

CASE REPORT

Primary colonic adenocarcinoma diagnosed with cutaneous shave biopsy

Nicholas B Abt,¹ Maame Efua S Sampah,¹ Romsai Tony Boonyasai,² Amit K Pahwa²

¹The Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

²Department of Medicine, The Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

Correspondence to

Dr Amit K Pahwa,
apahwa1@jhmi.edu

Accepted 9 June 2015

SUMMARY

A 67-year-old man presented to the emergency department with chronic weakness, fatigue and failure to thrive. On physical examination, he was found to have multifocal exophytic cutaneous masses in the pubic and scrotal regions. We obtained a shave biopsy, and subsequent histopathology demonstrated non-native tissue consistent with metastasis from a primary adenocarcinoma. We report this novel case of anogenital cutaneous metastases of colorectal adenocarcinoma.

BACKGROUND

Colonic adenocarcinoma is the fourth most common cancer worldwide and the second leading cause of cancer-related mortality in the USA.¹ Metastases to local and distant sites including liver, lung, peritoneum and bone are well established, and represent a major barrier to patient treatment and survival.^{1–2} However, cutaneous metastases from colonic adenocarcinoma occur in only 2.3–6% of cases, with abdominal skin being the most frequent site of metastasis.^{3–4} To the best of our knowledge, this is the first case reported of primary colonic adenocarcinoma diagnosed with a cutaneous shave biopsy of the metastases to the anogenital and scrotal regions.

CASE PRESENTATION

A 67-year-old man who sought no medical care in the previous decade presented to the emergency department (ED) with profuse haematochezia. His clinical history began 5 years prior to presentation, when he noticed intermittent blood-tinged stool. Initially, he self-managed this condition with over-the-counter fibre. He continued to note occasional diarrheal episodes intermixed with frank blood over the next several years. Approximately 2 years prior to presentation, cutaneous lesions appeared within and surrounding the intergluteal cleft extending to the pubic/scrotal area (figure 1). The patient remained unconcerned due to absence of pain and the lesions' slow growth. Four months prior to presentation, he noticed a reduced appetite in addition to increasing fatigue, lethargy and a diffuse, dull pressure sensation in the bilateral lower abdominal quadrants. Fever, night sweats and unintentional 105-pound weight loss over a 10-month period accompanied these symptoms. Six weeks prior to presentation, the patient developed bowel incontinence and, subsequently, bladder incontinence. He became so weak that he could not answer his telephone, thus neighbours grew concerned and called emergency medical



Figure 1 Photograph of the heterogeneous, exophytic nodules on the pubic and scrotal skin.

services. The patient was unaware of a family history of cancer. He had never been incarcerated, though he described occasional exposure to ex-inmates. He had no contact with immigrants and had no history of travel except for a trip to New Mexico 5 years prior to presentation. He had a remote history of heavy alcohol use, but no history of illicit drug use. He had not had sexual intercourse in almost two decades.

On presentation to the ED, the patient appeared acutely ill. His vital signs included temperature 97.5°F, pulse 107 bpm, blood pressure 94/56 mm Hg, respirations 20 breaths/min and oxygen saturation 92% on room air. On physical examination, he was cachectic and grey appearing, with pale conjunctivas. No lymphadenopathy was noted. Breath sounds were diminished on the right. His abdomen was non-tender and non-distended. Friable exophytic masses were observed in the anorectal region and extended down to the scrotum, which was swollen. Rectal examination yielded brown liquid stool, which was haemoccult positive. Rectal tone was normal. He was oriented to person, place and time. Cranial nerves were grossly intact bilaterally.

He had a small ulceration on his right shoulder and larger purulent ulcer on his right hip. The patient was admitted to the medical intensive care unit.

INVESTIGATIONS

Notable laboratory findings included initial haemoglobin of 5 g/dL, white cell count of 17 100 cells/mm³, alkaline phosphatase of 125 U/L and lactate of 3.9 mmol/L. The patient received vancomycin and piperacillin/tazobactam, 4 units of packed red blood cells, intravenous ferrous sulfate and



To cite: Abt NB, Sampah MES, Boonyasai RT, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-210046



Figure 2 CT of the abdomen demonstrating focal circumferential thickening of the sigmoid colon (red arrow) with extensive bilateral common and external iliac lymph node chains containing rim calcification (yellow arrows). Diffuse fat stranding is noted within the pelvic rim.

parenteral fluids. Active gastrointestinal (GI) bleeding ceased without direct intervention, resulting in haemodynamic stabilisation.

Chest CT angiogram (CTA) demonstrated multiple segmental and subsegmental pulmonary emboli in the left lower lobe and lingula with a small pericardial effusion. Multiple subcentimetre lower paraoesophageal and retrocaval lymph nodes were noted. Lower extremity duplex ultrasound showed a completely occlusive deep venous thrombosis extending from the left femoral to popliteal vein, and partially occlusive thrombus of the right mid-femoral and distal femoral veins.

Abdomen and pelvis CTA revealed focal circumferential thickening of the sigmoid colon with extensive retroperitoneal, pelvic and inguinal lymphadenopathy containing rim calcification (figure 2). Asymmetric thickening of the distal rectum with multiple fistulae and/or abscesses were noted along its right aspect. A destructive sacrococcygeal lesion presumed to be a locoregional metastasis was present. There was an enlarged oedematous scrotum with multiple skin lesions surrounding the intergluteal cleft, anus and scrotum, involving only dermal tissue without contiguous involvement from the primary cancer (figure 3).

A cutaneous lesion was biopsied from the right inguinal area, which demonstrated cutaneous epidermis overlying infiltrative non-native tissue within the dermis with irregular branching and

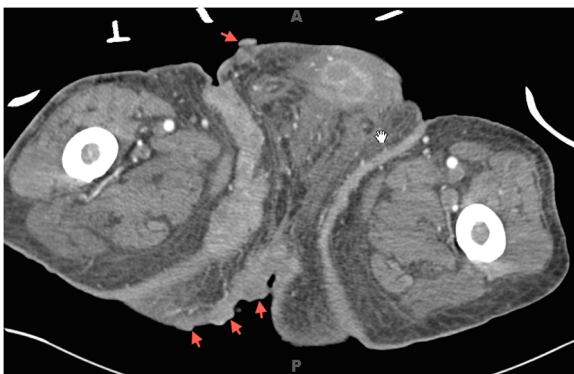


Figure 3 CT scan demonstrating multiple heterogeneous, exophytic nodules (red arrows) confined to the superficial skin on the inguinal, anogenital and scrotal skin. No direct extension from the primary colonic adenocarcinoma is seen in the CT series.

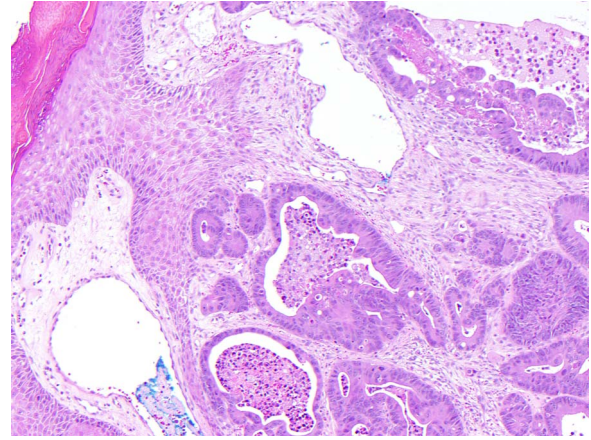


Figure 4 Histological sections with H&E staining demonstrating cutaneous epidermis overlying infiltrative non-native tissue within the dermis with irregular branching and cribriform glands, with pseudostratified columnar epithelium and luminal inflammatory debris, consistent with adenocarcinoma.

cribriform glands, with pseudostratified columnar epithelium and luminal inflammatory debris, consistent with metastasis from a primary adenocarcinoma (figure 4). Immunohistochemical staining was positive for cytokeratin 20 (CK20), a cytoskeletal protein specific to intestinal and goblet cells, and CDX-2 (figure 5), a homeobox protein biomarker for intestinal epithelium, identifying the primary adenocarcinoma as colonic in origin. Tissue was negative for CK7, a cytokeratin expressed in transitional carcinoma and anorectal adenocarcinoma, but not colonic adenocarcinoma. Oesophagogastroduodenoscopy and sigmoidoscopy were initially deferred due to the patient's haemodynamic instability. Urine and blood cultures were negative over the course of admission. HIV, rapid plasma reagin, *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and quantiferon gold testing were found to be negative.

DIFFERENTIAL DIAGNOSIS

Prior to biopsy, our differential diagnosis of these anogenital lesions consisted of cutaneous lymphoma, condyloma lata,

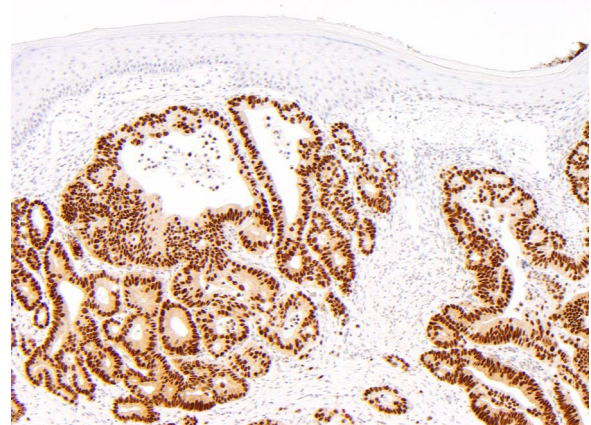


Figure 5 Immunohistochemical staining was positive for CDX-2, a homeobox protein biomarker for intestinal epithelium. Not shown: staining was also positive for cytokeratin 20 (CK20), a cytoskeletal protein specific to intestinal and goblet cells. However, samples were negative for CK7, a cytokeratin expressed in transitional carcinoma and anorectal adenocarcinoma cells, but not colonic adenocarcinoma cells. Staining was also negative for p16 and high risk HPV (16 and 18).

condyloma acuminatum, squamous or basal cell carcinoma, epidermolytic acanthomas, or atypical epidermal nevi. Given the anogenital distribution of the lesions, we also had a high level of suspicion for a pathology involving a sexually transmitted infection, including HPV or syphilis. Further, given that our patient presented with weakness and failure to thrive, neoplasia, and hence cutaneous lymphoma, was higher on our differential. Finally, due to the initial septic-appearing presentation, tuberculosis, atypical mycobacteria and fungi including coccidioidomycosis, histoplasmosis and blastomycosis, were considered.

Human papilloma virus (HPV) has a well-recognised aetiological role in anogenital, oropharyngeal and cervical cancers. More recently, increasing literature has shown an association between some colon cancers and HPV infection. Specifically, DNA of high-risk HPV strains 16 and 18 has been detected in up to 30% of tissue samples of colonic adenocarcinoma.⁵ However, in this case, immunohistochemical probing for p16, which is overexpressed in neoplastic cells due to inactivation of pRB by HPV protein E7, was negative. Staining for high-risk HPV strains 16 and 18 was also negative, indicating that the cutaneous lesions observed in this patient were not representative of an HPV-associated colonic adenocarcinoma.

TREATMENT

Given the patient's chronic GI bleed, we held heparin administration in the acute setting. We also discussed potential placement of an inferior vena cava filter, and risks and benefits of long-term anticoagulation with the patient, given the presence of multiple pulmonary emboli and deep venous thrombi. Finally, we provided the patient with information on risks and benefits of various approaches to treating metastatic cancer, including chemotherapy, palliative radiation and hospice care. The patient declined all interventions.

OUTCOME AND FOLLOW-UP

The patient was evaluated by the oncology and radiation oncology services. After extensive discussion related to goals of care, the patient declined all potential therapy, including palliative services, opting instead to receive 24-h care from family and friends.

DISCUSSION

Cutaneous metastases from primary lung and breast adenocarcinomas, as well as melanoma, have been widely observed.⁶ This phenomenon is a rare observation with primary colonic adenocarcinomas. When cutaneous metastases of colon adenocarcinoma are observed, they are primarily to abdominal skin, specifically to postoperative scar sites manifesting often as ulcerations, nodules, or bullae.^{5 7} In this patient, the cutaneous lesions from colonic metastases appeared as heterogeneously skin coloured and erythematous exophytic masses. We searched for articles using PubMed via keywords “(colonic adenocarcinoma) AND cutaneous) AND metastasis”, from 1950 until 1 September 2014. From those search results and to the best of our knowledge, this is the first case reported of primary colonic adenocarcinoma with metastasis to the anogenital and scrotal regions.

The choice of biopsy technique depends on clinical diagnosis and lesion morphology. In this patient with a rectal mass and several pelvic nodules, punch and shave biopsy were potential diagnostic approaches, since the patient had both sessile and pedunculated lesions. Punch biopsies contain the entire dermis, and thus are preferred for sessile lesions (where a larger tissue sample is desirable), and to look for potential lesions in dermis

or subcutis. However, this approach also requires sutures for haemostasis. Since cancer was one of the leading diagnoses and carcinomatous tissue tends to be friable and difficult to suture, we elected to shave biopsy a large pedunculated lesion. This sample yielded enough tissue to make the diagnosis, thus no further sampling was needed. We subsequently used heat cautery for haemostasis.

From previous cases, the median interval between diagnosis of internal malignancy and presentation of metastasis to the skin is estimated to be 33 months.⁸ Therefore, cutaneous metastases appear to be associated with advanced colonic adenocarcinoma. In this previously undiagnosed patient, the lesions appeared approximately 4–5 years after the onset of the patient's bloody stools. In a large retrospective study of a tumour registry, cutaneous masses were the first evidence of extranodal metastases in 11 of 413 (2.66%) patients.⁴ These cutaneous lesions were the first signs of metastases in our patient. With additional CTA, diffuse involvement of the lymphatic system was seen, with no other solid organ involvement. The CDX2+/CK20+/CK7–phenotype obtained via cutaneous biopsy, in conjunction with this data, supports the diagnosis of a colorectal adenocarcinoma, obviating the need to perform more invasive testing.

Learning points

- ▶ Visceral malignancies such as colonic adenocarcinomas may manifest as cutaneous metastases, and should be on the differential for heterogeneous, exophytic, nodular skin lesions.
- ▶ Cutaneous manifestations of this sort are uncommon because colonic adenocarcinoma is preventable with screening and treatable when identified in early stages. Thus, advanced manifestations such as cutaneous lesions are likely to be seen in patients who do not receive screening or lack access to medical care.
- ▶ In cases where signs and symptoms provide high suspicion for malignancy, it is important to consider that dermatological lesions may be indicative of distant metastasis.
- ▶ Utilisation of an appropriate dermatological biopsy with immunohistochemistry may yield a diagnosis of a primary visceral cancer, without the need for further invasive biopsy sampling.

Acknowledgements The authors would like to acknowledge Dr Matthew Tilson in the Johns Hopkins University School of Medicine Department of Dermatopathology for help with reading histopathology slides. They also thank Dr Nikita Barai, Dr Samuel Kim, Dr Thomas Johnson and Dr Dylan Lovin were part of the General Internal Medicine team that provided care for this patient. Dr Peter L Mattei from the Department of Dermatology also contributed.

Contributors NA and MESS contributed equally to this work, outlined the manuscript, coordinated laboratory and other studies and retrieved data concerning the case. NA, MESS, AKP and RTB wrote the manuscript.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Edwards BK, Ward E, Kohler BA, *et al*. Annual report to the nation on the status of cancer, 1975–2006, featuring colorectal cancer trends and impact of interventions

- (risk factors, screening, and treatment) to reduce future rates. *Cancer* 2010;116:544–73.
- 2 Ferlay J, Shin HR, Bray F, *et al*. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer* 2010;127:2893–917.
 - 3 Pereira WA, Humaire CR, Silva CS, *et al*. Sister Mary Joseph's nodule: a sign of internal malignancy. *An Bras Dermatol* 2011;86:S118–20.
 - 4 Lookingbill DP, Spangler N, Helm KF. Cutaneous metastases in patients with metastatic carcinoma: a retrospective study of 4020 patients. *J Am Acad Dermatol* 1993;29:228–36.
 - 5 Damin DC, Ziegelmann PK, Damin AP. Human papillomavirus infection and colorectal cancer risk: a meta-analysis. *Colorectal Dis* 2013;15:e420–8.
 - 6 Alcaraz I, Cerroni L, Rütten A, *et al*. Cutaneous metastases from internal malignancies: a clinicopathologic and immunohistochemical review. *Am J Dermatopathol* 2012;34:347–93.
 - 7 Saeed S, Keehn CA, Morgan MB. Cutaneous metastasis: a clinical, pathological and immunohistochemical appraisal. *J Cutan Pathol* 2004;2013:419–30.
 - 8 Browstein MH, Helwig EG. Patterns of cutaneous metastasis. *Arch Dermatol* 1972;2013:862–8.

Copyright 2015 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow