April Case of the Month

- 63-year-old female presented to the emergency department for bilateral lower extremity edema
- HPI:
  - 5 months duration with no improvement on diuretics.
  - Previous workup showed no evidence of cardiomyopathy or renal disease.
  - On exam, there was massive weeping anasarca up to the xiphoid process with cachexia of the face and upper extremities. Induration of the skin of the right abdomen was noted. A punch biopsy of the skin was performed.
- PMH:
  - Basal cell carcinoma of the skin
  - Hypothyroidism
  - COPD
  - Recent pulmonary embolism.

What is your diagnosis?

Signet ring cutaneous metastasis presenting with massive anasarca

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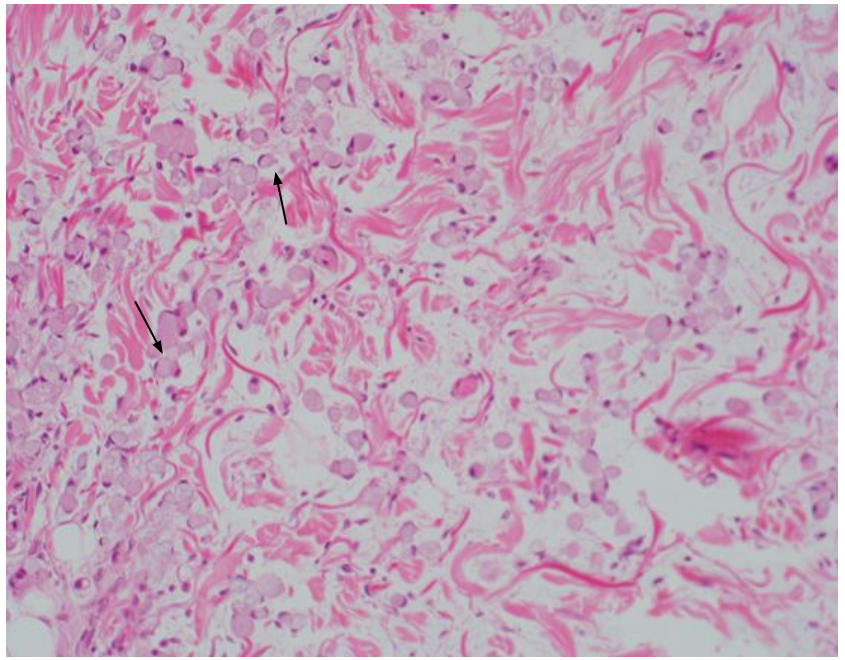
HPI

- 63-year-old female with a presented to the emergency department for evaluation of bilateral lower extremity edema
- HPI
  - 5 months duration with no improvement on diuretics.
  - Previous workup showed no evidence of cardiomyopathy or renal disease.
- PE
  - Massive weeping anasarca up to the xiphoid process with cachexia of the face and upper extremities.
  - Induration of the skin of the right abdomen was noted.
  - A punch biopsy of the skin was performed.
- **Medical History**: Basal cell carcinoma of the skin, hypothyroidism, COPD, and recent pulmonary embolism.
- **Social History**: Significant smoking history
- **Medications**: Home medications included Lasix 80mg PO daily and apixaban 5mg PO BID

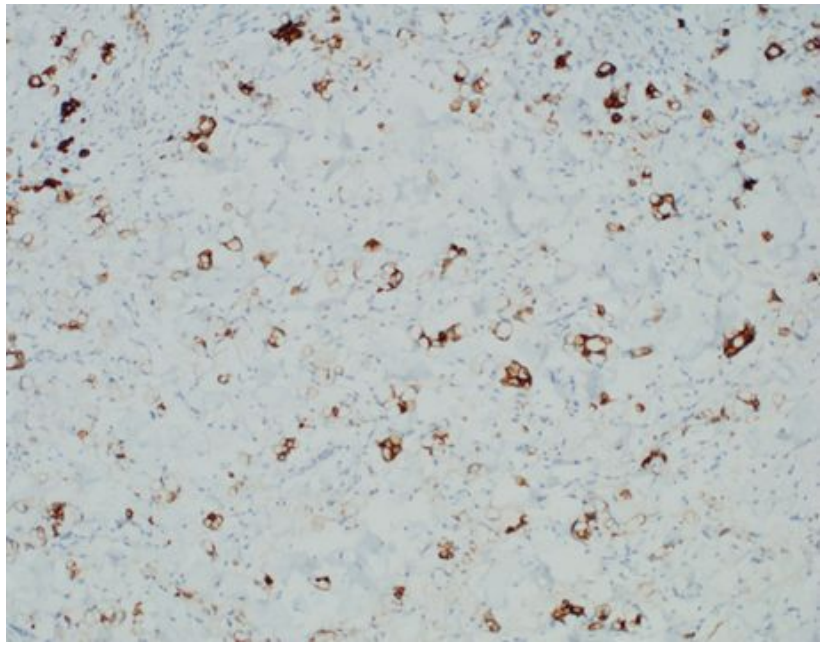
Pathology

Metastatic adenocarcinoma with signet ring cells

- Atypical cells with signet ring features as well as occasional gland formation within the subcutaneous soft tissue and reticular dermis.
- Immunostains
  - Positive for pancytokeratin, CK7, SATB2, and CDX-2.
  - Negative for GATA3 (marker for breast and bladder primary), synaptophysin and chromogranin (neuroendocrine markers), and CK20
  - Colloidal iron highlights mucin within tumor cells. CD68 highlight scattered macrophages.
- Favored a metastasis from the appendix based on immunostains, but cannot entirely exclude a colorectal or stomach primary.
- The immunohistochemical profile essentially exclude the possibility of this being a metastasis from the breast, bladder, and pancreatobiliary tract or a neuroendocrine carcinoma.



Hematoxylin & Eosin stain demonstrating signet ring cells (arrows).



100X Magnification of tissue stained with CK-7 (colorectal)

Discussion

- The most common type of visceral cancer to metastasize to the skin is breast cancer.[1]
- Signet ring-cell carcinoma is typically caused by stomach (e.g. *linitis plastica*), breast, bladder, or pancreatic cancer.[2]
- Cutaneous metastasis carries a very poor prognosis and can be the first indication of internal malignancy.
- This unique presentation of cutaneous metastasis also depicts the diagnosis of a visceral malignancy from skin involvement and the subsequent targeted search for a primary tumor based on histopathologic findings. In response to the skin biopsy, EGD, colonoscopy and ultimately PET/CT scan were performed.
- Unfortunately, no primary cancer was able to be identified.

Follow-up

- The patient died less than one month after initial presentation secondary to septic shock following initiation of comfort care. There was no autopsy performed and the primary tumor was never fully elucidated. Skin biopsy was the only clear proof of malignancy.

References

1. Wong CY, Helm MA, Helm TN, Zeitouni N. Patterns of skin metastases: a review of 25 years' experience at a single cancer center. Int J Dermatol. 2014;53(1):56-60.
2. 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.

Discussion questions - https://bit.ly/3wfC548

1) What is the most common type of visceral cancer to metastasize to the skin?

2) What are common origins of signet ring-cell carcinoma?