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Case Report

Eyelid Metastasis from Cervical Cancer: A Case Report

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Cervical cancer · Eyelid tumor · Tumor metastasis · Case report

Abstract
Metastatic malignant lesions of the eyelids are less than 1% of all eyelid tumors. Eyelid metastasis from the cervix, particularly the first sign of metastasis, has not been reported. A female presented to an ophthalmologist with a gradually increasing mass on the lateral edge of the lower eyelid for 2 months and was diagnosed with stage IB1 cervical cancer 3 years ago. We performed wide local excision of the eyelid mass. The mass was histologically and immunohistochemically similar to cervical cancer. Upon metastatic examination, no lesions involving other sites or lymph nodes were found. Subsequently, local radiation therapy yielded the desired results. In the present case, the possibility of metastasis from the cervix was not considered for the first time. More attention should be paid when identifying unexplained masses in patients with a history of malignant tumors.

Introduction

According to Global Cancer Statistics 2020, cervical cancer is the fourth leading cause of morbidity and mortality among women around the world [1]. Although the prevention, detection, diagnosis, and treatment of cervical cancer have improved over the past decade, mortality remains high.

The main metastatic routes of cervical cancer are the direct spread and lymphatic metastasis. Lymphatic vessels can spread cervical cancer to inguinal, mediastinal,

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supraclavicular, and pelvic lymph nodes. Patients with advanced cervical cancer usually have enlarged and indurated inguinal lymph nodes. Distant metastasis of malignant tumors usually occurs in the late stage; however, metastasis to the eyes and skin is extremely rare. Orbits [2], choroid [3], and iris [4] are reported sites of metastatic lesions. Skin metastasis of cervical cancer is very rare, ranging from 0.1% to 2% [5]. However, cervical cancer metastasis to the eyelid has not been reported. Herein, we present a rare case of a metastatic eyelid origin from cervical cancer.

Case Presentation

A 56-year-old female presented to see an ophthalmologist with complaints of a gradually increasing mass on the left eyelid during 2 months. The patient denied any subjective visual impairment, prior eye injuries, or other ophthalmologic disorders. On ophthalmic examination, a 5 × 6 mm painless mass, which was firm, unmovable, and nonulcerated, was found on the outer skin of the left lower eyelid margin. The patient's uncorrected visual acuity was 1.0 (logMAR) bilaterally. No abnormalities were detected by slit-lamp microscopy or direct ophthalmoscopy. The patient had a history of cervical cancer 3 years ago. After being diagnosed with HPV-16 positive stage IB1 cervical squamous cell carcinoma, she underwent total radical en bloc hysterectomy, pelvic lymph node dissection, and bilateral adnexectomy, followed by chemotherapy and radiation therapy. No abnormalities were found in 3 years of follow-up.

We performed wide local excision of the eyelid mass. Hematoxylin and eosin (H&E) staining of the tumor is shown in Figure 1a. Pathological result showed heterologous cell nests were distributed in clumps and flaks, with large nuclei and irregular nuclear membranes, and intercellular bridges were observed, which indicated a moderately differentiated carcinoma consisting of keratinizing squamous cell carcinoma. Immunohistochemical analysis showed positive staining for CK5/6, CK7, CK, P16, P63, and P40 and negative staining for Calponin, HMB45, SMA, and S100 (Fig. 1b–k). The HPV test of mass was HPV-16 positive. Combined with the patient's history and image of H&E staining, we hypothesized that this mass was a cervical eyelid metastasis. Gynecological examination revealed that the vaginal stump was tumor free. Physical examination revealed no enlargement of the cervical, preauricular, or submandibular nodes. Subsequently, we performed positron emission tomography-computed tomography and confirmed that no other sites of metastasis were present (Fig. 2). The patient subsequently underwent local radiotherapy. No other metastases were found during the 1-year follow-up period. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000534594).

Discussion

Cervical cancer, which is mainly caused by human papillomavirus (HPV) infection, is well characterized. HPV-16 is the most common high-risk HPV type in cervical cancer. The initiation and progression of cervical cancer ranging from cervical intraepithelial neoplasia (CIN I) to CIN II and then CIN III finally leads to cancer [6]. Direct local extensions and lymphatics are the most common methods used for the spread of cervical cancer. Hematogenous metastasis usually occurs in the late stages of cancer and affects the lungs, bones, and liver. Patients with advanced cervical cancer with recurrent or distant metastases have a poor prognosis, with a 1-year survival rate of only 15–20% [7]. Cutaneous

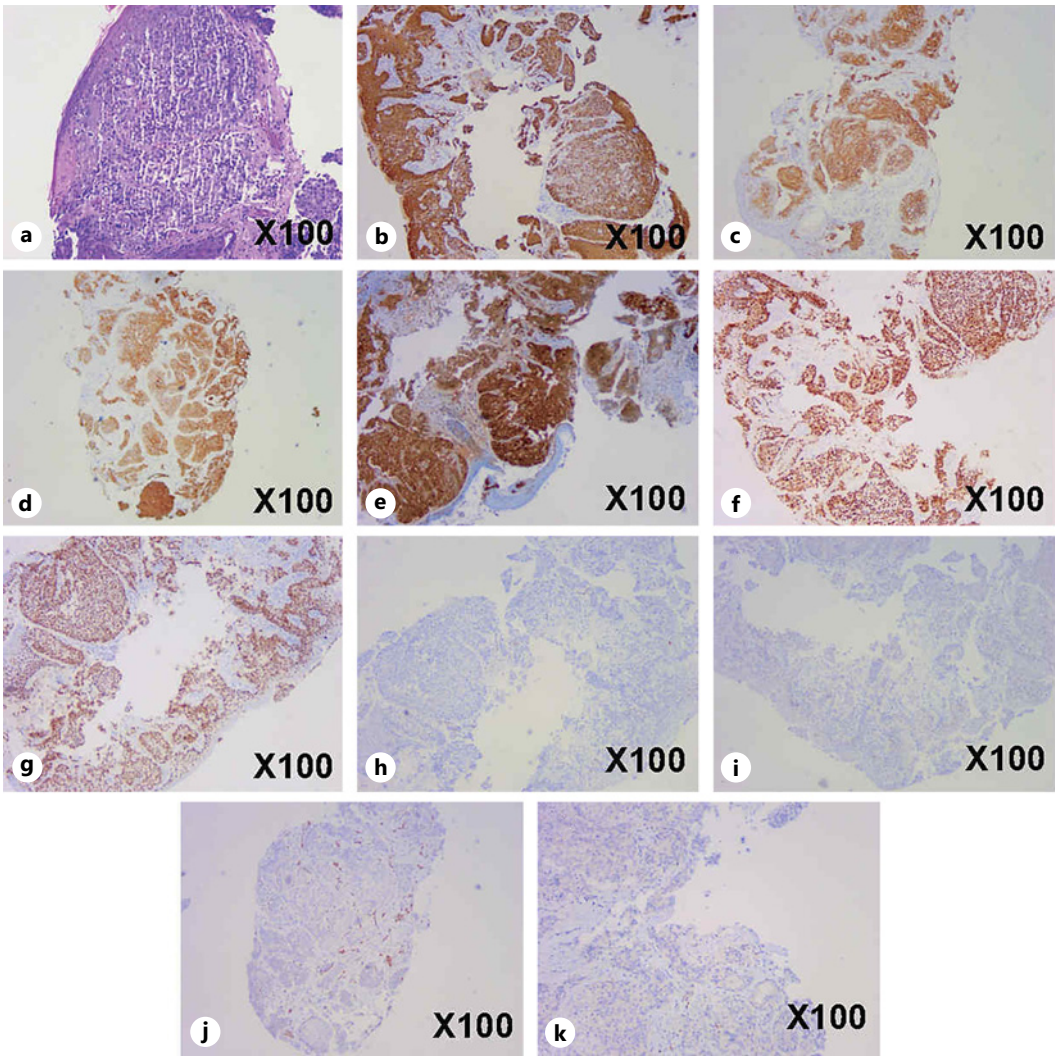

Fig. 1. Histochemical and immunohistochemical staining of eyelid mass (×100). **a** Histochemical staining. **b** CK5/6(+). **c** CK7(+). **d** CK(+). **e** P16(+). **f** P63(+). **g** P40(+). **h** Calponin(−). **i** HMB45(−). **j** SMA(−). **k** S100(−).

metastases are rare in cervical carcinoma. The most common sites of cutaneous metastases are the abdomen and lower extremities [8]. The prognosis for cervical cancer with cutaneous metastases is extremely poor. Usually, it takes 3 months from diagnosis to death for patients with cervical carcinoma metastases to the skin [5]. For our patient, she had a history of HPV-16 positive stage IB1 cervical squamous cell carcinoma. The result of H&E staining indicated this mass was a metastatic malignancy. Meanwhile, the same type of oncogenic HPV and the immunohistochemical analysis further supported our speculation that this mass was a cervical eyelid metastasis. Fortunately, our patient was diagnosed and treated promptly.

Most malignancies of the eyelids are primary, with 90% of them being basal cell carcinoma. Malignant metastatic lesions of the eyelids are rare, accounting for less than 1% of all eyelid tumors [9]. In female, the most frequent primary site is the breast and the lungs [10]. Eyelid metastasis can be the first symptom or first sign of metastasis from a known malignant

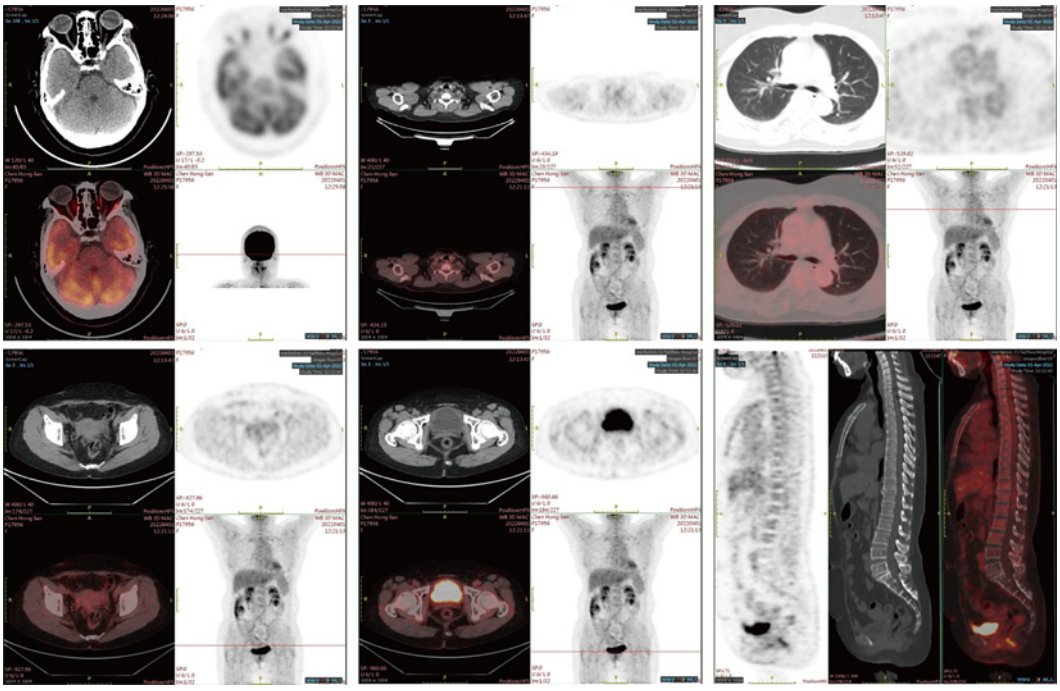

Fig. 2. PET-CT after the excisions of eyelid mass.

neoplasm and is associated with a poor prognosis. Metastases appeared 62 months after the diagnosis of the primary tumor [9], and the average survival time after presentation with eyelid metastases was 9.7 months [11]. After a literature search, we summarized a table of eyelid metastasis from other malignancies (Table 1).

Cervical cancer metastasis to the eyelid, particularly the first sign of metastasis, has never been reported. After a literature search, we found only 5 cases of orbital metastasis from cervical cancer to date. All these 5 patients had visual impairment, eye discomfort with other organs, and lymph node metastasis. In this case, the patient showed only a left lower eyelid mass without concomitant ocular or systemic symptoms. A firm, unmovable, and non-ulcerated mass was not considered a metastatic malignant lesion. Based on this case report, in the future, attention should be paid to patients with a history of cervical cancer as the main manifestation of skin and eyelid masses. Metastasis can be detected on time using pathological and immunohistochemical examinations, which is of great significance for treatment. We summarize that biopsy and wide local excision are appropriate to identify the property of eyelid metastasis and the managements of eyelid metastasis are mainly based on the treatments of primary tumor. If possible, chemoradiotherapy and targeted drugs are also alternative.

Hematogenous and lymphatic metastases are the two types of metastases that lead to different treatments and survival rates. Patients with lymphatic metastasis have a better prognosis than those with hematogenous metastasis [21]. PET/CT, which is more sensitive and specific than CT or MRI, is widely used to evaluate extra-pelvic metastases. Concurrent chemoradiotherapy is efficient and well tolerated in patients with lymphatic metastasis [22]. Chemoradiotherapy should be used in combination with surgery [23]. Eyelid metastases suggest hematogenous spread of cancer, even in the absence of other sites. The treatment of eyelid metastases aims to maximize the patient's quality of life and preserve their vision. For eyelid metastases, radiotherapy is the mainstay treatment that

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Table 1. Literature review on the management of eyelid metastasis and previous case reports

Primary tumor	Age, years	Gender	Clinical stage	Months to eyelid metastasis	Treatment	References
Breast cancer	79	Female	IV	2	Chemotherapy	Martorell-Calatayud et al. [12], 2010
Breast cancer	80	Female	NA	120	Surgical resection and followed up	Fonseca et al. [13], 2009
Breast cancer	77	Female	NA	24	Biopsy and followed up	Fonseca et al. [13], 2009
Breast cancer	50	Female	II	60	Biopsy and chemotherapy	Zhang et al. [14], 1995
Breast cancer	59	Female	I	84	Biopsy, fulvestrant, and palbociclib	Martin et al. [15], 2017
Lung adenocarcinoma	68	Male	NA	24	Biopsy	Tavakoli et al. [16], 2016
Non-small cell lung cancer	75	Male	IV	0	Chemotherapy	Joseph et al. [17], 2016
Lung cancer	50	Male	IV	0	Surgical resection and chemoradiotherapy	Latz et al. [18], 2009
Rectal cancer	57	Male	I	8	Neoadjuvant chemoradiotherapy, surgical resection, and chemotherapy	Paik et al. [19], 2020
Gastric cancer	58	Female	IV	24	Chemotherapy	Martorell-Calatayud et al. [12], 2010
Nasopharyngeal chondroid chordoma	63	Female	NA	36	Surgical resection and radiotherapy	Ren et al. [20], 2019

NA, not available.

controls tumor growth, preserves visual function, improves patient comfort, and alleviates symptoms in 80% of cases [24]. In a 1- to 2-week period, a dose of 20–40 Gy is recommended. According to the guideline of National Comprehensive Cancer Network, chemotherapy with or without radiation forms the basis of treatment of recurrent and/or metastatic cervical cancer patients. Our patient was recommended to perform chemoradiotherapy. Due to the serious side effects of chemotherapy, she refused to receive chemotherapy. Our patient accepted the radiotherapy and to have annual clinical and radiologic checkup. She has been followed up for more than 1 year without any evidence of tumor recurrence or metastasis.

Conclusion

In summary, our findings suggest that more attention should be paid to unexplained masses with a benign appearance in patients with cervical cancer. The mass should be biopsied and excised to identify its characteristics and sources, particularly in patients with a history of primary tumors. There is a limitation that we have not saved the photograph of eyelid mass.

Statement of Ethics

This study was approved by the Ethics Committee of the Taizhou Central Hospital (Taizhou University Hospital) (2023 L-04-05). Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of Interest Statement

The authors declare that they have no conflict of interest.

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Author Contributions

J.W. and B.S. performed the case study, prepared the figures, and wrote the manuscript. C.H. and N.G. participated in the collection of case data and literature, as well as in the completion of all documentary and article works. W.W. had given many constructive suggestions for this paper. All the authors have read and approved the final manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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