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A Case of Eye Lid Tissue Loss in The Patient of Breast Cancer on Chemotherapy: Diagnostic Dilemma

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Abstract

A 33-year-old woman on chemotherapy for breast carcinoma presented with loss of tissue of the right lower eyelid margin with madarosis and corneal descemetocele formation. The possibility of either metastasis or primary eyelid malignancy such as sebaceous cell carcinoma given her immunocompromised state was considered. Another possible cause of extensive inflammatory blepharoconjunctivitis was because of the ocular side effects of chemotherapeutic agents given for breast cancer. A tissue biopsy from the local area was performed and the patient was started on topical medications for symptomatic relief. Histopathology revealed chronic inflammatory disease of the eye with no evidence of malignant cells. Smear for grams stain showed few pus cells, few epithelial cells, and no microorganisms. Pus culture was sterile which further confirmed inflammatory disease of the eyelid. Eyelid inflammation was the possible outcome of a chemotherapeutic side effect in an immunocompromised state.

Keywords: ***Breast carcinoma; Eyelid tissue loss; Madarosis; Chemotherapy; Immunocompromised state; Chronic inflammation***

1. Introduction

Breast carcinoma is renowned for its varied presentations. While metastases to the bones and brain are relatively common, eyelid metastasis remains quite rare [1]. Ocular complications arising from antineoplastic agents used to treat breast carcinoma can significantly affect the quality of life for cancer patients. Recent advancements in oncologic treatments, including monoclonal antibodies, immunotherapies, antibody-drug conjugates, checkpoint inhibitors, and growth factor receptor

therapies, have led to an increase in ocular complications. These complications differ depending on the specific mechanisms of action of these therapies and pose considerable challenges in the management of cancer patients [2].

2. Case Report

This is a case report of a 35-year-old female patient who was diagnosed with advanced-stage carcinoma of the right breast. Sentinel lymph node biopsy was positive for axillary lymph node. She was treated with modified radical mastectomy with radical axillary lymph node dissection followed by two cycles of chemotherapy. Chemotherapy is ongoing, adhering to TCH schedule: Taxotere® (Docetaxel, Hospira National code 667214) 75 mg/ml, Carboplatin® (Carboplatin AUC6, Pfizer RxPathways, US) administered every 3 weeks with a total of six cycles, and Herceptin® (Tratuzumab, Roche Products Limited, UK) 6 mg/kg/12 months.

Following the first cycle, the patient had developed relevant signs of toxicity, such as conjunctival, vaginal, and anal grade 2 mucositis [2]. This development of symptoms forced the chemotherapy dose to be decreased to 75%, resulting in an improvement of the referred symptoms. She was diagnosed with cilia touching her eyes which were subsequently epilated on multiple occasions. She had denied any previous history of ocular complaints or treatment.

Three weeks following the initiation of chemotherapy, she presented to us with complaints of redness and intense pain, marked diminution of vision, discharge, and right lower lid tissue loss. On examination of the right eye, the vision was finger counting close to face with accurate projection of rays, intense conjunctival congestion was seen with stromal edema and descemetocele formation. Periorbital edema, crusting with meibomian gland disease, and lid tissue loss over her right lower lid were seen (FIG. 1). Schirmer test I was 5/6 mm and Schirmer II was 3/4 mm. The lacrimal meniscus was almost absent. The punctum was patent and well-positioned. The lacrimal system was normal.

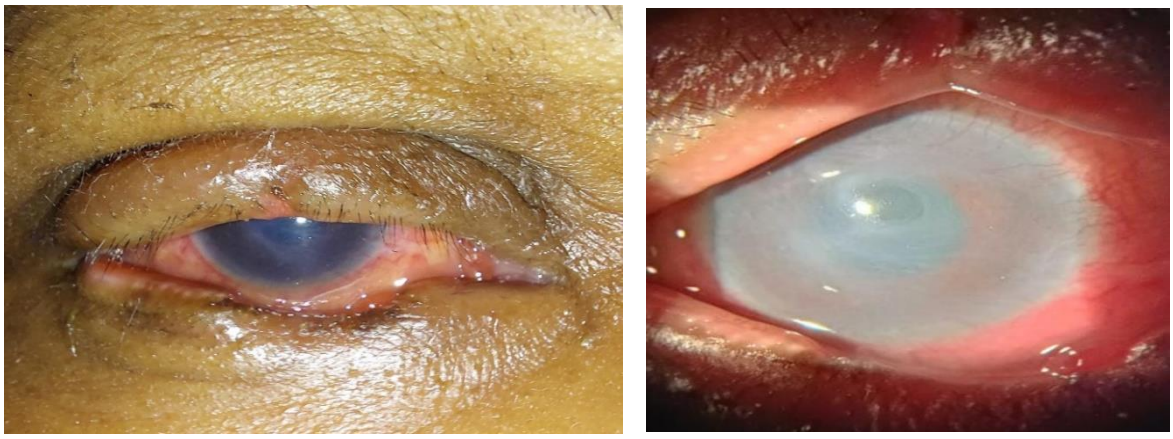

FIG. 1. **Condition of eyelid at the time of presentation.**

An incisional biopsy of the lower lid was done. The smear for gram stain shows few pus cells, few epithelial cells, and no microorganisms. The culture sensitivity of pus aspirate was sterile after 48 hours of incubation. The histopathological report was suggestive of inflammatory changes and a biopsy was planned. Histopathological examination of the excised portion

revealed chronic inflammation, dermal fibrosis with squamous metaplasia process, and abnormal epithelial differentiation. Immunofluorescence was negative, as no linear deposition of antibodies were found on the basal membrane. Ocular pemphigoid (OCP), Steven–Johnson disease, infections, rosacea blepharoconjunctivitis, atopic keratoconjunctivitis, or topical medication toxicity were all ruled out. Treatment was started in the line of inflammatory etiology, after a few days patient was symptomatically better.

3. Discussion

The loss of eyelid tissue and decompensated cornea can occur in a patient with breast carcinoma undergoing chemotherapy. The potential underlying causes of eyelid tissue loss in such cases include the toxicity of chemotherapeutic agents, metastasis of breast carcinoma, and primary eyelid carcinoma. Among these, chemotherapy-related adverse reactions are the most common, which can also impact vision through the formation of cataracts and the induction of corneal opacity [3]. Metastasis to the eyelids is rare, accounting for less than 1% of all malignant eyelid lesions [4].

In the ophthalmic literature, information on eyelid metastases has been reported mostly as individual case reports and a few small case series. Riley reported 15 cases of eyelid metastasis from a pathology laboratory and found that the most common primary tumor was breast carcinoma (6 [40%]), followed by skin melanoma (5 [33%]), gastric carcinoma (2 [13%]), uveal melanoma (1 [7%]), and lung carcinoma (1 [7%]) [5]. Later, Mansour and Hidayat reviewed 31 cases from the Armed Forces Institute of Pathology and found that the most frequent primary site was the breast (11 [35%]), followed by the skin (4 [13%]), gastrointestinal tract (3 [10%]), genitourinary tract (3 [10%]), and uvea (2 [6%]) [1].Chemotherapy for our patient was administered using a combination of docetaxel and carboplatin, along with trastuzumab. Docetaxel, a taxane-class antineoplastic agent, is utilized in advanced breast cancer cases to enhance patient survival rates; however, it may cause side effects such as eyelid alterations, potentially leading to cicatricial entropion or canalicular obstruction [6]. Several earlier case reports and studies have indicated that docetaxel can provoke severe inflammatory reactions in the cornea, which, if not appropriately managed, may result in corneal opacity [7].

Furthermore, research has demonstrated that epiphora, characterized by excessive tearing, occurs more frequently in patients receiving weekly docetaxel treatments compared to those on a three-week regimen [8,9]. Carboplatin is a widely utilized platinum-based chemotherapeutic agent known to potentially cause ocular toxicity. Common side effects include ocular pain, redness, blurred vision, and inflammation of the eyes and surrounding tissues. Less frequently reported side effects involve optic nerve edema accompanied by hemorrhages, macular edema, pigmentary maculopathy, uveal effusion glaucoma, exudative retinal detachment, bilateral metamorphopsia, irreversible vision loss, and optic atrophy [10]. In another study, abnormal ocular motility has also been noted with sub tenon injection of carboplatin [11]. Bilateral ischemic retinopathy was also seen in a combination therapy of carboplatin and paclitaxel. Treatments regarding severe ischemic retinopathy are limited to pausing treatment or pan-retinal laser treatment [12].

In the present case, the patient is presented with pain, redness, and marked diminution of vision which may be due to carboplatin-related toxicity. On the other hand, trastuzumab is specifically targeted against the extracellular domain of the human epidermal growth factor receptor 2 and can result in increased tear production, swelling of the eyelids, conjunctivitis,

discharge, lacrimal canalicular stenosis, and corneal epithelium changes [13]. She developed lower eyelids chronic cicatricial inflammation and severe dryness soon after the first cycle of the treatment. The chronic inflammatory process resulted in meibomian glands dysplasia, evolving with acquired distichiasis/ trichiasis and finely tissue loss. Three other cases of similar eyelid inflammation associated with the use of docetaxel have previously been reported, starting 5 days to 7 years, and 8 months after trastuzumab or even after cessation of treatment, similar to our case [14]. The pathology biopsy of our patient confirmed the presence of chronic inflammation, fibrosis, and squamous metaplasia. It has been reported that both docetaxel and trastuzumab can lead to significant inflammation and stromal fibrosis in the mucosal lining of the lacrimal drainage apparatus. However, our patient did not develop stenosis in this area. It is known that docetaxel may affect both the upper and lower eyelids, while trastuzumab has been associated with effects primarily on the lower eyelids [15].

4. Conclusion

Eyelid tissue loss and corneal opacity can occur as rare complications in breast carcinoma patients undergoing chemotherapy. When patients receive multiple chemotherapeutic agents, it becomes challenging to attribute specific ocular side effects to a particular drug, as similar toxicities are often observed across different treatments. In addition, primary eyelid carcinoma or metastasis to the eyelid may also lead to tissue loss and abnormalities in the eyelid margin; however, histopathological examination has ruled out these possibilities in the current case. Considering the ocular manifestations presented, the adverse effects of chemotherapy may result in immunosuppression. Both oncologists and ophthalmologists need to collaborate for the early management of such cases. A proactive and multidisciplinary approach is crucial to prevent disease progression and minimize complications.

5. Statement of Ethics

Verbal & written consent was obtained to publish case details including the clinical photograph.

6. Conflicts of Interest

There are no conflicts of interest.

7. Disclosure Statement

The authors declare that they have no financial disclosures.

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