

# UC Davis

## Dermatology Online Journal

### Title

Metastatic renal clear cell carcinoma masquerading as a pyogenic granuloma on the lip

### Permalink

<https://escholarship.org/uc/item/6394q7wg>

### Journal

Dermatology Online Journal, 27(11)

### Authors

Williams, Josiah  
Depcik-Smith, Natalie  
Williams, Todd  
et al.

### Publication Date

2021

### DOI

10.5070/D3271156090

### Copyright Information

Copyright 2021 by the author(s). This work is made available under the terms of a Creative Commons Attribution-NonCommercial-NoDerivatives License, available at <https://creativecommons.org/licenses/by-nc-nd/4.0/>

Peer reviewed

# Metastatic renal clear cell carcinoma masquerading as a pyogenic granuloma on the lip

Josiah Williams<sup>1</sup> BS, Natalie Depcik-Smith<sup>2</sup> MD, Todd Williams<sup>3</sup> MD, Steven R Feldman<sup>1,4,6</sup> MD PhD

Affiliations: <sup>1</sup>Center for Dermatology Research, Department of Dermatology, Wake Forest School of Medicine, Winston-Salem, North Carolina, USA, <sup>2</sup>Aurora diagnostics, Greensboro, North Carolina, <sup>3</sup>Dermatology and Skin Surgery Center, Asheboro, North Carolina, USA <sup>4</sup>Department of Pathology, Wake Forest School of Medicine, Winston-Salem, North Carolina, USA, <sup>5</sup>Department of Social Sciences & Health Policy, Wake Forest School of Medicine, Winston-Salem, North Carolina, USA, <sup>6</sup>Department of Dermatology, University of Southern Denmark, Odense, Denmark

Corresponding Author: Steven R Feldman MD PhD, Wake Forest School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157, Tel: 336-716-7740, Fax: 336-716-7732, Email: [sfeldman@wakehealth.edu](mailto:sfeldman@wakehealth.edu)

## Abstract

Metastases to the face are rare. We report on a patient with a history of renal cell carcinoma who presented with a 1.2cm violaceous papule on his lower lip. Although clinically thought to be a pyogenic granuloma, biopsy revealed metastatic renal cell carcinoma recurring after 7 years of latency.

*Keywords: medical dermatology, metastasis, oncology, renal cell carcinoma*

## Introduction

Skin metastases in general occur in up to 10% of cancer patients, but facial metastases occur in less than 0.5% of patients with metastatic cancer [1,2]. Renal carcinomas involve cutaneous metastases in approximately 8% of cases [1]. Herein, we describe renal clear cell carcinoma metastasizing to the lower lip.

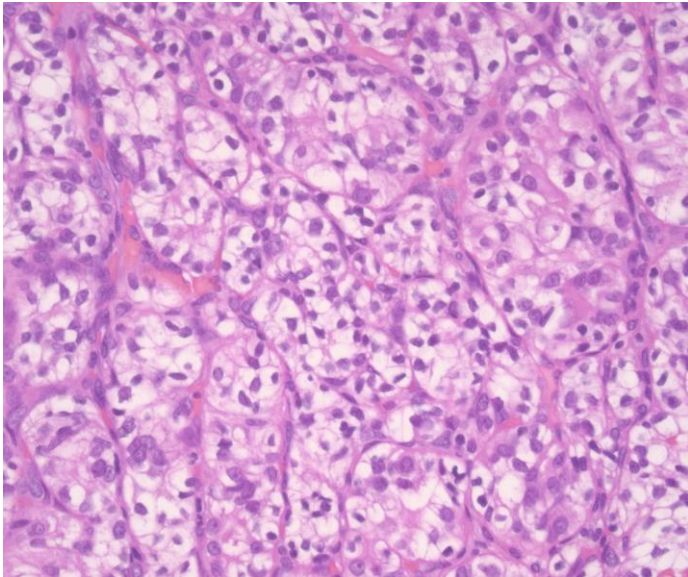
## Case Synopsis

A 59-year-old man was referred to our dermatology clinic by his primary care provider for a lesion on his lower lip. The nodule had been present for one month and was growing. It was painless but irritating to the patient because it protruded from his lip. On examination, he exhibited a 1.2cm protruding, violaceous nodule located centrally on the lower lip

and crossing the vermilion border. There was a small area of overlying crust distally, and the lesion bled easily on manipulation (**Figure 1**). Clinically this lesion was thought to be a pyogenic granuloma, with a differential diagnosis that included squamous cell carcinoma and metastatic disease. The nodule was removed by shave biopsy and sent to pathology. The biopsy results were consistent with metastatic renal clear cell carcinoma (RCCC), showing a background of arborizing thin-walled vessels and positivity for



**Figure 1.** Lower lip nodule at time of referral. A 1.2cm protruding, violaceous nodule that bled with manipulation located on the patient's lower lip, crossing the vermilion border.



**Figure 2.** H&E of original biopsy at 40x magnification. Microscopy demonstrates dermal proliferation and sheets of cells with clear cytoplasm and distinct membrane admixed in a background of arborizing small thin-walled vessels.

CK7, PAX-8, CD10, vimentin, and cytokeratin AE1/AE3 (**Figures 2, 3**). The patient was promptly referred to the department of urology for further evaluation and treatment. Unfortunately, he has persistently avoided follow-up at the time of writing this report and has not yet obtained a staging CT scan.

Additional history from the patient was pertinent for kidney surgery many years ago for “cancer” without any known sequelae thereafter. According to medical records uncovered after his presentation, he underwent right-sided radical nephrectomy over 7 years prior for Stage II RCCC. A CT scan performed 8 months after his surgery showed no evidence of metastatic spread, but afterwards he was lost to follow up. His risk factors for urologic malignancy included cigarette use (1 pack-per-day for 20-30 years prior to diagnosis of his cancer, at which point he stopped smoking) and exposure to agricultural chemicals for two years at a previous job. He was overweight (Body Mass Index 29.5) but had no history of diabetes or hypertension and no family history of cancer.

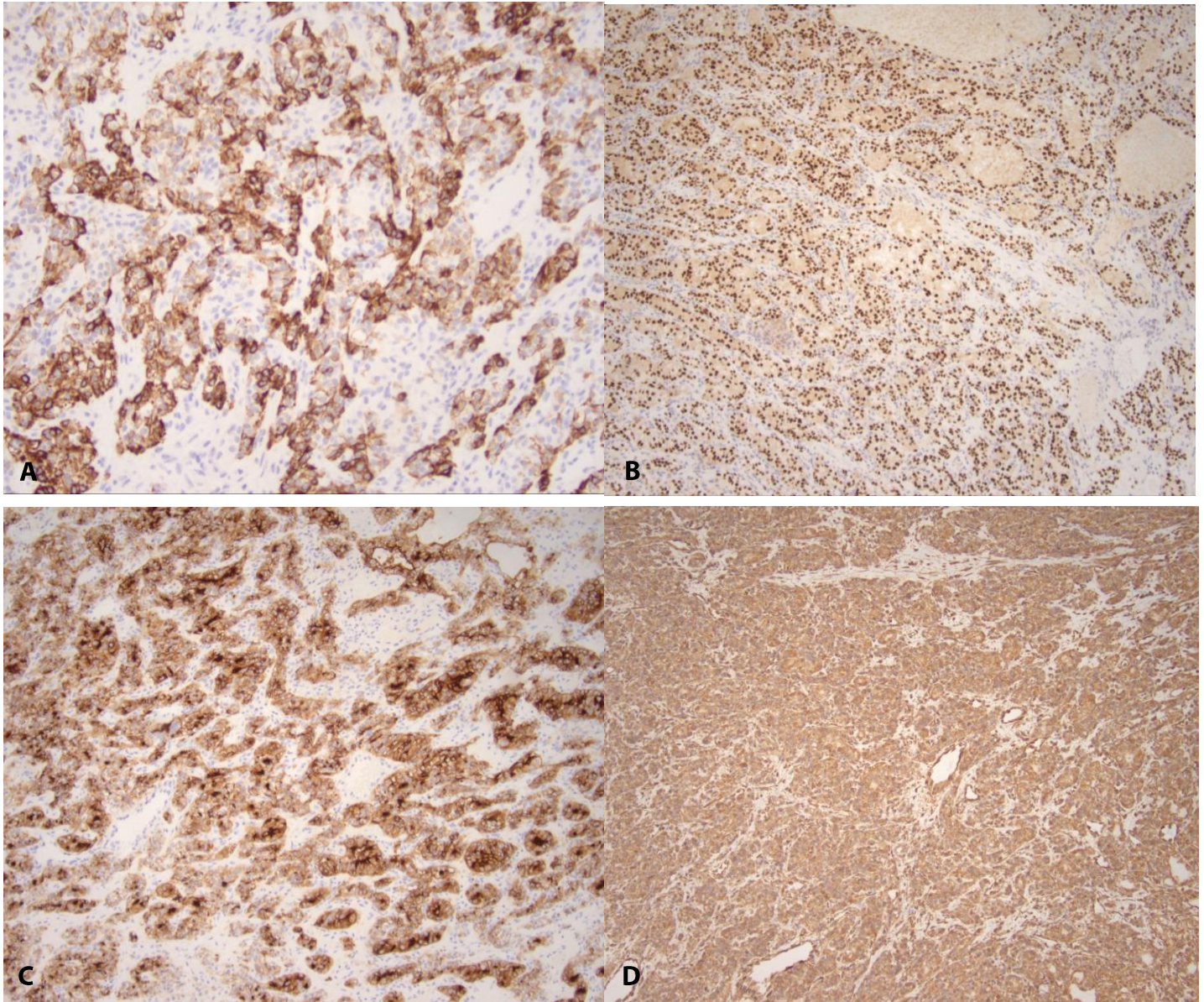
## Case Discussion

Renal clear cell carcinoma is the most common subtype of renal cell carcinoma, constituting 80 to 90

percent of all renal cell carcinomas and about 70 to 80 percent of all kidney cancers [3]. The 10-year survival range for RCCC is 71% [3]. The survival in cases of distant metastasis is less favorable and varies based on multiple prognostic factors [4]. Overall, metastatic renal cell carcinoma has an average 5-year survival of about 12% [5]. The most common locations of metastasis for RCCC are the lungs, bone, brain, liver, lymph nodes, and adrenal glands. [3] Renal clear cell carcinoma can metastasize to the skin in about 8% of cases but typically occurs on the extremities, prior surgical sites, or the scalp [1,6].

The route of metastasis in this case is likely hematogenous, which is a common mechanism for RCCC. [3] Angiogenesis is a key feature of cancers that successfully metastasize and RCCC is naturally pro-angiogenic since the majority of cases involve a dysfunction of the Von-Hippel-Lindau (VHL) gene [3,7]. In healthy cells this gene product promotes ubiquitination and inactivation of hypoxia-inducible factor a [3]. Decreased ubiquitination of this factor creates a pro-angiogenic environment.

The metastatic spread in this case is curious not only because of the location of metastasis but also because the cancer was latent for nearly 7 years. It is not uncommon for metastatic events to present years after the primary tumor is removed [7]. A similar case was recently reported of a 45-year-old woman who developed a pyoderma gangrenosum-like nodule on the chin that turned out to be renal cell carcinoma; this also developed 7 years after what was thought to be successful treatment of the primary tumor [8]. An important clinical question that arises is whether circulating tumor cells (CTCs) implanted in this patient’s lip 7 years after his original tumor was excised or whether these cells extravasated 7 years ago and remained dormant for this period of time. Dormancy is thought to occur after metastatic tumor cells have already extravasated through a vessel wall and become established at a distant site [9]. If this is the case, this patient’s CTCs implanted in his lip many years ago. Once tumor cells implant in a distant site, dormancy can occur when cells enter long periods of quiescence (cell-cycle arrest), although dormancy



**Figure 3.** Immunohistochemical staining. The cells were positive for **A)** CK7, **B)** PAX-8, **C)** CD10, and **D)** vimentin.

has also been hypothesized to occur as a balance between proliferation and cell death rather than arrest of the cell cycle [9]. The exact mechanism is still controversial and triggers that lead to proliferation after a period of dormancy are currently speculative [9].

## Conclusion

Metastases to the face are uncommon. Renal clear cell carcinoma metastasizing to the lip is a rare

phenomenon observed in this patient that otherwise could have clinically been misdiagnosed. This underscores the importance of pathologic evaluation of excised lesions and the value of considering malignancy in the differential diagnosis of atypical cutaneous lesions.

## Potential conflicts of interest

The authors declare no conflicts of interest.

## References

1. Alcaraz I, Cerroni L, Rütten A, Kutzner H, Requena L. Cutaneous metastases from internal malignancies: a clinicopathologic and immunohistochemical review. *Amer J Dermatopathol*. 2012;34:347-393. [PMID: 2261733].
2. Hashimi Y, Dholakia S. Facial cutaneous metastasis of colorectal adenocarcinoma. *BMJ Case Rep*. 2013;2013:bcr2013009875. [PMID: 24177455].
3. Arora RD, Limaiem F. Renal Clear Cell Cancer. 2020. <https://pubmed.ncbi.nlm.nih.gov/33085377/>. Accessed on December 29, 2021. [PMID: 33085377].
4. Klatte T, Rossi SH, Stewart GD. Prognostic factors and prognostic models for renal cell carcinoma: a literature review. *World J Urol*. 2018;36:1943-1952. [PMID: 29713755].
5. Padala SA, Barsouk A, Thandra KC, et al. Epidemiology of Renal Cell Carcinoma. *World J Oncol*. 2020;11:79-87. [PMID: 32494314].
6. Hussein MR. Skin metastasis: a pathologist's perspective. *J Cutan Pathol*. 2010;37:1-20. [PMID: 19922483].
7. Hirshberg A, Berger R, Allon I, Kaplan I. Metastatic tumors to the jaws and mouth. *Head Neck Pathol*. 2014;8:463-474. [PMID: 25409855].
8. Chelliah P, Shah KM, Vandergriff T, Nijhawan RI. Pink nodule of the chin: an unusual presentation of metastatic carcinoma. 2021; *Dermatol Online J*. 25:15.
9. Wells A, Griffith L, Wells JZ, Taylor DP. The dormancy dilemma: quiescence versus balanced proliferation. *Cancer Res*. 2013;73:3811-3816. [PMID: 23794703].