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Malignant pleural effusion from squamous cell carcinoma of the vulva: extremely rare metastatic pattern of a rarely metastasizing cancer

Abstract

The discovery of a malignant pleural effusion indicates metastatic disease and thus invariably results in the highest possible cancer stage. Although the female reproductive tract overall is a common primary tumor site giving rise to malignant pleural effusion, vulvar carcinoma stands out for its propensity for locoregional spread rather than distant metastasis. Our case contributes to the extremely limited number of published descriptions of thoracic involvement by vulvar carcinoma, with malignant pleural effusion being a particularly unusual pattern.

Key words: vulvar carcinoma, squamous cell carcinoma, malignant pleural effusion, pleural metastases

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Introduction

Malignancy is second only to infection as the commonest cause of exudative pleural effusion [1]. Lung is the primary tumor site most closely associated with pleural metastasis, followed by breast cancer. Among extrathoracic solid neoplasms, cancer of the female reproductive tract accounts for the highest percentage of malignant pleural effusions (MPE) [2]. Epithelial ovarian carcinoma (EOC) is the most common gynecological malignancy implicated in MPE, but primaries from virtually every female reproductive organ have been reported to metastasize to the pleura [3, 4]. This list includes vulvar cancer, which is the fourth commonest gynecological malignancy in the United States after uterine, ovarian, and cervical cancers [5]. Squamous cell carcinoma (SCC) accounts for the vast majority of vulvar cancer cases. Only six percent of patients present with distant metastases and, among these, pleural involvement is one of the rarest patterns

[6]. Herein we report a case of MPE due to metastatic SCC of the vulva. To our knowledge, this is only the second such case description in the English-language literature.

Case presentation

A 63-year-old Caucasian woman presented to our institution with new onset of dyspnea and non-productive cough. Additional history was significant for a 5 × 6 cm nodular right vulvar lesion with central ulceration and early extension into the ipsilateral vagina evaluated and biopsied one week previously. At that time, palpable right inguinal lymphadenopathy (LAN) was also present. Biopsy material demonstrated moderately differentiated, non-keratinizing SCC. She was afebrile, and her oxygen saturation on room air was 94%. Lung auscultation revealed decreased breath sounds at both bases. Routine laboratory evaluation was unremarkable. Frontal radiograph of the chest showed bilateral

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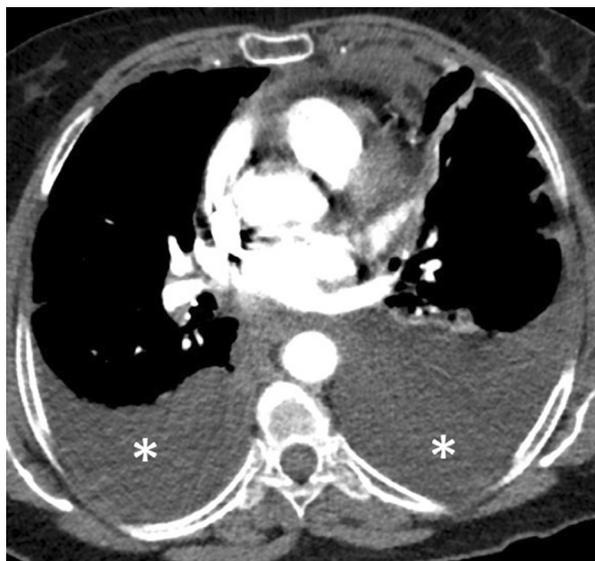


Figure 1. Chest computed tomography axial image set to soft tissue window demonstrating bilateral pleural effusions, left greater than right (asterisks)

pleural effusions, left greater than right. Subsequent computed tomography (CT) of the chest confirmed this finding (Figure 1). Left-sided thoracentesis was performed, yielding exudative pleural fluid. Microscopic examination revealed scattered atypical cells with high nucleus to cytoplasm ratio, irregular nuclei, and prominent nucleoli. Rare mesothelial cells and abundant mixed inflammatory cells were also identified. Immunohistochemical staining for calretinin and WT-1 highlighted the mesothelial cells. Staining for the squamous cell marker p40 was negative in the atypical cells. These cytological findings were non-diagnostic for establishing the presence of MPE. Repeat left pleural fluid cytology yielded similar results. As the next step, ¹⁸fluorodeoxyglucose positron emission tomography (¹⁸FDG-PET)/CT scanning was ordered. Besides hypermetabolic enhancement of the vulva with regional LAN, it demonstrated increased ¹⁸FDG uptake along both pleural surfaces but more prominently on the right with a maximum standardized uptake value (SUV) of 6.64 (Figure 2). No other suspicious foci of ¹⁸FDG activity were detected. In light of concern for metastatic malignancy to the pleura, she underwent video-assisted thoracoscopic surgical pleural biopsy of the more intensely ¹⁸FDG-avid right side. On intraoperative inspection, numerous pleural nodules were observed. Histology of the abnormal pleura showed invasive, non-keratinizing, poorly-differentiated SCC with areas of necrosis (Figure 3). These findings were morphologically

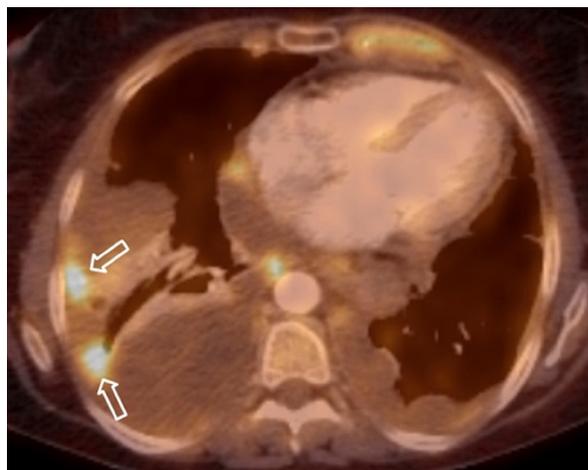


Figure 2. Representative axial fused PET/CT image showing hypermetabolic foci along the right pleural surface (arrows). The left pleural space also demonstrated areas of increased metabolic activity (not shown)

concordant with the previously obtained malignant vulvar tissue. The patient started and completed six cycles of platinum-based chemotherapy with Cisplatin and Paclitaxel. Computed tomography imaging immediately following this regimen demonstrated a robust tumor response. Unfortunately, during the subsequent treatment holiday, she experienced catastrophic relapse and passed away under hospice care approximately 8 months after the discovery of her MPE.

Discussion

In aggregate, gynecological cancer is the third most common solid tumor to give rise to MPE [2]. As is true of all other solid malignancies, pleural involvement by gynecological cancer signifies stage IV disease and is associated with poor survival [7]. In order to create pleural fluid accumulation, thoracic metastases need to both increase pleural capillary permeability and decrease pleural lymphatic drainage. While gynecological cancers with access to the peritoneal cavity such as ovarian and fallopian primaries are capable of transcoelomic spread into the pleural space, the predominant mechanism of pleural implantation in most cancers, presumably including vulvar carcinoma, is lympho-hematogenous dissemination. Even though the clinical picture and radiology could be highly suggestive of MPE, especially in patients with known malignancy, only positive cytohistology can definitively establish this diagnosis. The least invasive and therefore the most practical initial source of a pathological specimen in suspected cases is pleural fluid

withdrawn during thoracentesis and processed for cytology. The approximate overall cytological yield in MPE is a disappointing 50%, a number that can exceed 80% in exfoliative cancers such as ovarian adenocarcinoma and can fall under 30% in non-exfoliative cancers such as SCC [8, 9]. It

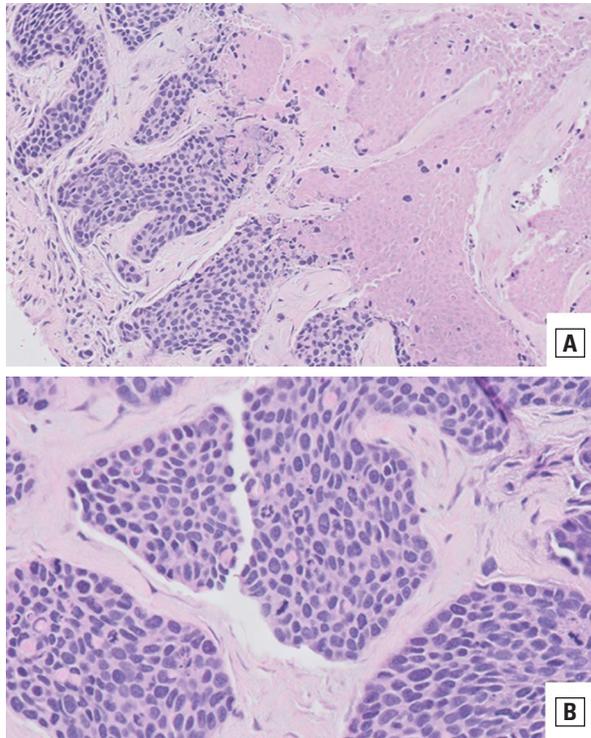


Figure 3. **A.** Low-power view of the pleural biopsy showing nests of neoplastic squamous cells in a fibrotic background with associated necrosis (Hematoxylin & eosin, original magnification $\times 200$). **B.** High-power view allowing better appreciation of the pleomorphic nuclei and eosinophilic cytoplasm of the neoplastic squamous cells. There is no evidence of keratinization. Numerous mitotic figures are present (H&E, original magnification $\times 400$)

is thus not surprising that pleural involvement could not be confirmed by fluid cytology in our patient despite repeat sampling.

As mentioned, the majority of vulvar carcinoma cases remain localized — with potential invasion of nearby structures — or spread only as far as the regional lymph nodes [6]. The list of metastatic sites reported in the literature includes the central nervous system [10], breast [11], heart [12], lung [13], liver [13], bone [13], skin [13], and muscle [14]. We were able to find only a single published case describing pleural metastases from vulvar carcinoma, also with biopsy-proven squamous histology of pleural implants [15]. In that report, the presence of vulvar carcinoma was likewise known prior to detection of MPE as in our case, but pleural involvement occurred much later in the disease course: it signified recurrence approximately one year after initial diagnosis and vulvectomy. In contrast to our case, however, the original vulvar specimen was not available for correlation. Table 1 summarizes the differences and similarities between our case and the one published previously.

Conclusion

While not an uncommon gynecological malignancy, vulvar cancer is at the same time an exceedingly rare source of pleural metastases. Squamous cell carcinoma, the usual histology of vulvar cancer, is associated with poor cytological yield of pleural fluid sampling, so our case both illustrates a very unusual metastatic pattern and reminds that suspicion for MPE ought to be maintained despite negative pleural fluid cytology and despite a rarely metastasizing cancer.

Table 1. Comparison of features of the present case with those of the single previously published report.

Source	Erra <i>et al.</i> [15]	Present case
Publication year	2016	2020
Diagnosis of vulvar carcinoma	Historical	Confirmed at reporting institution
Age at MPE diagnosis	76 years	63 years
Histology of pleural implants	SCC	SCC
Timeline of MPE detection	1 year after diagnosis	1 week after diagnosis
Pattern of pleural involvement	Unilateral (right)	Bilateral
Symptoms	Dyspnea, chest pain	Dyspnea, dry cough
Mode of MPE diagnosis	Thoracoscopy with pleural biopsy	Thoracoscopy with pleural biopsy
Inguinopelvic lymph node involvement	No	Yes (by PET)
Treatment history of primary site	Vulvectomy	None

MPE — malignant pleural effusion; PET — positron emission tomography; SCC — squamous cell carcinoma

Conflict of interest

None declared.

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