Title
CK7 negative anaplastic thyroid carcinoma presenting as cutaneous metastases to the scalp

Journal
Dermatology Online Journal, 24(11)

Authors
McKenzie, Grant W
Callen, Jeffrey P
Haeberle, M Tye

Publication Date
2018

DOI
10.5070/D32411042006

CK7 negative anaplastic thyroid carcinoma presenting as cutaneous metastases to the scalp

Grant W McKenzie[1] BS, Jeffrey P Callen[2] MD, M Tye Haeberle[2] MD

Affiliations: [1]School of Medicine, University of Louisville, Louisville, Kentucky, USA, [2]Division of Dermatology, University of Louisville, Louisville, Kentucky, USA

Corresponding Author: M. Tye Haeberle, University of Louisville School of Medicine, Division of Dermatology, 3810 Springhurst Boulevard, Suite. 200, Louisville, KY 40241, Tel: 502-583-1749, Email: tye.haeberle.derm@gmail.com

Abstract

Anaplastic thyroid carcinoma (ATC) is an extremely rare but aggressive form of thyroid cancer. Although local tissue invasion is characteristic of this disease, systemic metastases are a common clinical finding. Our case discusses an unusual presentation of cutaneous metastases to the scalp in a patient with a remote history of ATC. It also highlights the utility of immunohistochemical staining in determining the origin of a tumor when the source of primary malignancy is not readily identifiable.

Keywords: Anaplastic thyroid carcinoma, metastasis, scalp, skin, immunohistochemistry

Introduction

Anaplastic thyroid carcinoma (ATC) is one of the rarest tumors of the thyroid gland, representing only 1.7% of recognized thyroid cancers, with patients typically presenting in their sixth or seventh decade of life [1]. Anaplastic thyroid carcinoma carries a dismal prognosis, with a median survival of 4 to 12 months after diagnosis [2]. Although a multi-modal therapeutic approach incorporating surgery, radiation, and chemotherapy is the current standard of care for this disease, therapies are aimed more toward palliation than a curative intent [3]. This case report describes ATC presenting as multiple cutaneous metastases to the scalp, discusses other dermatologic conditions considered within both the clinical and histological differential diagnosis, and demonstrates how immunohistochemical staining can be used for determining the origins of an undifferentiated neoplasm.

Case Synopsis

A man in his 50's with an unknown past medical history presented to clinic with multiple nodules on his scalp for several months. He described the lesions as pruritic, irritated, and non-healing. The patient reported vague flu-like symptoms, including body-wide aches. He was not talkative on examination and denied any history of major illness. Outside medical records were not readily accessible. Clinical examination revealed several erythematous,

Figure 1. *One of several erythematous scalp nodules.*

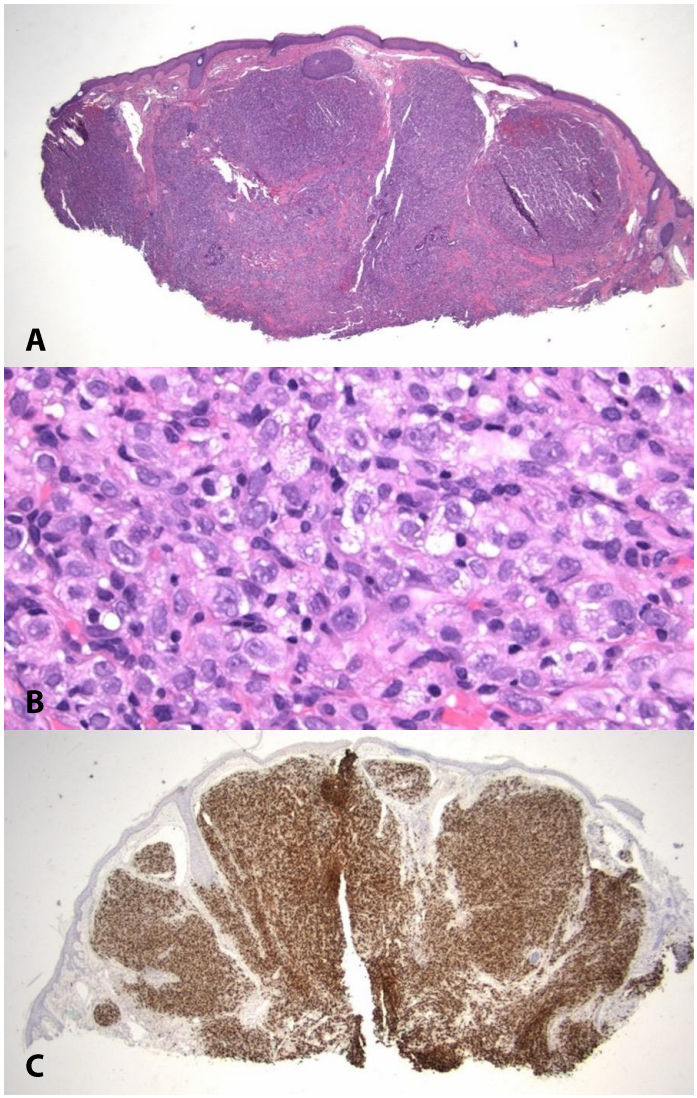

Figure 2. *Shave biopsy specimen, H&E. A, 4×; B, 400×. C) TTF-1 immunohistochemistry, 4×.*

violaceous nodules scattered bilaterally across his scalp (**Figure 1**). A shave biopsy was performed on one of the lesions for further histopathologic analysis.

Histologic evaluation revealed a dermal based nodule with sparing of the overlying epidermis. Hematoxylin-eosin staining showed cells of moderate atypia with pleomorphism. Mitoses were not abundant. A mild lymphocytic infiltrate was present (**Figure 2A, B**). Immunohistochemical analysis showed pan-cytokeratin (CKAE1/3) positivity as well CK7 and CK20 negativity. CK5/6, SOX-10 and CD30 were also negative. CD45 highlighted the lymphocytic infiltrate but not the cells of interest. Further immunohistochemical stains PAX-8, TTF-1, and PSA were ordered to evaluate for a $CK7^-/CK20^-$ tumor of the skin concerning for metastatic disease, which revealed both TTF-1 and PAX-8 positivity (**Figure 2C**).

In the interim, a primary relative of the patient phoned the office to report that the patient had recently been admitted to the hospital and found to have disseminated metastatic disease. They also communicated that he had a history of an unknown type of thyroid cancer. Outside medical records were obtained and reviewed, showing that the patient had been treated with a thyroidectomy and adjuvant radioactive iodine the year prior for anaplastic thyroid carcinoma. The patient was later admitted to a local hospital with widespread disease, including central nervous system metastases with secondary hemorrhage. The patient declined further therapy and was released to hospice care. He passed away 1 month after presentation to clinic.

Case Discussion

Metastatic disease must be considered within the differential in a patient presenting with multiple new onset scalp nodules, especially in light of a history of malignancy as our patient later was found to have. Although local invasion of central neck structures is a hallmark of ATC, systemic metastases are estimated to be found in 50% of patients at initial presentation, with lungs, bone, and brain as common sites [4]. Reviews of cutaneous presentation of metastatic disease have revealed metastases of thyroid carcinoma tend to occur on the scalp and head [5]. Overall, the scalp is an uncommon site for cutaneous metastases, shown to account for only 7% of all skin metastases [6]. With the absence of a reliable past medical history in a patient with suspected cutaneous metastases, histologic and immunohistochemical assessment is crucial in delineating the tumor of origin when the source of primary malignancy is not readily identifiable [7].

This case has several unusual findings histopathologically. Thyroid carcinomas typically will have a $CK7^+/CK20^-$, $TTF\text{-}1^+$, $PAX\text{-}8^+$ immunohistochemical profile [7, 8]. Our patient's disease was $CK7^-$, which has been reported to occur in 16% of

anaplastic thyroid carcinomas [9]. This is, to our knowledge, the first report of a CK7$^-$ ATC metastasizing to the scalp. Furthermore, in contrast to differentiated thyroid cancers, anaplastic carcinoma is less likely to stain positive for TTF-1. Our patient's disease was TTF-1$^+$, shown in one review to comprise only 13.7% of anaplastic thyroid carcinomas [10].

With the ability to mimic clinically a variety of benign and malignant entities, a high index of suspicion is required in order to accurately diagnose metastatic disease to the scalp. Cutaneous metastases may present as either solitary or multiple skin lesions, thus lending to a broad clinical differential diagnosis [11]. Pilar cysts are keratin-filled, epithelial-lined cysts arising from the outer root sheath of hair follicles. These cysts often present as multiple mobile, well-circumscribed nodules with a predilection for the scalp. However, the rapid lesion growth as seen in our patient would be an atypical finding [12]. Epidermoid cysts may present similarly as mobile dermal nodules on the scalp, but these lesions are most often skin-colored, yellow, or white with a central punctum [12]. Cutaneous metastases may easily be mistaken for vascular tumors. For men in particular, both renal cell carcinoma and lung cancer have a disproportionate propensity to metastasize to the scalp, with breast carcinoma being the most common in women [13]. The rapid growth of this patient's lesions could suggest a lobular capillary hemangioma (pyogenic granuloma). Generally, these vascular tumors are solitary and have a history of bleeding, unlike the presentation in our patient [14]. Lastly, the erythematous and violaceous nature of our patient's lesions coupled with the inability to rule out an immunocompromised state made both bacillary angiomatosis and Kaposi sarcoma possibilities.

Histologically, thyroid carcinoma metastatic to the skin may have overlapping features with primary cutaneous neoplasms with similar histopathological characteristics [15]. Diagnoses considered within the histological differential included sebaceous carcinoma, xanthogranuloma, and lymphomatoid papulosis. Sebaceous carcinoma is a malignant tumor of sebaceous glands that presents as a painless mass, in some instances multifocal, with predilections for the head, neck, and in particular the periorbital region. However, sebaceous carcinoma typically stains positive for CK7 [16]. Xanthogranulomas are benign, asymptomatic nodules composed of histiocytic cells that occur most frequently during infancy and childhood. Histology is characterized by macrophages and foamy cells. These lesions would not be CKAE1/3 positive [16]. Lymphomatoid papulosis is a recurrent lymphoproliferative disease with self-regressing papulo-nodular skin lesions characterized on histology by a diffuse, sheet-like CD30$^+$ lymphoid proliferation, which was not seen in this patient [16].

Conclusion

In summation, cutaneous metastases may be the first systemic sign of malignancy, or as in this patient, an ominous sign of tumor recurrence and progression. This case highlights the need for gathering a comprehensive patient history and thorough medical record searching whenever a malignant process is considered within the differential diagnosis. In the absence of such, the judicious application of specialized testing, such as immunohistochemistry, can provide invaluable information about the origins of otherwise undifferentiated neoplasms and help guide therapeutic approaches.

References

1. Hundahl SA, Fleming ID, Fremgen AM, Menck HR. A National Cancer Data Base report on 53,856 cases of thyroid carcinoma treated in the US, 1985-1995. *Cancer.* 1998;83(12):2638-48
2. Are C, Shaha AR. Anaplastic thyroid carcinoma: biology, pathogenesis, prognostic factors, and treatment approaches. *Ann Surg Oncol.* 2006;13(4):453-64. [PMID: 16474910].
3. Xia Q, Wang W, Xu J, Chen X, Zhong Z, Sun C. Evidence from an updated meta-analysis of the prognostic impacts of postoperative radiotherapy and chemotherapy in patients with anaplastic thyroid carcinoma. *Onco Targets Ther.* 2018;11:2251. [PMID: 29719407].
4. Nagaiah G, Hossain A, Mooney CJ, Parmentier J, Remick SC. Anaplastic thyroid cancer: a review of epidemiology,

pathogenesis, and treatment. *J Oncol*. 2011;2011:542358. [PMID: 21772843].

5. Nashan D, Meiss F, Braun-Falco M, Reichenberger S. Cutaneous metastases from internal malignancies. *Dermatol Ther*. 2010;23(6):567-80. [PMID: 21054703].
6. Krathen RA, Orengo IF, Rosen T. Cutaneous metastasis: a meta-analysis of data. *South Med J*. 2003;96(2):164-8. [PMID: 12630642].
7. Lin F, Liu H. Immunohistochemistry in undifferentiated neoplasm/tumor of uncertain origin. *Arch Pathol Lab Med*. 2014;138(12):1583-610. [PMID: 25427040].
8. Bejarano PA, Nikiforov YE, Swenson ES, Biddinger PW. Thyroid transcription factor-1, thyroglobulin, cytokeratin 7, and cytokeratin 20 in thyroid neoplasms. *Appl Immunohistochem Mol Morphol*. 2000;8(3):189-94. [PMID: 10981870].
9. Lam K, Lui M, Lo C. Cytokeratin expression profiles in thyroid carcinomas. *Eur J Surg Oncol*. (EJSO). 2001;27(7):631-5. [PMID: 11669590].
10. Ordóñez NG. Value of thyroid transcription factor-1 immunostaining in tumor diagnosis: a review and update. *Appl Immunohistochem Mol Morphol*. 2012;20(5):429-44. [PMID: 22531688].
11. Hu SC, Chen GS, Lu YW, Wu CS, Lan CC. Cutaneous metastases from different internal malignancies: a clinical and prognostic appraisal. J Eur Acad Dermatol Venereol. 2008;22(6):735-40. [PMID: 18312322].
12. Thomas VD, Snavely NR, Lee KK, Swanson NA. Chapter 118. Benign Epithelial Tumors, Hamartomas, and Hyperplasias. In: Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, Wolff K, editors. Fitzpatrick's Dermatology in General Medicine, 8e. New York, NY: The McGraw-Hill Companies; 2012.
13. Lookingbill DP, Spangler N, Helm KF. Cutaneous metastases in patients with metastatic carcinoma: a retrospective study of 4020 patients. *J Am Acad Dermatol*. 1993;29(2 Pt 1):228-36. [PMID: 8335743].
14. Mathes EF, Frieden IJ. Chapter 126. Vascular Tumors. In: Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, Wolff K, editors. Fitzpatrick's Dermatology in General Medicine, 8e. New York, NY: The McGraw-Hill Companies; 2012.
15. Dahl PR, Brodland DG, Goellner JR, Hay ID. Thyroid carcinoma metastatic to the skin: a cutaneous manifestation of a widely disseminated malignancy. *J Am Acad Dermatol*. 1997;36(4):531-7. [PMID: 9092737].
16. LeBoit PE, Burg G, Weedon D, Sarasin A. Pathology and genetics of skin tumours: WHO Classification of Tumours. 3rd ed. IARC press; 2006.