

Eyelid metastasis from lung adenocarcinoma

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ABSTRACT

Purpose: To report an unusual case of lung metastasis presenting as an eyelid lesion.

Observations: An 82-year-old man presented with a right upper lid lesion of 2 weeks' duration proven to be adenocarcinoma of the lung.

Conclusions and importance: Metastasis to the eyelid is a rare occurrence. We present a review of the literature emphasizing factors contributing to its low incidence.

1. Introduction

We report a case of a secondary malignancy of the eyelid, briefly review the literature, and discuss the prognostic implications for the patient. Further, we suggest factors for the low incidence of metastases to the eyelid.

2. Case report

An 82-year-old White man presented with a 2-week history of a rapidly growing right upper eyelid mass (Fig. 1). One year prior, he was diagnosed with adenocarcinoma of the lung. He had ceased smoking cigarettes 28 years earlier.

Pertinent findings on his ocular examination were a 2.5- x 1.5-cm mass with surface keratinization and telangiectasia arising from the medial part of the upper eyelid and involving the superior punctum. Associated with the lesion were distortion and loss of eyelashes in addition to a reactive discharge. Best corrected visual acuity was 20/20 in right eye and 20/25 in his left eye. Intraocular pressure was normal in both eyes, and the function of the extraocular muscles was normal. Except for the presence of pseudophakia, the anterior and posterior segments were normal.

From the clinical examination of this lesion, the differential diagnosis included keratoacanthoma, pyogenic granuloma, foreign body granuloma, and malignancy (Video 1). Written informed consent was obtained from the patient and his family, and the lesion was resected.

The eyelid laxity permitted a 1-stage simple excisional biopsy with primary repair (Video 2).

Supplementary video related to this article can be found at <https://doi.org/10.1016/j.ajoc.2020.100991>.

Histopathology revealed a poorly differentiated carcinoma. The neoplasm appeared to bear a significant resemblance to the patient's previously diagnosed pulmonary carcinoma (Fig. 2 and Fig. 3).

Tumor cells expressed cytokeratin (CK) with pan CK, low-molecular-weight CK, and high-molecular-weight staining preparation. CK immunoperoxidase assays supported the diagnosis of carcinoma. Scattered tumor cells expressed CK 5 and 6 with a rare cell expressing CK 7 (Fig. 4). CK 20 was not expressed by the tumor. Both thyroid transcription factor 1 (TTF-1, also known as NK2 homeobox 1) and genetic marker p63 were expressed in scattered neoplastic nuclei (Fig. 5). The morphologic and immunophenotypic similarities between the eyelid lesion and the lung carcinoma, with the shared expression of TTF-1, indicated that the eyelid lesion was metastatic from the lung adenocarcinoma.

After a tumor board consultation and discussion with the patient and his family, three care options were offered: (1) reoperation with excision of the previous surgical margins with frozen section control for complete excision of the lesion; (2) local radiation therapy to prevent recurrence; or (3) close monitoring for recurrence. The patient chose the last option along with in-home hospice. He expired 3 months later.

Abbreviations: CK, Cytokeratin; TTF-1, Thyroid Transcription Factor 1.

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Fig. 1. Right upper eyelid mass at presentation.

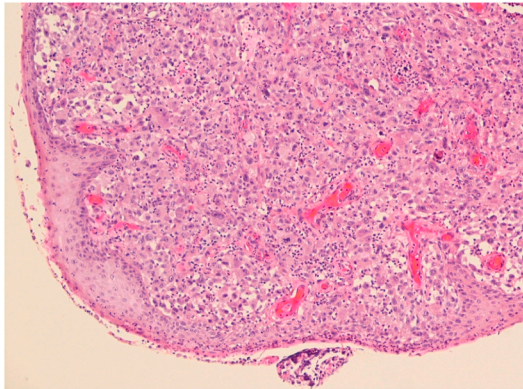


Fig. 2. Low-power hematoxylin and eosin stain demonstrates that the neoplasm does not involve the epithelium. There is no evidence of epithelial dysplasia (carcinoma in situ), suggesting that the eyelid is not the primary site.

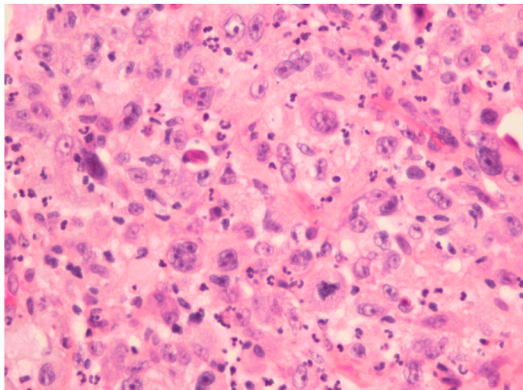


Fig. 3. High-power hematoxylin and eosin stain reveals wall-to-wall nuclear pleomorphism and abundant mitotic activity.

3. Discussion

Although neoplasms of the eyelid are common, metastatic disease of the eyelid is not. Large retrospective case series reviews from various sources have reported a similar incidence. A review study of 1502 eyelid lesions examined histopathologically found only one case (0.07%) to be the result of metastasis.¹ Another large series of 2023 eyelid malignant tumors identified three cases of metastasis with an incidence of 0.6%. When all biopsy specimens submitted were included, the incidence fell to 0.1%.² Riley reviewed 15 cases from the literature and added 15 cases collected from the tissue registry of Mayo Clinic from 1922 to 1969.³ Mansour and Hidayat⁴ reported 31 cases of eyelid metastasis and

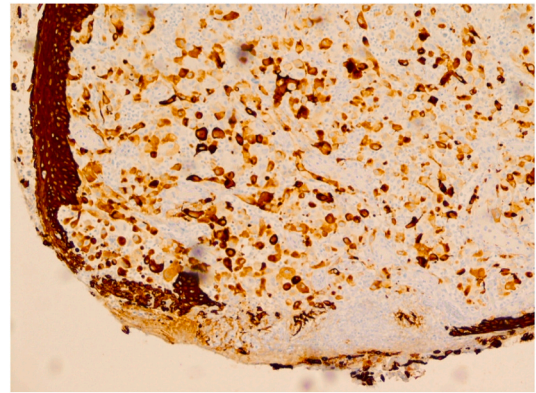


Fig. 4. High-molecular-weight cytokeratin stain.

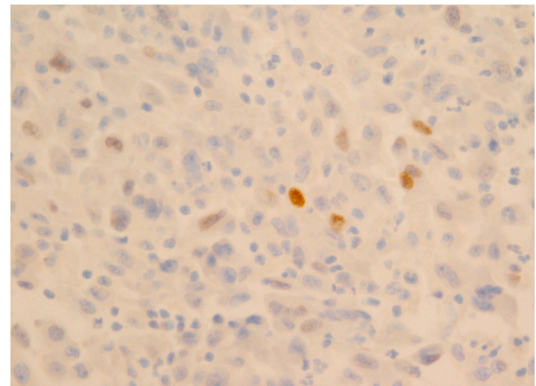


Fig. 5. Thyroid transcription factor-1 stain.

documented the frequency of the primary cancer site as follows: breast (n = 11; 35%), followed by the skin (n = 4; 13%), gastrointestinal tract (n = 3; 10%), genitourinary tract (n = 3; 10%), and uvea (n = 2; 6%). The high proportion of breast metastases has been attributed to the long survival times in these patients and explains the preponderance of women exhibiting metastatic eyelid disease.

Immunohistochemical stains provide guidance for the pathologist toward a tissue of origin for poorly differentiated or undifferentiated tumors. A panel of stains is typically employed to aid interpretation.

CKs are a heterogeneous group of intermediate-sized, water-soluble, filamentous, structural proteins in the cytosol of cells. CKs predominate in epithelial cells but are not exclusive to them. There are more than 25 subtypes of CKs, and they are characterized by their pH and molecular weight.

CK 5 and 6 are basic high-molecular-weight CKs supporting a carcinoma diagnosis when positive.⁵ The low-molecular-weight CK 7 and 20 differ in pH; CK 7 is basic and CK 20 is acidic. CK 7 is a good marker for lung and breast carcinomas, whereas CK 20 predominates in carcinomas of gastrointestinal and urogenital origin. TTF-1 is a primary marker in tissues of lung and thyroid origin.⁶ Immunoperoxidase stains provide additional help in the identification of ambiguously differentiated lung carcinomas.⁷

A small case series provided the scope of tissue types that have been reported to be the origin of metastasis to the eyelid. These include squamous cell carcinoma of the esophagus,² thyroid carcinoma,^{3,8} transitional cells of the bladder,² gastric adenocarcinoma,^{1,9,10} colon adenocarcinoma,¹¹ squamous cell carcinoma of the lung,¹² parotid carcinoma,^{13,14} and melanoma.^{3,15,16} The majority of cases occurred after the patient carried a known primary cancer diagnosis, with the metastatic site presenting months to decades after the discovery of the primary malignancy.

The clinical presentation in these cases varied considerably in appearance, location within the eyelid, and speed of growth. These included an innocuous lump under the eyelid skin, inflammatory nodules imitating chalazia with associated hemorrhagic epiphora, and a localized mass distorting the eyelid structures. All reported cases that we found were unilateral except for one. A report by Martorell-Calatayud et al. of two separate cases of different primary malignancies with bilateral, symmetric eyelid involvement demonstrates the diagnostic dilemma for the clinician who is confronted by such a rare situation. The bilateral eyelid periorbital swelling was easily confused with contact dermatitis or the multiple systemic conditions associated with periorbital and eyelid edema.¹⁷

This case prompted us to consider whether metastasis is rarer than the incidence of cutaneous metastasis in general. The eyelids compose approximately 1% of the total skin area when measured using the palm surface area technique.¹⁸ We postulate that because the incidence of cutaneous metastasis has been reported to be 5%, it can be inferred that eyelid metastasis should be expected to occur approximately 0.05% of the time.¹⁹ This correlates well with the findings of Arnold and colleagues.¹

Although eyelid metastasis is usually observed in patients with a known malignancy, as in our patient, eyelid lesions can also be the initial sign of a malignancy.²⁰ Mansour and Hidayat⁴ reported that in 45% of their cases, the eyelid metastasis preceded the discovery of the primary neoplasm (referred to as precocious metastasis).⁴ It is worth noting that the largest case series in the literature was reported well before the present era. This suggests that both the availability of a myriad of noninvasive imaging modalities and the more effective cancer therapies than were previously available have led to much earlier diagnosis of primary malignancies. We speculate that the end result has been to reduce the frequency of unusual metastatic events.

4. Conclusions

Although metastasis to the eyelid from a remote malignancy is uncommon, the incidence correlates well with the fractional share of the total dermis represented by the eyelids. Except for metastasis from the breast, metastatic disease to the eyelid from other sites tends to herald a poor prognosis and early demise.^{4,21} Clinicians should be aware that malignant disease may present in the form of a common, nonmalignant lesion. A careful medical history may increase the probability of detecting such an uncommon presentation and lead to an earlier investigation and diagnosis. Immunohistochemistry and genetic testing for tumor markers are the mainstay of primary site determination. Excision with or without radiation for local control of disease or the use of comfort measures has a role in patient care that is dependent on disease burden, prognosis, and patient acceptance.

Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

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Authorship

All authors attest that they meet the current ICMJE criteria for

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Prior submission of content

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Declaration of competing interest

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References

1. Arnold AC, Bullock JD, Foos RY. Metastatic eyelid carcinoma. *Ophthalmology*. 1985; 92(1):114–119.
2. Weiner JM, Henderson PN, Roche J. Metastatic eyelid carcinoma. *Am J Ophthalmol*. 1986;101(2):252–254.
3. Riley FC. Metastatic tumor of the eyelids. *Am J Ophthalmol*. 1970;69(2):259–264.
4. Mansour AM, Hidayat AA. Metastatic eyelid disease. *Ophthalmology*. 1987;94(6): 667–670.
5. Peigu GC, Weiss LM. Expression of cytokeratin 5/6 in epithelial neoplasms: an immunohistochemical study of 509 cases. *Mod Pathol*. 2002;15(1):6–10.
6. Krishna M. Diagnosis of metastatic neoplasms: an immunohistochemical approach. *Arch Pathol Lab Med*. 2010;134(2):207–215.
7. Zhou F, Moreira AL. Lung carcinoma predictive biomarker testing by immunoperoxidase stains in cytology and small biopsy specimens: advantages and limitations. *Arch Pathol Lab Med*. 2016;140(12):1331–1337.
8. Bianciotto CG, Demirci HY, Shields CL, Shields JA. Simultaneous eyelid and choroidal metastases 36 years after diagnosis of medullary thyroid carcinoma. *Ophthalmic Plast Reconstr Surg*. 2008;24(1):62–63.
9. Kuchle M, Holbach L, Schlötzer-Schrehardt U. Gastric adenocarcinoma presenting as an eyelid and conjunctival mass. *Eur J Ophthalmol*. 1992;2(1):3–9.
10. Rodríguez-García C, González-Hernández S, Pérez-Robayna N, Martín-Herrera A, Sánchez R, Guimera F. Eyelid metastasis as an initial presentation of a gastric carcinoma. *J Am Acad Dermatol*. 2010;63(2):e49–50.
11. Ostriker PJ. Metastasis of adenocarcinoma of the colon to the conjunctival surface of the lid. *AMA Arch Ophthalmol*. 1957;57(2):279–281.
12. Ahamed R, Ram R, Shannon J, Winter RK. Eyelid metastasis from lung carcinoma. *Clin Exp Ophthalmol*. 2006;34(6):509–610.
13. Wright JC, Meger GE. Metastatic bronchogenic carcinoma of the eyelid. *Am J Ophthalmol*. 1962;54:135–137.
14. Miyazaki S, Shiraki K, Umetani Y, Kumoi T. Unusual case of metastatic carcinoma of the eyelid. *Jpn J Ophthalmol*. 1982;26(3):302–307.
15. Rosenberg C, Finger PT. Cutaneous malignant melanoma metastatic to the eye, lids, and orbit. *Surv Ophthalmol*. 2008;53(3):187–202.
16. Ramirez R, Ivan D, Prieto VG, et al. Cutaneous melanoma metastatic to the eyelid and periocular skin. *Ophthalmic Plast Reconstr Surg*. 2010;26(2):88–94.
17. Martorell-Calatayud A, Requena C, Díaz-Recuero JL, et al. Mask-like metastasis: report of 2 cases of 4 eyelid metastasis and review of the literature. *Am J Dermatopathol*. 2010;32(1):9–14.
18. Rhodes J, Clay C, Phillips M. The surface area of the hand and the palm for estimating percentage of total body surface area: results of meta-analysis. *Br J Dermatol*. 2013;169(1):76–84.
19. Lookingbill DP, Spangler N, Sexton FM. Skin involvement as a presenting sign of internal carcinoma: a Retrospective study of 7316 cancer patients. *J Am Acad Dermatol*. 1990;22(1):19–26.
20. Lyndon WM, John VL, Richard LA. Metastatic disease first presenting as eyelid tumors: a report of two cases and review of literature. *Ann Ophthalmol*. 1987;19(1): 13–18.
21. Brady LW, O'Neill EA, Farber SH. Unusual sites of metastases. *Semin Oncol*. 1977;4 (1):59–64.