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Case Report

Cutaneous metastasis of serous ovarian carcinoma

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Abstract

Ovarian carcinoma ranks among the top causes of cancer-related fatalities among women in the United States.[1] In the spectrum of ovarian carcinomas, low-grade serous ovarian carcinoma (LGSOC) is a relatively rare form, constituting only 2-5% of all ovarian carcinomas.[2] Although metastasis to the peritoneum and other organs is frequently observed, cutaneous metastasis of ovarian carcinoma is uncommon, occurring in less than 4% of cases and occurring even less often in the serous subtype.[3] Owing to its rare and variable presentation, cutaneous involvement in ovarian carcinoma is particularly challenging to recognize. Patients presenting with skin lesions in the setting of a history of ovarian carcinoma should raise suspicion for cutaneous metastasis. We present a rare case of LGSOC with non-nodular cutaneous involvement presenting as asymptomatic erythematous papules and hyperpigmented patches on the upper chest, abdomen, and lower back.

Introduction

Ovarian carcinoma ranks among the top causes of cancer-related fatalities among women in the United States.[1] Low-grade serous ovarian carcinoma (LGSOC) is a rare subtype, accounting for 2-5% of cases, whereas high-grade serous ovarian carcinoma (HGSOC) constitutes approximately 70%.[2-4] LGSOC tends to have an earlier average age of onset (55.5 years versus 63.6 years), a slower progression (99 months versus 57 months), and more resistance to chemotherapy.[2] Cutaneous manifestations of internal malignancies, although rare, may even be the presenting feature of malignancies.[1,5] Cutaneous metastases of ovarian carcinoma are uncommon, occurring somewhere between 0.9%-4%, further emphasizing the importance of recognizing cutaneous manifestations and their potential impact on patient's clinical course.[3,4] Herein, we discuss a rare case of cutaneous metastasis in a patient with LGSOC presenting with non-nodular cutaneous manifestations.

Case Synopsis

A 35-year-old woman with an extensive history of recurrent stage IV LGSOC was seen in consultation for a two-week history of a worsening erythematous rash that was unresponsive to topical diphenhydramine, hydrocortisone 1%, and calamine lotion. In 2015, tissue specimens from the bilateral ovaries, fallopian tubes, bladder, cecal peritoneum, omentum, and right hemidiaphragm were consistent with stage IV LGSOC (ER/PR+, p16+, p53-, Wt-1+). Lab workup at the time was significant for elevated CA 125 (62U/mL). Family history was negative for breast and ovarian cancers. However, genetic analysis conducted by FoundationOne®CDx (Cambridge, MA) revealed a missense mutation in BRCA1 interacting protein C-terminal helicase 1 (BRIP1) mutation, which has been linked to an increased risk of ovarian cancer.[5]

Over the course of 8 years, her recurring malignancy was treated with various chemotherapies including first-line therapy (carboplatin, paclitaxel 175, bevacizumab), second-line therapy (fulvestrant), third-line therapy (carboplatin, paclitaxel, bevacizumab), fourth-line therapy (avutometinib), and fifth-line therapy (cytoxan, bevacizumab). At the time of evaluation, the patient was on maintenance therapy with letrozole and ribociclib.

The patient was hospitalized for a small bowel obstruction and had well-demarcated, slightly erythematous, non-scaling, non-blanchable papules with a slightly digitate appearance on the abdomen and upper chest on exam (**Figure 1A**). Multiple hyperpigmented patches with poorly demarcated borders were noted on her lower back (**Figure 1B**). A punch biopsy of an erythematous papule on her left abdomen revealed superficial dermal invasion of AE1/AE3 positive cells present within and sur-

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Figure 1. ***A)*** *Well-demarcated, slightly erythematous, non-scaling, non-blanchable papules with a slightly digitate appearance on the abdomen and upper chest on exam.* ***B)*** *Multiple hyperpigmented patches with poorly demarcated borders were noted on the patient's lower back.*

rounding the superficial dermal vasculature (Figure 2A-C). Cells were positive for cytokeratin 7 (CK7) and PAX8 and negative for cytokeratin 20, confirming the diagnosis of metastatic cutaneous ovarian carcinoma.

Case Discussion

As the fifth-leading cause of cancer-related deaths in women in the United States, ovarian cancer is the most lethal gynecologic malignancy.[1] This high mortality rate is attributed to diagnosis in advanced stages and its propensity to metastasize.[1,5,6] The development of cutaneous metastasis in ovarian carcinomas is felt to be related to an intricate interplay between cancer subtype, severity, metastasis routes, and prior medical and surgical history. Metastasis most commonly occurs through intraperitoneal seeding to the peritoneal cavity but can also infiltrate the pelvic and para-aortic nodes via lymphatic channels and spread hematogenously to distant sites.[6] Prior laparoscopic surgery, particularly in the setting of malignant ascites or intraperitoneal metastases, can provide a route of direct implantation, which may increase risk of cutaneous spread.[1] Additionally, a history of anti-vascular endothelial growth factor treatments, such as bevacizumab, which is commonly used for ovarian cancer, has been shown to predispose patients to cutaneous metastases via acquired resistance and subsequent angiogenesis.[1,7]

Cutaneous metastases of ovarian carcinoma are rare and, in most cases reported in literature, the abdomen, chest, or previous sites of intra-abdominal surgeries are sites of cutaneous spread.[7] The most common presentation of cutaneous metastasis in ovarian carcinoma is solitary to multiple umbilical nodules, referred to as Sister Mary Joseph nodules (SJN).[1] However, there are many case reports of cutaneous metastases presenting as nodules in non-umbilical sites. Non-SJN metastases have also been rarely reported in literature with various cutaneous morphologies. Cormio, Li, Bernecker, Yilmaz, and Achimas et al have reported cutaneous metastases in ovarian carcinoma presenting as ulcerated herpetiform/zosteriform lesions, reticulate erythema, indurated plaques, erythema annulare-like lesions, cellulitis, and lymphangitis, respectively.[7-11]

Cutaneous metastasis in ovarian carcinoma is correlated with an unfavorable prognosis, with a median survival of four months.[8] The most prognostic factor is the duration between diagnosis of ovarian carcinoma and the appearance of skin symptoms; longer intervals (>40 months) indicate a more favorable prognosis.[1,8] Interestingly, the presence of metastases in surgical scars suggests a more favorable outcome, whereas metastatic lesions in nonsurgical scar areas are linked to higher mortality rates.[1] Unfortunately, therapeutic management poses difficulties and is guided by metastasis location, comorbidities, and patient care objectives. The most effective treatment course for cutaneous metastasis remains uncertain; however, chemotherapy, surgical removal, and radiation have all been used.[1]

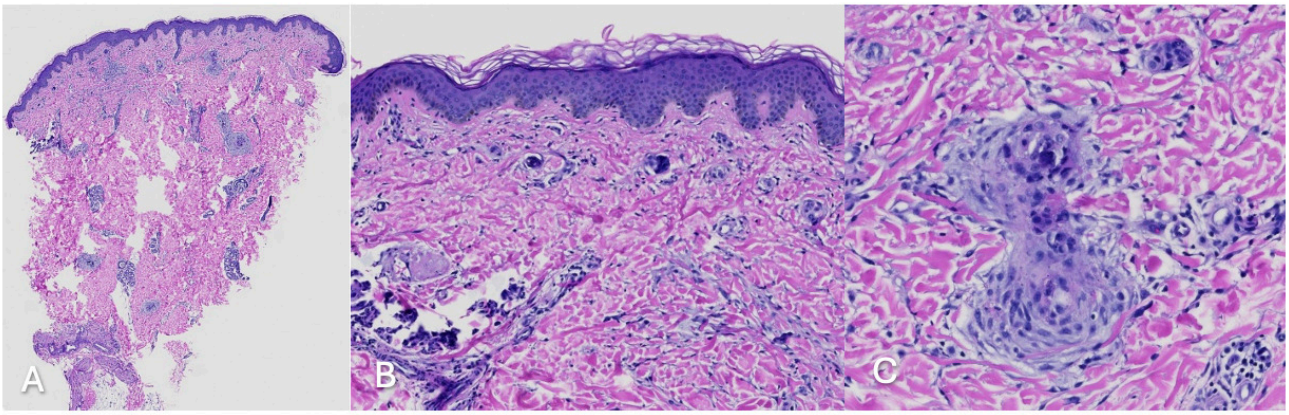


Figure 2. ***A)*** *H&E, 100× revealing a subtle, nonspecific, infiltrate in upper dermis.* ***B)*** *H&E, 200× revealing an atypical interstitial and intravascular epithelioid cell population.* ***C)*** *H&E, 400× revealing an atypical interstitial and intravascular epithelioid cell population.*

Conclusion

In conclusion, cutaneous metastasis should remain in the differential diagnosis in patients with a history of cancer and unexplained dermatologic lesions of any morphology. Furthermore, unique or uncharacteristic dermatologic findings should not rule out the possibility of metastasis, such as non-SJN lesions in a patient with ovarian carcinoma and still warrant a comprehensive diagnostic workup. Our case of cutaneous metastasis of LGSOC presenting as asymptomatic erythematous papules and hyperpigmented patches exemplifies the importance of maintaining high clinical suspicion for possible cutaneous metastasis to aid in early diagnosis and appropriate subsequent management.

Conflicts of interest

The authors declare no conflicts of interest.

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