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Case Report

Late recurrence of sigmoid carcinoma mimicking primary vulvar cancer: case report and review of the literature

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Abstract: Objective: To demonstrate a unique case report about late and isolated vulvar metastasis of sigmoid adeno-carcinoma with review of the literature. Material-method: 57 year old postmenopausal patient with prior sigmoid colon cancer history was admitted with isolated vulvar mass. Immunohistochemistry (IHC) and KRAS gen mutation analysis following surgery were performed to discriminate the metastasis from a vulvar primary malignancy. Further imaging techniques were also performed to exclude additional tumours. Results: Immunohistochemistry (IHC) and KRAS gene mutation analysis revealed isolated metastasis of the colonic adeno-carcinoma in the vulva. Conclusion: Isolated and late occurring vulvar metastasis of colonic origin is very unusual. Careful evaluation and IHC is useful for such cases.

Keywords: Colon, immunohistochemistry, metastasis, sigmoid, vulva

Introduction

Metastases to the female genital tract from other malignancies are rare and the most common extra-genital primary sites are breast and gastrointestinal system [1, 2]. In such cases, ovaries are most often affected, while isolated vulvar metastasis is extremely uncommon and constitutes 5–8% of all vulvar tumours [3]. Considering both early and late recurrences, distinguishing the metastatic lesion from primary carcinoma is crucial for both management and prognosis. Herein, late recurrence of sigmoid colon cancer presenting with vulvar solid mass is reported and discussed within current literature.

Case Report

A 57-year-old postmenopausal woman was admitted with the complaint of a newly recognized irregular vulvar mass that had been present for 2 months. She had been operated 2 years ago for sigmoid colon adeno-carcinoma (T4a, N0, M0, stage 2, Dukes B) in another institution followed by six cycles of adjuvant chemotherapy with 5-fluorouracil and folic acid. The period after the completion of chemotherapy with follow-up colonoscopies and further investigations were uneventful until present day. She had a negative Pap test which was obtained a year ago and a normal mammography that was performed 2 years ago. On her physical examination, a 2-cm firm, irregular mobile mass was detected on the lateral side of the left vulva that was >1cm away from vulvar midline. Recto-vaginal examination was unremarkable and there were no palpable inguinal lymph nodes. Laboratory results including tumour markers were all considered as normal (Ca 125: 7,6 U/ml, Ca 19-9: 11,9 U/ml, Ca 15-3: 5,5 U/ml, CEA: 16,42). Transvaginal sonography (TVS) revealed thin endometrial echo (<5mm) and atrophic bilateral ovaries. Computerized tomography (CT) scan of the pelvis demonstrated asymmetric thickening of the left vaginal wall suggestive of suspicious mass (**Figure 1**). Neither enlarged lymph nodes nor

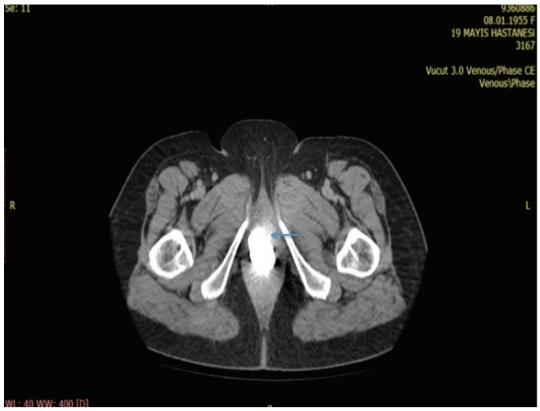

Figure 1. CT scan of the pelvis; asymmetric thickening of left vaginal wall suggestive of vulvar mass.

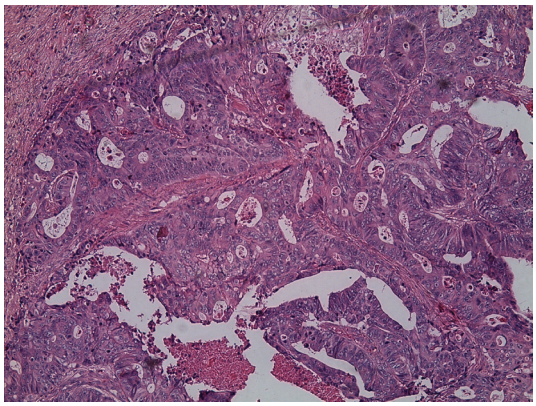

Figure 2. Atypical epithelial cells with large vesicular nuclei and with prominent nucleoli that infiltrating the vulva epithelium and stroma (hematoxylin eosin x10).

further suspicious masses were detected in the pelvis. Wide local excision of vulvar lesion with ipsilateral groin dissection was performed. Histopathology revealed atypical epithelial cells with large vesicular nuclei and with prominent nucleoli infiltrating the vulva epithelium and stroma. Central necrosis and high mitotic activity was also reported in tumour clusters (**Figure 2**). CK-20 IHC examination of tumour cells revealed diffuse and strong cytoplasmic staining pattern (**Figure 3**). Contrarily, there was no CK-7 staining pattern observed in tumour cells (**Figure 4**). Additionally, KRAS gene mutation analysis revealed wild-type colonic adenocarcinoma without mutation in exon 2 (codon 12 and 13). Lymph node specimens were all reported as tumour free. These features were considered as strongly suggestive for vulvar metastasis of the colonic origin.

Discussion

Genital tract metastases of the gynecologic malignancies are common, however metastases arising from extra-genital cancers are relatively rare [1]. The most common extra-genital tumours that metastasize through the genital tract are well defined in the literature, namely colon-rectum cancers (37%) and breast cancers (34%), followed by stomach, appendix and other uncertain primary cancers [1]. These malignancies generally metastasize to female genital tract by using hematologic route or by lymphatic spreading and usually present themselves as solid masses. Ovaries are most often affected, whereas uterus and other sites such as vulva account approximately less than 10% [1, 2].

As part of the female genital tract, primary malignancy of the vulva is rare, with 3580 new cases predicted for the year 2009 in USA [5]. Histopathology is generally squamous cell carcinoma; the prognosis is strongly correlated with the lymph node involvement and with the stage of disease; five-year survival rates varies from 78.5% in FIGO stage I to 13.0% in stage IV disease [4]. Metastatic lesions of the vulva are much more uncommon and reflect peculiar histopathology other than squamous cell carcinoma. These lesions may be observed with additional malignancies as a consequence of widespread disease, hence frequently represent a pre-terminal event. Cervical, ovarian and endometrial cancers are the most common gynecologic malignancies tending to spread to the vulva [6, 7], however gastro-intestinal system is the most frequent extra-genital site. Dehner firstly defined the clinical and morphological features of metastatic disease to the vulva in his retrospective analysis and identified 22 cases [6]. Likewise, Neto et. al. reported the largest series in the literature consisting of 66 cases of metastatic disease to the vulva, seen at the MD Anderson Cancer Centre between 1944 and 2001 [7]. In 46.5% of cases, the primary tumour was of gynecologic origin; whereas in 43.9% of cases, the primary tumour was originated from gastro-intestinal tract. Similarly, Cohen et. al. retrospectively analyzed 1513 vulvar and vaginal biopsy specimens and reported a total number of 4 metas-

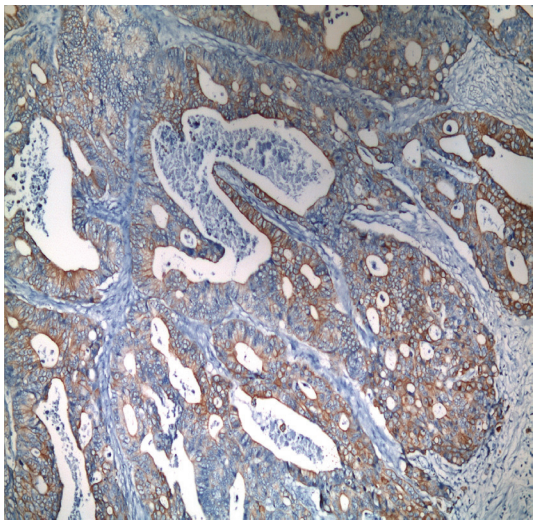

Figure 3. Diffuse and strong cytoplasmic staining pattern of malignant cells with CK-20 (x10).

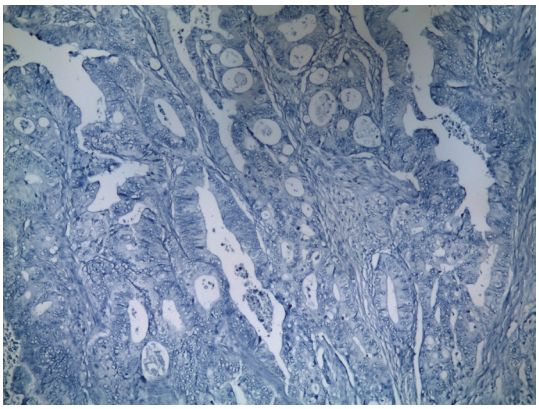

Figure 4. There was no staining observed with CK-7 in malignant cells (x10).

tases to the vulva arising from cutaneous melanoma, lymphoma, breast and renal-cell carcinomas [8].

As the most common extra-genital site spreading through the female genital tract, colorectal cancer is the third most common malignancy for both genders worldwide and approximately 20% of patients with this cancer obviously have metastatic disease at their clinical presentation [5, 9]. Recurrent colorectal carcinoma usually develops within the first 5 years after resection, occurring by local extension or implantation and/or lymphatic dissemination. Carcinoembryonic antigen (CEA) is currently the only laboratory test recommended for routine surveillance. The liver is the most common site of distant metastasis and other common sites are; regional lymph nodes, lungs, and peritoneum [10]. Moreover, isolated splenic, testicular, vaginal cuff and even urethral metastasis have also been reported [11-14]. Genital tract involvement is an extremely rare event for colonic metastasis and if it occurs, ovaries are most often affected followed by vaginal involvement. Mazur et. al. reported 56 cases of metastatic colo-rectal malignancies to the female genital tract [1]. The major site of metastasis was reported as ovaries (71.4%), followed by vagina (19.6%), endometrium (3.6%), cervix (3.6%) and salpinx (1.8%). Interestingly, there was no vulvar lesion reported (0/56). On the other hand, lesions that masquerade primary gynecologic malignancies were noted [15] where even pathologic Pap tests with high-grade lesions or atypical glandular cells have been reported as a result of gynecologic tract recurrence [16]. Clinical presentations of the colo-rectal metastases to the lower genital tract are various and may be conflicting for a clinician.

Metastatic lesions with unknown or suspected primaries warrant careful histopathologic assessment since management strategies and prognosis completely depend on accurate diagnosis. Within this perspective, many data has been accumulated on the use of immunohistochemicals (IHC) CK-7 and CK-20 to predict the origin of metastatic lesions, especially investigating adenocarcinomas with unknown primaries. In general, lung, breast, endometrium, vagina and ovarian tissues contain CK-7 but not the colon. However, CK-20 is found almost exclusively in the gastrointestinal tract and urothelium [17-19]. Thus, IHC staining of tumor sections with these two cytokeratins is useful to distinguish the existence of colonic adenocarcinomas from others. According to the literature, phenotype CK7–/CK20+ pattern is available in approximately 75–95% cases of colorectal cancers [20], whereas the phenotype CK7+/CK20– favors primary tumors of the lung, breast, biliary tract, pancreas, ovary and endometrium [21]. In the current report, vulvar tissue samples were all considered as positive for CK-20 and negative for CK-7, as it was strongly suggestive for colonic metastasis to the vulva. Additionally, KRAS gene mutation analysis pointing wild-type colonic adenocarci-

noma without mutation in exon 2 (codon 12 and 13) supports above mentioned metastasis. In this case, after considering medical history, IHC report and the KRAS analysis of the patient, further treatment and surveillance plan have been decided. In summary, IHC is crucial in reflecting exact origin of the tumor and guiding clinicians to handle and manage complex metastatic cases.

Careful gynecologic evaluation of patients with prior malignancies is mandatory since this group represents high-risk for any further metastasis and unusual recurrences in the genital tract. Moreover, these patients even the ones who have had prior hysterectomy should also be evaluated with periodic gynecologic examinations including careful inspection of external genitalia, TVS and periodic Pap test. Unusual metastases that present themselves as gynecologic malignancies could be possible and therefore careful IHC assessment should be kept in mind. Imaging techniques including MRI and CT should also be taken into consideration since concurrent metastases as a consequence of widespread disease may accompany initial lesions.

Consequently, isolated vulvar metastases from a colonic adenocarcinoma can easily be misdiagnosed as primary vulvar carcinoma rather than a relapse. Therefore, before the final decision, clinicians should precisely distinguish the primary lesion from metastasis. Careful evaluation of patients with a thorough physical examination, appropriate imaging techniques and IHC is crucial for such complex cases.

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Disclosure statement

There are no financial or commercial interests to declare regarding the authors of the study.

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