

4-1-2021

Signet-ring cutaneous metastasis presenting with massive anasarca

Neel Raval

Washington University School of Medicine in St. Louis

Leonid Shmuylovich

Washington University School of Medicine in St. Louis

John Strickley

Washington University School of Medicine in St. Louis

Tiffany Y Chen

Albany Medical Center

Ilana S Rosman

Washington University School of Medicine in St. Louis

See next page for additional authors

Follow this and additional works at: https://digitalcommons.wustl.edu/oa_4

Recommended Citation

Raval, Neel; Shmuylovich, Leonid; Strickley, John; Chen, Tiffany Y; Rosman, Ilana S; and Musiek, Amy, "Signet-ring cutaneous metastasis presenting with massive anasarca." *JAAD Case Reports*. 10, 123 - 125. (2021).

https://digitalcommons.wustl.edu/oa_4/399

This Open Access Publication is brought to you for free and open access by the Open Access Publications at Digital Commons@Becker. It has been accepted for inclusion in 2020-Current year OA Pubs by an authorized administrator of Digital Commons@Becker. For more information, please contact vanam@wustl.edu.

Authors

Neel Raval, Leonid Shmuylovich, John Strickley, Tiffany Y Chen, Ilana S Rosman, and Amy Musiek

Signet-ring cutaneous metastasis presenting with massive anasarca



Neel Raval, BS,^a Leonid Shmuylovich, MD, PhD,^a John Strickley, MD,^a Tiffany Y. Chen, MD,^c
Ilana S. Rosman, MD,^{a,b} and Amy Musiek, MD^a
St. Louis, Missouri and Albany, New York

Key words: anasarca; case report; dermatology; edema; Hoffman's syndrome; metastasis; signet-ring cell carcinoma.

INTRODUCTION

Signet-ring cell carcinomas (SRCC) are poorly-differentiated neoplasms that generally arise from gastrointestinal or breast tissue and are associated with poor prognosis.¹ Malignant signet-ring cells contain abundant cytoplasmic mucin and a peripherally displaced nucleus. Of note, these neoplasms have an unusual tendency to infiltrate surrounding tissues, which is thought to be due to the loss of E-cadherin.² This is clearly illustrated by the gastric SRCC variant, known as "linitis plastica," which can result in the thickening of the stomach wall.³ Similarly, SRCC can metastasize to the peritoneum, leading to omental caking, a classic radiologic pattern describing the infiltration of omental fat by soft-tissue material (eg, Krukenberg tumors). Dermatologists seldom identify SRCC in practice, most probably due to a combination of their sporadic prevalence and wide-ranging cutaneous manifestations. Here, we report a remarkable case of SRCC presenting with massive anasarca diagnosed solely via skin biopsy.

CASE REPORT

A 63-year-old woman with a history of basal cell carcinoma, hypothyroidism, and tobacco use presented to the emergency department from her nursing home complaining of bilateral lower extremity edema coupled with a rapid decline in overall health. Edema of the lower extremities inexplicably began about 5 months prior to admission. During the interim, she experienced gradual weight loss from her face and upper body, diffused

Abbreviation used:

SRCC: Signet-ring cell carcinoma

hair loss from the scalp, and significant orthopnea, ultimately requiring her transfer to a skilled nursing facility. While there, she suffered a pulmonary embolism and had several inconclusive workups for her gross deterioration. Aggressive diuresis failed to provide any significant relief from edema, which prompted her hospital admission.

On physical examination (Fig 1, A and B), she had a massive indurated edema of the lower body extending to the inframammary area, which stood in stark contrast to the cachectic appearance of the upper extremities, chest, head, and neck. The lower extremity skin was thickened and leathery, with very faint overlying scattered erythema on the pretibial areas alone. No frank nodularity, papules, ulcerations, or violaceous lesions were found.

Initial diagnostic workup revealed hemoglobin of 7.9 g/dL, elevated erythrocyte sedimentation rate (89 mm/hr), and elevated thyroid-stimulating hormone (18.6 mIU/mL) with depressed free T4 (0.72 ng/dL). A computed tomography scan showed evidence of diffuse body wall edema and skin thickening with hypertrophy and calcification of the proximal lower extremity musculature. These changes were uniformly distributed, although slightly worse in dependent areas (sacrum and proximal thighs). When taken together with hypothyroidism, these imaging findings suggested a

From the Division of Dermatology^a and Department of Pathology & Immunology, Washington University School of Medicine, St. Louis,^b and Department of Pathology, Albany Medical Center.^c
Funding sources: None.

IRB approval status: Not applicable.

Correspondence to: Amy Musiek, MD, Division of Dermatology, Washington University School of Medicine, 4590 Children's Place, Campus Box 8123, St. Louis, MO 63110. E-mail: amusiek@wustl.edu.

JAAD Case Reports 2021;10:123-5.
2352-5126

© 2021 by the American Academy of Dermatology, Inc. Published by Elsevier, Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

<https://doi.org/10.1016/j.jidcr.2021.02.009>

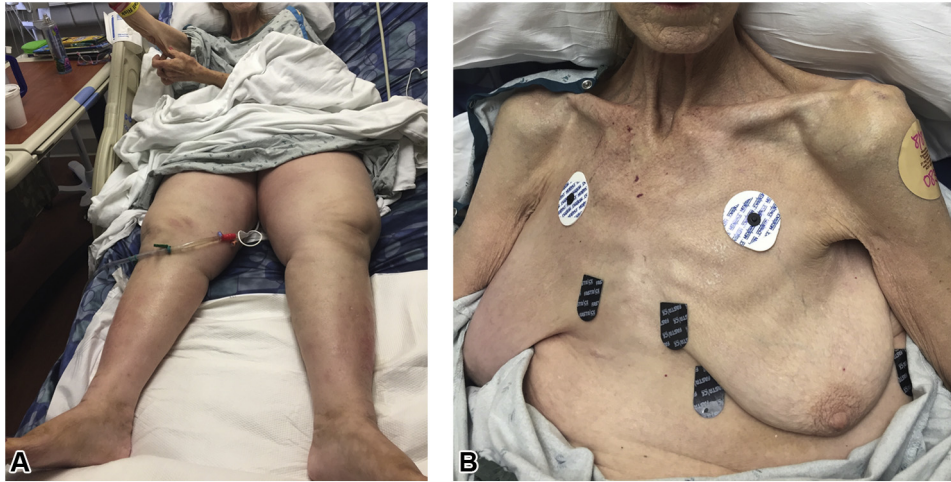


Fig 1. Clinical presentation. **A**, Indurated edema of bilateral lower extremities. **B**, Edema extending to the inframammary area with cachexia of upper extremities and thorax.

diagnosis of Hoffman's syndrome, a rare form of hypothyroid myopathy presenting with muscular pseudohypertrophy. Nevertheless, clinical uncertainty necessitated further evaluation.

The dermatology department was consulted and a skin biopsy was performed from the most superior region of the anterior abdominal wall. This location was chosen as it was typical of the edematous changes seen throughout, as well as to avoid the static changes that can occur after lower leg biopsies. On histopathologic examination (Fig 2, A and B), there was tremendous edema with scattered cells having a signet-ring morphology within the deep reticular dermis and subcutis. Lesional cells stained positive with pancytokeratin, CK7, SATB2, and CDX-2, which was suggestive of a non-cutaneous primary malignancy. GATA3, CK20, and neuroendocrine markers, synaptophysin and chromogranin, were negative. Colloidal iron highlighted mucin within atypical cells and no lymphovascular invasion was observed. Collectively, the histopathologic and immunophenotypic findings pointed to a metastatic SRCC of gastrointestinal origin.

Subsequently, the patient underwent abdominal ultrasonography, esophagogastroduodenoscopy, colonoscopy with biopsy, and fluorodeoxyglucose-positron emission tomography with computed tomography. Tumor marker studies were notable for elevated CEA, CA 19-9, CA 15-3, and CA 125 antigen. Imaging studies, as well as tissue biopsies of colonic and esophageal mucosa, failed to identify a primary SRCC.

The patient was transferred to the medical oncology department for further management, with a diagnosis of metastatic adenocarcinoma due to the

presence of signet-ring cells. She tolerated inpatient folinic acid, 5-fluorouracil, and oxaliplatin therapy and was referred to a skilled nursing facility with plans for outpatient follow-up. Regrettably, she succumbed to septic shock soon after discharge and no autopsy was performed.

DISCUSSION

We present a remarkable case where a patient with immense edema of the abdomen and lower extremities was diagnosed with metastatic visceral adenocarcinoma (SRCC) solely via skin biopsy.

Physicians must consider several pathophysiologic mechanisms when evaluating skin thickening and lower extremity edema. Iatrogenic culprits include medications (ie, dihydropyridine calcium channel blockers) or surgical lymph node dissections. Infectious etiologies (eg, lymphatic filariasis) should be ruled out in those with pertinent travel histories. Infiltrative processes, such as amyloidosis, myxedema, or sarcoidosis, present unique challenges when they are not accompanied by classic symptoms (weight gain/loss, fatigue) or other typical features (hair/nail changes, uveitis). These features can prolong arriving at the correct diagnosis, which is worrisome for both patient and physician. Our case determined that SRCC is the infiltrative process responsible for anasarca, which has not yet been reported.

In prior literature, cutaneous metastases from SRCC are described as papulonodular, sclerodermoid, or inflammatory-appearing lesions.⁴ Illustrative examples of these reactionary patterns include carcinoma *en cuirasse* and carcinoma erysipeloides, often in the setting of metastatic gastric or breast SRCC.^{4,5} These

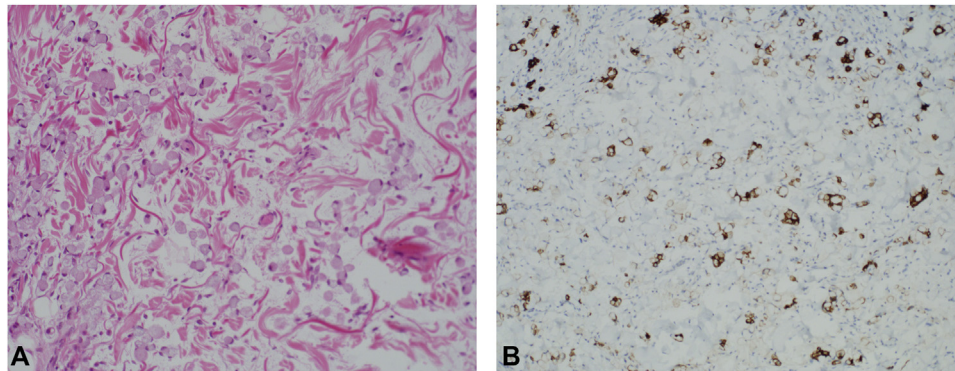


Fig 2. Histopathology. **A**, Signet-ring cells. (Hematoxylin-eosin stain; original magnification: $\times 200$.) **B**, Tissue stained with CK-7 (colorectal). (Original magnification: $\times 100$.)

distinct morphologies can provide strong clues for the dermatologist but are scarcely observed in common practice. Furthermore, SRCC can mimic benign processes, such as allergic contact dermatitis,⁶ or appear as localized, asymptomatic scarring.⁷ In addition to obtaining a comprehensive history and performing a full body skin examination, these reports on cutaneous manifestations of SRCC emphasize that the clinician must harbor a high index of suspicion and a low threshold for accepting skin biopsy results to avoid delays in diagnosis and treatment.

After a biopsy, gross histopathologic evaluation and targeted immunostaining are essential and will often help in identifying the primary cancer. Painter et al provided a concise review of relevant immunohistochemical markers that dermatologists may encounter.⁸ In our case, the presence of signet-ring cells prompted immunostaining for common gastrointestinal malignancies with CK-7/CK-20, SATB2, and CDX-2, in addition to GATA3 for breast and bladder primaries.⁶ Negative synaptophysin and chromogranin militated against a neuroendocrine etiology.

To summarize, dermatologists should consider a diagnosis of SRCC when faced with a confusing clinical picture that could be explained by an infiltrative process. Moreover, this case underscores the powerful diagnostic utility of a skin biopsy, which provided the only evidence for an internal malignancy in this case.

Conflicts of interest

Dr Musiek reports the following: Kyowa - advisory board; Helsinn - advisory board; Elorac, Sologenix, miRagen, Connect, Pfizer, and Menlo - investigator. Author Raval and Drs Shmuylovich, Strickley, Chen, and Rosman have no conflicts of interest to report.

REFERENCES

1. Chu PG, Weiss LM. Immunohistochemical characterization of signet-ring cell carcinomas of the stomach, breast, and colon. *Am J Clin Pathol.* 2004;121(6):884-892.
2. Chan JK, Wong CS. Loss of E-cadherin is the fundamental defect in diffuse-type gastric carcinoma and infiltrating lobular carcinoma of the breast. *Adv Anat Pathol.* 2001;8(3):165-172.
3. Pernot S, Voron T, Perkins G, Lagorce-Pages C, Berger A, Taieb J. Signet-ring cell carcinoma of the stomach: Impact on prognosis and specific therapeutic challenge. *World J Gastroenterol.* 2015; 21(40):11428-11438.
4. Kaur S, Aggarwal P, Dayal S, Sangwan A, Jain VK, Jindal N. Cutaneous metastasis from signet-ring gastric adenocarcinoma in a carcinoma en cuirasse pattern: an unusual clinical-diagnostic sequence. *Indian J Dermatol.* 2015;60(6):637.
5. Oliveira GM, Zchetti DB, Barros HR, Tiengo A, Romiti N. Breast carcinoma en Cuirasse—case report. *An Bras Dermatol.* 2013; 88(4):608-610.
6. Ahn SJ, Oh SH, Chang SE, et al. Cutaneous metastasis of gastric signet ring cell carcinoma masquerading as allergic contact dermatitis. *J Eur Acad Dermatol Venereol.* 2007;21(1): 123-124.
7. Aneiros-Fernandez J, Husein-ElAhmed H, Arias-Santiago S, et al. Cutaneous metastasis as first clinical manifestation of signet ring cell gastric carcinoma. *Dermatol Online J.* 2010;16(3):9.
8. Painter JT, Clayton NP, Herbert RA. Useful immunohistochemical markers of tumor differentiation. *Toxicol Pathol.* 2010;38(1): 131-141.