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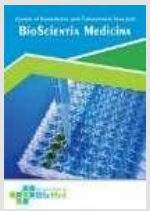

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Direct Closure Technique for Superior Palpebra Defect in Sebaceous Gland Carcinoma Palpebra

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A B S T R A C T

Background: Sebaceous Gland Carcinoma (SGC) palpebra is a malignancy tumor on the palpebra that originates from the sebaceous gland. These tumors can spread peripherally through intraepithelial or pagetoid growths. The main management is surgery, and the defect reconstruction is performed according to the size and area of the defect. **Case presentation:** A 53-year-old female patient came with a mass on the upper eyelid of the right eye for 1 year, which progressively grew in size and stuck to the eyelid, with no bleeding and no pain. The history of treatment has not provided an adequate response for the last 1 year. Visual acuity was 6/12 in both eyes, and a mass was found approximately 8x8 mm in size, nodular, fixed, and accompanied by madarosis. The histopathological examination showed a palpebral sebaceous gland carcinoma. There was no enlargement of submandibular or parotid lymph nodes. The patient underwent a wide excision of the upper eyelid lesion. Then, the defect was reconstructed by direct closure technique. The patient has been controlled 4 weeks of follow-up. The functional and cosmetic outcomes were satisfied. **Conclusion:** After a month of follow-up, no recurrence occurred. Reconstruction with direct closure technique has good results in terms of anatomy, function, and cosmetics.

1. Introduction

The eyelid or palpebra is a complex structure in the body that plays a crucial role in protecting the integrity of the eyeball and the tear film through its dynamic movements. Dysfunction of the eyelid can lead to disturbances in visual acuity, discomfort, and even blindness. Eyelid abnormalities can result from trauma, tumors, and congenital disorders. The most common malignant tumors affecting the eyelid include basal cell carcinoma, squamous cell carcinoma, sebaceous gland carcinoma, and malignant melanoma. Malignant eyelid tumors fall within the category of adnexal eye tumors and can affect various structures in both the upper and lower eyelids. They can be distinguished through histopathological examination.[1-3]

Eyelid malignancies account for 5-10% of all skin malignancies, with an incidence of 15 cases per 100,000 population per year. Sebaceous gland carcinoma is one form of malignancy of the eyelid that originates from the sebaceous glands. Sebaceous gland carcinoma accounts for 1-5.5% of all eyelid malignancies. The incidence is higher in Asian populations compared to Western populations. It is more common in women than in men, with a ratio of 2:1. The incidence increases above the age of 50, peaking in the 60-69 age group. Sebaceous gland carcinoma is characterized by a progressive nature, significant recurrence rates, and relatively high mortality.[2,3]

Sebaceous gland carcinoma most commonly arises from the meibomian glands located within the tarsal layer. This highly aggressive tumor can also originate from the sebaceous glands found in eyelashes, the caruncle, and eyebrow hairs. The tumor growth resembles a chalazion, and its contents, which

resemble those of a chalazion, should always be histologically examined when recurrent. Fat staining should be performed on tissue if sebaceous gland carcinoma is suspected. This tumor can be multifocal and may spread peripherally through intraepithelial or pagetoid growth. Metastases and spread to the orbital cavity often occur.[1,2]

2. Case Presentation

A 54-year-old woman presented with a complaint of a lump on her upper right eyelid that had been present for approximately 1 year. The lump on the upper right eyelid has progressively increased in size, particularly over the past 6 months. Initially, it was a small lump, about the size of a soybean, but it rapidly grew larger. The lump initially caused itching, and the patient frequently scratched it. It appeared reddish, uneven, without eye discharge, non-tender, and did not easily bleed. The lump was uncomfortable and felt like an obstruction on the eyelid. There was no redness in the eye and no secretions. The patient had a biopsy performed 4 months ago with the result of Anatomic Pathology is sebaceous gland carcinoma. Surgical plans were made, but the patient didn't follow up due to the pandemic. She had medical attention several times at local health centers, where it was initially diagnosed as inflammation, and she was given antibiotic ointment, but there was no improvement. She was then referred to hospital.

Over the last four months, the patient had been using herbal remedies for the lump, but there was no change. There were no complaints of lumps in other parts of the body. The patient had no history of diabetes mellitus, had a 5-year history of hypertension, and was taking Amlodipine. She was a non-smoker, but her husband frequently smoked indoors and while working in the fields. She had no history of wearing glasses, no history of trauma, and no history of eye surgery. No family members had similar complaints. The patient worked as a farmer and was often exposed to outdoor sunlight.

The physical examination of the patient showed a blood pressure of 140/90 mmHg, a heart rate of 84 times/minute, a respiratory rate of 20 times/minute, temperature of 36,5°C. Results of an ophthalmological examination of both eyes showed visual acuity at 20/40. There were no abnormalities in the cornea, anterior segment, iris, pupil, or lens. A mass was observed on the upper eyelid of the right eye, measuring 8x8x3 mm. It was solitary, located 5 mm from the superior punctum, with an uneven surface, firm in texture, not easily prone to bleeding, no pus, fixed to the superior margin, and non-paintful. Fundoscopic examination results of both eyes showed clear media, rounded papillae with firm boundaries, blood vessels aa:vv = 2:3, retina: bleeding (-), exudate (-), with Rf fovea (+), IOP: 14 mmHg.

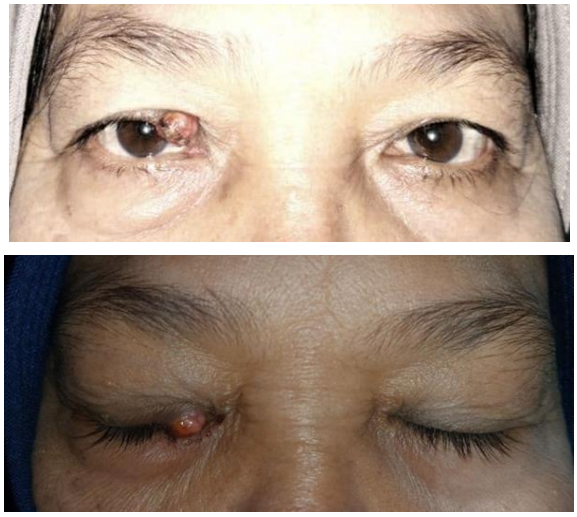


Figure 1. The clinical appearance of the patient shows a mass on the upper right eyelid.

The patient was diagnosed with sebaceous gland carcinoma of the right upper eyelid and planned for a wide excision surgery with a direct closure technique under general anesthesia.

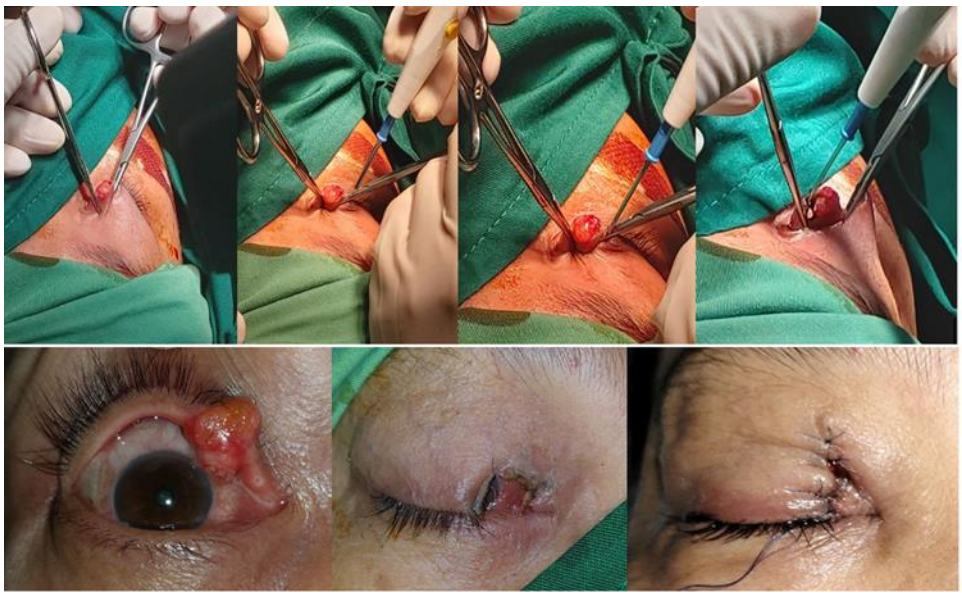
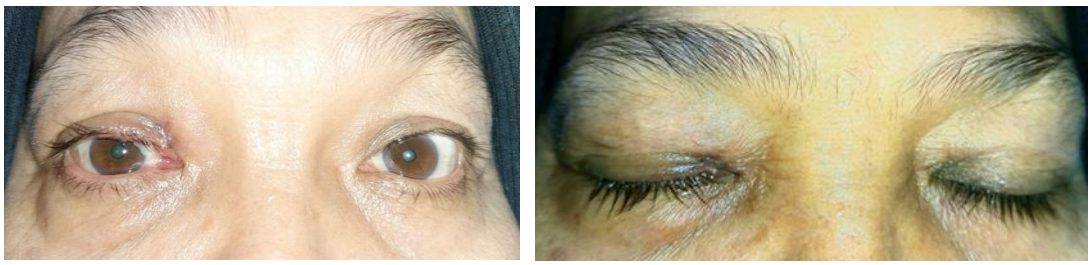


Figure 2. Direct closure technique.

After 1 month of follow up, the patient has not reported any additional complaints, and there is no recurrence detected. Reconstruction with direct closure technique has good results in terms of anatomy, function and cosmetics.

1-week post operation

1-week post operation



1 month follow up

Figure 3. The evaluation of the patient from the beginning to 1 month post-operation.

3. Discussion

A case of sebaceous gland carcinoma (SGC) has been reported in the right ocular (OD) region, which was treated with a wide excision procedure followed by upper eyelid (OD) reconstruction through direct closure. SGC is a malignancy originating from the sebaceous glands and is commonly found in the head and periocular areas. It falls into the category of adnexal tumors as it originates from the epidermal components and is the second most common eyelid tumor after basal cell carcinoma (BCC). This tumor is extremely rare and develops slowly, with an estimated incidence of about 1-6% of eyelid malignancies, more frequently found in Asians than Westerners. Women are more commonly affected by this tumor, with a ratio of 2:1. The incidence is highest in individuals over 50 years of age, peaking in the 60-69 age group.[4-6]

Diagnosing sebaceous gland carcinoma in this case was based on the patient's medical history, ophthalmological examination, and supporting tests. The patient, a 54-year-old woman, reported a history of a lump on the upper right eyelid that initially resembled a soybean but gradually grew in size and became uncomfortable. Initially, the patient thought it was just a common lump, itching, not painful, with a history of ineffective treatment for the past year. Clinically, this tumor is often challenging to diagnose in the early stages due to its variable presentation. Early clinical presentations can resemble benign lesions, often resembling a chalazion, blepharoconjunctivitis, or meibomianitis that does not respond completely to antibiotic therapy (Masquerade syndrome). Suspicion of sebaceous gland carcinoma should be considered for eyelid lesions that do not respond adequately to the given management, as experienced by the patient who had been seeking treatment for the past year and had even tried herbal remedies.[7-9]

The patient also has age-related risk factors, being over 50 years old, and is female, which aligns with the literature reference previously reported, where this condition is more commonly found in women and individuals over 50 years old. SGC predominantly affects the upper eyelid in 2/3 of cases, 20% in the lower eyelid, and 4-7% in the caruncle. The location of the tumor in the upper eyelid in this patient is consistent with a study conducted by Kaliki et al., which found that it occurs twice as often in the upper eyelid compared to the lower eyelid. The higher presence of meibomian and Zeis glands in the upper eyelid plays a significant role in why this tumor is more frequently found in that area.[6-8]

In the patient's ophthalmological examination, a mass was found on the upper right eyelid, measuring approximately 8x8x3 mm. It was nodular, firm, fixed, accompanied by madarosis (loss of eyelashes), and not associated with tenderness upon touch. This corresponds with the literature, where nodular SGC typically presents as a discrete, firm, immobile solitary nodule, often located on the tarsal plate with a yellowish appearance. The eyelid is a predilection site for this tumor, as the eyelid consists of meibomian glands on the tarsus, Zeis glands in the hair follicles near the eyelashes, sebaceous glands in the caruncle, hair follicles of the eyebrows, and facial skin. Sebaceous gland carcinoma is more frequently found on the skin of the eyelids compared to other parts of the body.[6,8,9]

The most common location on the eyelid is in the Meibomian glands, but it can also occur in the Zeis glands, sebaceous glands of the caruncle, and pilosebaceous glands of the eyelids and eyebrows. Lesions originating from the Zeis glands are typically small, yellowish nodules located on the edge of the eyelid just in front of the gray line or appear as diffuse or nodular thickening of the eyelid associated with eyelash loss. This is due to the neoplastic involvement of the eyelash follicles. Tumors originating from the sebaceous glands of the caruncle appear as masses located in the subconjunctival space, multilobular, grayish-yellow in color, and covered by intact epithelium. The etiology of sebaceous gland carcinoma (SGC) is not yet fully understood, but there are risk factors that play a role in the occurrence of SGC. These risk factors include advanced age, gender, Asian ethnicity, sunlight exposure, and immune system

disorders. Environmental and genetic factors also play a role. Risk factors in this patient include prolonged sunlight exposure due to working as a farmer, advanced age, and being female.[2,8,9]

Gradual genetic damage can explain the multifocal nature of sebaceous carcinoma and the stepwise progression from dysplasia to cancer over an extended period. Inactivation of Rb and p53 mutations, HIV, human papillomavirus infection, prior radiation therapy, and exposure to carcinogenic substances are possible risk factors. Two crucial factors that can be used to distinguish SGC from other adnexal tumors are, first, SGC originates from multifocal sites, and second, unlike basal cell carcinoma (BCC), which spreads radially, SGC spreads superficially, a characteristic known as pagetoid spread. One of the typical features of sebaceous gland carcinoma variants is pagetoid invasion, which is intraepithelial infiltration of the conjunctiva or the epidermal layer of the eyelid. The lesions also do not appear destructive, unlike the presentation of BCC (basal cell carcinoma) and SCC (squamous cell carcinoma). In BCC, the lesion appears as irregular lesion edges, often as nodules, sometimes with ulcers at the center, and it is locally destructive. In SCC, there are irregular lesion edges, ulcers, and hyperkeratosis. A comprehensive ophthalmological examination of the eyelid and ocular surface is important to identify pagetoid invasion and multicentric tumor lesions.[8-10]

A common clinical presentation of several sebaceous gland carcinomas that may go unnoticed when examining patients includes persistent unilateral conjunctivitis, blepharitis, meibomitis, or blepharoconjunctivitis. This presentation is due to the tendency of sebaceous gland carcinoma cells to invade the overlying epithelium, forming single-cell nests or multiple cells (pagetoid invasion), complete replacement of the entire epithelial thickness (intraepithelial carcinoma), or as cells with small nests that typically lack intracellular bridges and often compress adjacent epithelial cells. Pagetoid cells exhibit hyperchromic nuclei and excessive vacuolated cytoplasm containing varying amounts of lipid.[8,10,11]

Sebaceous gland carcinoma can undergo direct spread into nearby structures (orbit, paranasal sinuses, intracranial cavity). Tumors that invade the orbit have a poor diagnosis. Moderate to poorly differentiated tumors with infiltrative features are often associated with perineural infiltration and invasion into the lymphatic lumens, leading to metastasis to preauricular and cervical lymph nodes. Direct orbital invasion occurs in 19% of cases, and metastasis to preauricular and cervical lymph nodes or both in 23% of cases. Lymph node evaluation is necessary to assess the presence of metastasis. Upon physical examination, this patient did not exhibit lymph node enlargement or lymphatic nodules, which is supported by radiological findings that do not show pulmonary metastases.[10-12]

A definitive diagnosis of a tumor case requires a pathological tissue examination. Microscopic histopathological examination is the gold standard in diagnosing and confirming SGC. Most patients have well-differentiated tumors. The tumor cells are arranged in sheets or lobules with central necrosis. The cytoplasm appears pale frothy, and exhibits vacuolar features. The cell nuclei are hyperchromatic, and cell staining shows a positive result for specific lipid stains like the oil red O stain. Tumor excision, besides serving a histopathological diagnostic purpose, can also prevent recurrence. Histopathological diagnosis errors can occur but can be avoided with the assistance of specific staining such as oil red O stain and adipophlin.[10-12]

The histopathological diagnosis of sebaceous gland carcinoma can be categorized into histopathological classifications as well differentiated, moderately differentiated, and poorly differentiated. In well-differentiated tumors, the neoplastic cell appearance demonstrates sebaceous differentiation. These cells have abundant, finely vacuolated cytoplasm that typically appears soapy or hazy. Vacuoles often lead to nuclear membrane indentations. Nuclei are centrally located or slightly toward the periphery of the cell. Areas of sebaceous differentiation are often found in the center of the tumor lobules. Moderately

differentiated tumors exhibit only a few areas of highly differentiated sebaceous cells, with the majority consisting of neoplastic cells with prominent nuclei and excessive eosinophilic cytoplasm. In contrast, poorly differentiated tumors contain cells with pleomorphic nuclei, prominent mitotic activity, and scant cytoplasm, indicating a moderate increase in mitotic activity.[10,12,13]

In this patient, in accordance with the results of the Anatomic Pathology examination, a well-differentiated presentation was observed. The tissue exhibited a surface covered with stratified squamous epithelium. The dermal layer beneath contained proliferating cells with oval nuclei and clear, vacuolated cytoplasm, forming lobules separated by fibrovascular tissue septa. Hyperemic capillaries, necrotic foci, and clusters of necrotic cells were also visible. Sebaceous gland carcinoma presents in four histopathological patterns: lobular, comedocarcinoma, papillary, and mixed. The lobular pattern consists of well-defined lobules of varying sizes. Comedocarcinoma is characterized by prominent central lobules with pronounced necrosis, often comprising lipids. Papillary resembles papillae of neoplastic cells on the conjunctival surface. The mixed pattern indicates a combination of lobular with comedocarcinoma or a combination of papillary with lobular. In this patient, the histopathological pattern identified was lobular.[11-13]

The primary treatment option for sebaceous gland carcinoma (SGC) cases on the eyelid is surgery. The treatment aims to remove the malignant lesion to prevent local or systemic spread. Surgical options include wide excision of the tumor, radiotherapy, chemotherapy, orbital exenteration, or radical neck dissection. Wide excision is usually performed for tumor lesions localized on the eyelid, with the excision margins typically extending 3-4 mm beyond the tumor to ensure that the excision margins are free from the tumor. Wide excision with control often involves a frozen section or Mohs microsurgery, which is also used as an alternative to obtaining tumor-free excision margins. The use of Mohs microsurgery techniques has been reported to reduce recurrence rates in various cases.[14-16]

Orbital exenteration is usually recommended for cases with large or multifocal tumors with extensive and advanced spread involving diffuse and/or pagetoid orbital involvement. Radical neck dissection is performed in cases with lymph node spread and regional metastasis. The role of radiotherapy in SGC has been extensively studied, with varying results. Cryotherapy can be used as an adjuvant treatment. Neoadjuvant chemotherapy using carboplatin and 5-fluorouracil (5-FU) has been shown to reduce morbidity in patients with nodular metastasis. Recent studies on the expression of estrogen receptors, progesterone receptors, and androgen receptors show a potential role for hormonal therapy in SGC patients. Wide excision with excision margins extending about 3-4 mm beyond the tumor size was performed on the patient, considering the localized nature of the tumor lesion on the upper eyelid.[14-16]

Full-thickness defects on the eyelid following tumor excision require reconstruction to maintain the anatomical and physiological integrity of the eyelid. The primary considerations for eyelid reconstruction include forming a stable eyelid margin, achieving adequate eyelid closure, creating the anterior and posterior lamellae, and achieving good cosmetic outcomes. The posterior lamella, which includes the tarsal plate and palpebral conjunctiva, and the anterior lamella, consisting of skin, subcutaneous tissue, and the orbicularis oculi muscle, require sufficient blood supply.[16-18]

Full-thickness eyelid defects involving less than one-third of the entire eyelid can be reconstructed using the direct closure technique. Defects involving up to 50% of the eyelid margin can be reconstructed using direct closure with or without lateral canthotomy or superior cantholysis. Defects involving more than 50% of the eyelid margin can be reconstructed using a combination of flaps and grafts, as described in Figure 2. A relatively straightforward method for reconstructing full-thickness defects larger than 50% on the upper eyelid is by using a flap

consisting of the anterior and posterior lamellae taken from the lower eyelid, known as the Cutler-Beard flap.[2,17]

In this patient, surgical management was performed with wide excision of the tumor, resulting in a defect on the upper eyelid measuring less than 50%. Therefore, reconstruction of the upper eyelid can be achieved through direct closure. Reconstruction in patients with small defect sizes and closely located wound edges is done using minimal tissue removal to achieve a good reconstruction outcome with fewer complications. Direct closure is generally performed when the defect involves a margin < 33%. In elderly individuals with more laxity skin, it can be done when the defect involves a margin of up to < 40%. The technique involves closing the wound with two sutures: the inner side with Vicryl 6.0 and the skin with Prolene 6.0.[9,18,19]

Sebaceous gland carcinoma is one of the tumors associated with a relatively high recurrence and metastasis rate. In the absence of metastasis, reported mortality rates range from 0-15%. However, the presence of metastasis leads to a worse prognosis, with 5-year mortality rates reaching 50-67%. Research by Takahashi et al. and Kaliki et al. has reported several risk factors that play a role in the occurrence of recurrence and metastasis in sebaceous gland carcinoma, including involvement of the upper and lower eyelids, canthal involvement, multisentric tumor lesions, diffuse eyelid thickening, lesion size greater than 10 mm, perivascular, lymphovascular, and orbital invasion, poor differentiation, duration and duration of symptoms, infiltrative pattern, and the presence of pagetoid invasion of the skin or conjunctiva.[18-20]

Tumors originating from Zeis glands have a better prognosis. The mortality rate for SGC is around 5-10%, with metastasis reported in 6-29% of cases. Approximately 14-25% of patients show metastasis to lymph nodes and/or hematogenous spread to the liver, lungs, brain, and bones. SGC has a recurrence rate of up to 33% of all cases. According to the American Joint Committee on Cancer (AJCC), categories T2b or higher are associated with an increased rate of regional lymphatic metastasis, affecting up to 25% of all cases. Categories T3a or higher increase the risk of distant metastasis and death. In an AJCC study of 50 patients with SGC, 5 (10%) experienced mortality.[19-21]

The prognosis for this patient's case is quo ad vitam dubia ad bonam and quo ad functionam dubia ad bonam because the clinical presentation of the patient shows a lesion size of less than 10 mm, no involvement of the upper and lower eyelids, and no evidence of perivascular, lymphovascular, or orbital invasion, which are favorable prognostic factors. Other examination results did not reveal any evidence of metastasis to regional lymph nodes or other organs, as supported by the patient's X-ray results. As for quo ad sanactionam (doubtful to appropriate action) for the patient, it is because of the relatively high recurrence rate in SGC cases. Therefore, regular follow-up is necessary, especially to monitor for potential recurrence or metastasis, even though extensive excision has been performed. If risk factors contributing to recurrence or metastasis are identified, then consideration of post-surgical adjuvant therapy such as cryotherapy, systemic and topical chemotherapy, or radiation can be given, particularly in cases with pagetoid involvement.[18,20,21]

4. Conclusion

Sebaceous gland carcinoma is a malignancy originating from the sebaceous glands, which occurs more frequently in women, especially those above the age of 50, with a predilection for the upper eyelid, as observed in the patient. Clinical presentation in the early stages can resemble benign lesions. Suspicion of sebaceous gland carcinoma should be considered for eyelid lesions that do not respond adequately to the provided management. A comprehensive examination of the eyelid and ocular surface is crucial for identifying pagetoid invasion and spread to adjacent structures. Microscopic histopathological examination is the standard for diagnosing and confirming SGC, utilizing special staining techniques such as oil red O

stain. Extensive excision of the tumor lesion resulted in a full-thickness defect on the upper eyelid measuring less than 33%, and direct closure was performed considering the small defect size, close wound edges, minimal tissue removal, with fewer complications, and good results in terms of anatomy, functional and cosmetics.

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