Abstract. Background: Lung cancer is the second most common malignant tumor, with increasing incidence in the female population. The most frequent metastatic sites are the regional lymph nodes and surrounding areas as well as liver, adrenal gland, bones and brain. Metastases in the vagina of primary lung cancer have not been previously reported. Case Report: Lung cancer was diagnosed in a 67-year-old, postmenopausal woman. Two years following partial lung resection (right apical lobe, R0-resection, CR), the patient complained of increasing problems with urination. A suspect tumor was identified with palpation and confirmed sonographically. Histological and immunohistochemical examinations of a vaginal excisional biopsy revealed metastatic adenocarcinoma, with the staining reactivity as primary lung neoplasm. Anterior exenteration was performed. Conclusion: Some cases of vaginal metastases from extragenital tumors have been previously reported. This is the first report of vaginal metastases from primary lung cancer. We suggest that adenocarcinoma especially tend to form metastases in the female genital tract. The present case emphasizes that, in women with unclear symptoms and findings in the small pelvis (e.g. urination problems, suspect vaginal tumor), the formation of such metastases should be taken into account.

Case Report

We report on a case of a 67-year-old postmenopausal woman with a suspected vaginal tumor situated adjacent to the urethra. The tumor was palpable and sonographically identifiable. It was thought to be a progression of the adenocarcinoma of the lung (Stage IB, pT2 N0 cM0 G3), which was first surgically treated in July 2001 by partially lung resection (right apical lobe, R0-resection, complete remission). The patient had suffered from increasing problems of spontaneous urination since October 2002. Emptying of the bladder was only achieved by self catheterisation. Since June 2003, the woman had complained about pain in the right and lower part of the abdomen, in the bladder and the spine as well as about vaginal bleeding. Her past medical history revealed an abdominal hysterectomy in 1973 and two surgical treatments for a cystocele. In addition, she suffered from diabetes mellitus type II, valvular insufficiency and hypothyreodism. On her initial evaluation, a 5-cm round tumor at the vaginal vault with spreading to the urethra was diagnosed by pelvic examination (palpation) and transvaginal sonography. Cystoscopy failed due to an unpassable stenosis of the urethra. An excisional biopsy of the vagina revealed an undifferentiated adenocarcinoma.

The preoperative abdominal computerized tomography scan demonstrated no periurethral tumor mass, but a mass in the left adrenal gland. The bone scintigraphy revealed no evidence of metastases in the bones. A laparotomy was performed. Macroscopically, the pelvic cavity was occupied by a gray neoplasm (6.5 x 5 x 4.5 cm) infiltrating the vaginal vault and involving the entire bladder surface. Anterior exenteration with bilateral salpingo-oophorectomy, colpectomy, plevine lymphadenectomy, infracolic omentectomy, resection of the bladder and formation of an ileum conduit were performed (R0-resection).

The final histological result revealed an undifferentiated large cell adenocarcinoma with invasion of the vaginal wall (G3; Figure 1). The adnexa, bladder, omentum and lymph nodes were not affected.
Figure 1. Large tumor cells with extensive cellular and nuclear polymorphy, but no glandular arrangement (HE, original magnification x150).

Figure 2. Immunohistochemistry. The atypical epithelial compounds react positively for CK20 (original magnification x150).

Figure 3. Immunohistochemistry. The atypical epithelial compounds react positively for CK7 (original magnification x150).
Immunohistochemical analysis demonstrated intense reactivity of tumor cells (atypical epithelial compounds) for cytokeratin 7 (CK7) and cytokeratin 20 (CK20) (Figures 2 and 3), but they were negative for cytokeratin 5 and 6 (CK5 and CK6) as well as negative for thyroid transcription factor 1 (TTF-1) and thyreoglobulin. With the proliferation marker MIB-1, up to 20% of the tumor cell nuclei were positively marked. The recently treated lung cancer, in combination with the immunohistological examinations and pathological features, led to the diagnosis of a periurethral vaginal metastasis of the known lung cancer. A local neoplasia of the urogenital tract was unlikely due to the negativity of CK5/6. With the endorsement of the immunohistochemical analysis (TTF-1, CK5/6), the most probable diagnosis was a periurethral vaginal metastasis of the known lung cancer. In a complete clinical work-up, no other primary tumor was found.

With regards to the multimorbidity of the woman, doctors employed no further aggressive treatment. The patient was disease-free after five months.

Discussion

Extragenital tumor metastatic to the female genital tract is a rare occurrence. While pulmonary metastases of adenocarcinoma of the vagina are reported frequently in the literature (2), there have been no reports on vaginal metastases of lung cancer. However, one report analysed the origin of metastases in the female genital tract; in 149 out of 325 cases, metastases originated from extragenital primaries (3). The metastases originated from extra- or intragenital primaries, and they were most frequently localized in the ovaries (4, 5) and vagina (Table I). The majority of the extragenital metastases were adenocarcinomas from the gastrointestinal system, but a variety of other primaries did occasionally spread to the genital tract. Mazur et al. (3) showed that the most common primary of metastases in the vagina is an extragenital tumor, mostly of the gastrointestinal tract.

Cytokeratins (CK) 20 and 7 have been used successfully in studies determining primary location of adenocarcinomas from metastases. Yeh et al. (4) found that the monoclonal antibody panel for TTF-1, CK7 and CK20 may facilitate discrimination between primary and metastasized adenocarcinomas and identify tumors of pulmonary origin. Primary pulmonary adenocarcinomas usually show expression of CK20, but are negative for CK7 (6). With regard to the positivity of CK 7 and 20 in our immunohistochemical investigations of the vaginal tumor tissue, the lung origin seems to be uncommon. However, several studies showed that histological features of metastasis are not always specific to the origin. Fernandez (7) showed, in immunohistochemical

Table I. Metastatic tumors presenting as possible primary lesions, extragenital and genital primaries [modified from Mazur et al. (4)].

<table>
<thead>
<tr>
<th>Primary site</th>
<th>Site of metastasis</th>
<th>Ovary</th>
<th>Salpinx</th>
<th>Endometrium</th>
<th>Cervix</th>
<th>Vagina</th>
<th>Vulva</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extragenital</td>
<td>Colon, rectum</td>
<td>18</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>7</td>
<td>0</td>
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<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Stomach</td>
<td>4</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Breast</td>
<td>3</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Uncertain</td>
<td>8¹</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Miscellaneous</td>
<td>6²</td>
<td>0</td>
<td>0</td>
<td>2³</td>
<td>2⁴</td>
<td>1⁵</td>
</tr>
<tr>
<td>Genital</td>
<td>Ovary</td>
<td>-</td>
<td>-</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Salpinx</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Endometrium</td>
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<td>1</td>
<td>-</td>
<td>-</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Cervix</td>
<td>2</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Vagina</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Vulva</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>43</td>
<td>2</td>
<td>10</td>
<td>5</td>
<td>16</td>
<td>13</td>
</tr>
</tbody>
</table>

Total no. of metastatic tumors: 89.

¹Includes five tumors with Krukenberg patterns, probably originating in the gastrointestinal tract.
²Jejunal adenocarcinoma (1), ileal carcinoid (1), gallbladder (1), pancreas (1), kidney (1), lung (1).
³Melanoma of thoracic skin (1), lung (1).
⁴Bladder (2).
⁵Kidney (1).

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studies, an expression of CK7, but not of CK20 in 79% of cases with metastases from lung adenocarcinomas, an expression of CK7 and CK20 only in 19% and no expression of CK7 or CK20 in 2%. This report underlines that the immunohistochemical pattern CK7+/CK20+ is a rare finding in metastases from lung adenocarcinoma independent from the pattern of the original tumor site, as we demonstrated in immunohistochemical investigations. Furthermore, CK 7 and 20 can be used to distinguish lung from colonic metastatic carcinoma and are rather suggestive of a lung origin in double positivity for CK7 and CK20, as has been reported in our case. Primary urogenital tumors usually show strong positivity for CK 5 and 6 (CK5+/CK6+), but both cytokeratins were negative in all sections of our vaginal tumor issue (CK5-/CK6-). In our patient, the primary tumor of the adenocarcinoma in the vagina could be the gastrointestinal tract, a common extragenital site for vaginal metastases. But the typical pattern for gastrointestinal tumors is CK20+/7- (8, 9), which is in contrast to our findings. These reports support the immunohistological findings and support the view, that the origin of the vaginal metastases described was adenocarcinoma of the lung.

Conclusion

Metastases to the female genital tract are infrequent but, regardless of site, the survival rate is poor. We present a case of vaginal metastasis from a primary lung cancer which is, to our knowledge, the first reported case. Our case provides an example that, in women with unclear symptoms and findings in the small pelvis (e.g. urination problems, vaginal tumors), the formation of such metastases should be taken into account. To identify the primary site of a metastatic vaginal tumor, clinicians should not forget the lungs since the incidence of lung cancer in females is increasing. Furthermore, a monoclonal antibody panel for TTF-1, CK7 and CK20 may facilitate discrimination between primary and metastasized vaginal adenocarcinomas and the identification of pulmonary origin.

References


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