-receptor positive. This is a
determining factor for its prognosis, since type II involves higher grade
tumors such as papillary serous or clear cell carcinomas, and is diag-
nosed at advanced stages [6].

There are few reports in the literature on the association between
skin metastasis and the most probable routes of dissemination. Casimiro
et al. [1] reported that skin metastasis tends to develop close to the
primary tumor, as in the present case.

Some of the most common sites of skin metastases from malignant
lower genital tract tumors include the abdominal wall, the vulva and
the chest. Metastases to the scalp and extremities have been reported,
principally when the endometrium is the primary site [1,5]. These
lesions may vary morphologically and may present in the form of
macules, papules, nodules, hard plaques or purple plaques [1].

With respect to the vulva as a site of metastasis, Dehner [3] found
8.4% of metastatic tumors of the vulva in a series of 262 cases of malig-
nant tumors at this site. Likewise, Neto et al. [4] reported 66 cases be-
tween 1944 and 2001; however, only six of these involved endometrial
carcinoma. The majority of metastatic tumors consisted of nodules and
involved the labia majora. Only one case involved the clitoris. In 87% of
cases, the patient died at a mean of 7.5 months after diagnosis, reflect-
ning the fact that this is normally a terminal condition.

Giordano et al. [7] reported a case of hepatic and vulvar metastasis in
the form of a plaque on the commissure of the labia majora 8 months
after hysterectomy for a grade 3 endometrioid adenocarcinoma. The
same authors recommend investigating distant metastasis in visceral
organs following diagnosis of vulval metastasis from an endometrial
carcinoma. In the present case, metastasis to the lungs was also found.
The diagnosis of clitoral metastasis was made concomitantly with diag-
nosis of the primary site and distant metastasis. Furthermore, the clito-
ral lesion was more undifferentiated than the primary tumor; a finding
that is in agreement with the report made by Mandal et al. [8].

About 60% of skin metastases occur as adenocarcinomas and are
often more poorly differentiated than the primary tumor [1]. These
lesions may even lose some immunohistochemical characteristics
[9]. As shown in the present case, although the primary tumor was a
grade II endometrioid adenocarcinoma, the metastatic lesion on the
clitoris had the characteristics of a carcinoma with glandular and squa-
mous differentiation in a clear-cell pattern.

Endometrial carcinoma may originate from different germ cell
lineages and the simultaneous existence of more than one type is not
uncommon. Clear-cell variants occur in fewer than 5% of cases of endo-
metrial cancer. These variants are very similar to those found in the
ovary, vagina and cervix and may even have a particular propensity
for extraterine disease in a pattern that resembles ovarian epithelial
cancer. In the case reported here, the possibility of the existence of a
mixed endometrial tumor cannot be discarded; hybrid and mixed
tumors may coexist, i.e. an endometrioid carcinoma may have a serous
component [10].

Fig. 1. A) Metastatic nodular lesion of the clitoris. B and C) Biopsy of a lesion showing invasive carcinoma with glandular and squamous differentiation, clear-cell pattern (magnification of
20× and 40×, respectively).

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Analyzing the different forms of dissemination of endometrial tumors, Dehner [3] remarked that the fact that vascular involvement is common tends to confirm that this is the mode of dissemination to the vulva and the route of distant metastasis. However, the possibility of lymphatic dissemination cannot be discarded in this case, since advanced or type 2 endometrial tumors behave in a similar way to malignant ovarian neoplasia, with dissemination to the round ligaments and to the pelvic lymph nodes [1,10].

When skin metastasis is present, the mean survival time is 3–6 months, with mortality of more than 70% in the first year following diagnosis, confirming without a doubt the pattern of poor prognosis [1].

Conclusion

Skin metastasis from an endometrial carcinoma has a poor prognosis and rapid and aggressive progression. Little is known on the association between endometrial cancer and metastasis to the clitoris. So, it is necessary to emphasize the importance of early diagnosis and intervention, and raising awareness about regular gynecological exam, encouraging women to take care of their health.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Conflicts of interest statement

The authors declare that there are no conflicts of interest associated with this paper.

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