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

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...
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, $^{18}$fluorodeoxyglucose positron emission tomography ($^{18}$FDG-PET)/CT scanning was ordered. Besides hypermetabolic enhancement of the vulva with regional LAN, it demonstrated increased $^{18}$FDG 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 $^{18}$FDG 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 $^{18}$FDG-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 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 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 et al. [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

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Conflict of interest

None declared.

References:

1. Feller-Kopman D, Light R, Feller-Kopman D, et al. Pleural disease. N Engl J Med. 2018; 378(8): 740–751, doi: 10.1056/NEJMra1403503, indexed in Pubmed: 29466146.

2. Clive AO, Kahan BC, Hooper CE, et al. Predicting survival in malignant pleural effusion: development and validation of the LENT prognostic score. Thorax. 2014; 69(12): 1096–1104, doi: 10.1136/thoraxjnl-2014-205285, indexed in Pubmed: 25109651.

3. Wang JG, Cox PG. A woman in her 30s with a history of cervical cancer presents with shortness of Breath and pleuritic chest pain. Chest. 2017; 151(5): e115–e118, doi: 10.1016/j.chest.2016.10.048, indexed in Pubmed: 28463134.

4. Hiensch R, Meinhof K, Leytin A, et al. Clinically occult primary fallopian tube carcinoma presenting as a malignant pleural effusion. Clin Respir J. 2017; 11(6): 1086–1090, doi: 10.1111/crj.12423, indexed in Pubmed: 26646473.

5. Siegel RL, Miller KD, Fedewa SA, et al. Cancer statistics, 2017. CA Cancer J Clin. 2017, 67(1): 7–30, doi: 10.3322/caac.21387, indexed in Pubmed: 28055105.

6. Weinberg D, Gomez-Martinez RA. Vulvar cancer. Obstet Gynecol Clin North Am. 2019; 46(1): 125–135, doi: 10.1016/j.ogc.2016.09.008, indexed in Pubmed: 30683259.

7. Ataseven B, Chiva LM, Harter P, et al. FIGO stage IV epithelial ovarian, fallopian tube and peritoneal cancer revisited. Gynecol Oncol. 2016; 142(3): 597–607, doi: 10.1016/j.ygyno.2016.06.013, indexed in Pubmed: 27335253.

8. Porzel JM, Esquerda A, Vives M, et al. Etiology of pleural effusions: analysis of more than 3,000 consecutive thoracenteses. Arch Bronconeumol. 2014; 50(5): 161–165, doi: 10.1016/j.arbres.2013.11.007, indexed in Pubmed: 24160097.

9. Arnold DT, De Poussea D, Perry S, et al. Investigating unilateral pleural effusions: the role of cytology. Eur Respir J. 2018; 52(5), doi: 10.1183/13993003.01254-2018, indexed in Pubmed: 30262573.

10. Dursun P, Ayhan A, Tarhan NC, et al. Cerebellar metastasis in squamous cell vulvar carcinoma. Arch Gynecol Obstet. 2009; 279(1): 69–71, doi: 10.1007/s00404-008-0635-2, indexed in Pubmed: 18379804.

11. Vicus D, Korach J, Friedman E, et al. Vulvar cancer metastatic to the breast. Gynecol Oncol. 2006; 103(3): 1144–1146, doi: 10.1016/j.ygyno.2006.07.037, indexed in Pubmed: 17095246.

12. Linder R, Lauterbach R, Reiss A. A case of recurrent vulvar carcinoma with cardiac metastasis: case report and review of the literature. Int J Gynecol Pathol. 2020; 39(4): 400–403, doi: 10.1097/PGP.0000000000000624, indexed in Pubmed: 31433376.

13. Pries K, Haeringer N, Grimm D, et al. Patterns of distant metastases in vulvar cancer. Gynecol Oncol. 2016; 142(3): 427–434, doi: 10.1016/j.ygyno.2016.07.090, indexed in Pubmed: 27401841.

14. Steele DM, Hegstrand LR, Julian TM, et al. An unusual presentation of metastatic squamous cell carcinoma of the vulva. Gynecol Oncol. 1990; 39(2): 218–220, doi: 10.1016/0090-8258(90)90436-o, indexed in Pubmed: 2227599.

15. Erra S, Patrucci G, Speranza G, et al. Unusual pleural effusion from vulvar squamous cell carcinoma: report of a case and review of the literature. Pathologica. 2016; 108: 148–150.