Large Diffuse Cutaneous Metastases Secondary to Rectal Mucinous Adenocarcinoma

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ABSTRACT
Cutaneous metastases as the initial manifestation of colorectal cancer are rare, with an incidence below 1%. They usually occur in patients with advanced disease and may present with variable clinical features mimicking infectious conditions. Early recognition is essential for timely diagnosis and appropriate management.
We report the case of an immunosuppressed kidney transplant recipient who developed cutaneous lesions initially suspected to be herpes zoster. Owing to the lack of response to antiviral therapy, a skin biopsy was performed and revealed metastatic mucinous carcinoma. Immunohistochemical findings supported a colorectal origin, and imaging studies identified a primary rectal tumor with metastatic disease.
This case highlights the importance of including cutaneous metastases in the differential diagnosis of atypical skin lesions, particularly in immunocompromised patients, and underscores the pivotal role of biopsy and immunohistochemistry in identifying neoplasms of initially unknown origin.

***Keywords**: cutaneous metastases; colorectal cancer; mucinous adenocarcinoma; immunosuppression; herpes zoster*

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INTRODUCTION

Cutaneous metastases from colorectal cancer are an uncommon manifestation, with a reported incidence of less than 1% among affected patients.[1–3] Within the spectrum of cutaneous metastases arising from solid tumors, colorectal cancer represents a relatively rare etiology compared with malignancies more commonly associated with skin involvement, such as breast and lung cancer.[3]
Clinically, these lesions demonstrate marked morphologic heterogeneity. They may present as firm subcutaneous nodules, infiltrative plaques, or, less frequently, as atypical lesions mimicking infectious processes such as herpes zoster.[4] This broad clinical spectrum may complicate diagnosis and delay appropriate treatment, particularly in immunocompromised patients.
The presence of cutaneous metastases generally reflects advanced systemic dissemination and is associated with a poor prognosis, with a reported median survival of less than 1 year from the time of diagnosis.[4,5] In this setting, early recognition is essential, as it may facilitate timely therapeutic optimization and guide appropriate clinical management.
Mucinous rectal carcinoma represents a distinct histologic subtype characterized by abundant extracellular mucin production and unique biologic behavior, including a greater propensity for peritoneal dissemination and differential therapeutic response patterns compared with conventional adenocarcinoma.[6] Although cutaneous involvement is exceedingly rare, its recognition may represent the first manifestation of metastatic disease or tumor progression.

CASE

An 81-year-old woman with a medical history significant for hypertension, chronic kidney disease secondary to polycystic kidney disease, and deceased-donor kidney transplantation performed in 2011 with preserved graft function presented for evaluation. She was receiving immunosuppressive therapy with sirolimus (2 mg/day) and methylprednisolone (4 mg/day). Her medical history was also notable for neuropathy, peripheral arterial disease, and right above-knee amputation.
The patient presented with painful vesicular lesions involving the right lower extremity stump, initially interpreted as herpes zoster in the setting of immunosuppression (Fig. 1). However, because of the lack of response to antiviral therapy and persistence of the lesions, a skin biopsy was performed.
Histopathologic examination revealed dermal infiltration by neoplastic cells suspended within abundant extracellular mucin, forming characteristic mucin pools consistent with mucinous carcinoma (Fig. 2). Immunohistochemical analysis demonstrated positivity for cytokeratins AE1/AE3, CK20, and CDX2, and negativity for CK7, TTF1, PAX8, CD10, and GATA3, findings consistent with cutaneous metastasis of colorectal origin.
Given the suspicion of metastatic disease from an initially unknown primary tumor, CT of the chest, abdomen, and pelvis was performed, demonstrating irregular mural thickening of the lower rectum, mesorectal, retroperitoneal, and inguinal lymphadenopathy measuring up to 26 mm (Fig. 3), as well as multiple pulmonary nodules suggestive of metastatic disease.
Endoscopic evaluation and rectal MRI were not performed due to the patient's clinical condition and the confirmed tumor origin based on histopathologic and imaging findings.
Microsatellite instability testing was not performed because the patient was not considered a candidate for immunotherapy given her immunosuppressed status.
The case was discussed at a multidisciplinary tumor board, and systemic treatment with capecitabine was initiated. After 3 cycles of chemotherapy, disease stabilization was observed in both the cutaneous lesions and the primary tumor. However, tumor progression was confirmed 8 months after diagnosis, leading to a transition to palliative and symptom-directed care. The patient died 11 months after the initial diagnosis.

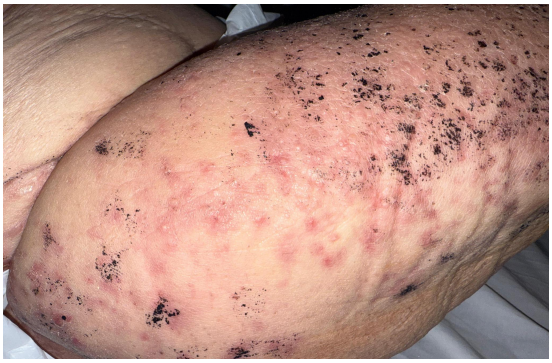

Figure 1. *Vesicular cutaneous lesions on the right lower extremity stump, initially interpreted as herpes zoster.*

DISCUSSION

Cutaneous metastases from colorectal carcinoma are an uncommon manifestation, with a reported incidence of less than 1% of cases, and typically reflect advanced systemic disease.[1–3] In most patients, they occur in the setting of known metastatic disease; therefore, their presentation as an initial manifestation or as a finding leading to the diagnosis of the primary tumor is exceptional.

From a clinical standpoint, colorectal cutaneous metastases most frequently involve the abdominal wall, perineal region, and surgical scars, a distribution associated with mechanisms of direct extension or tumor implantation.[4,7] However, less common sites have also been reported, including the chest, head and neck, and extremities; the latter represent a particularly rare presentation, as observed in the present patient.[7–9]

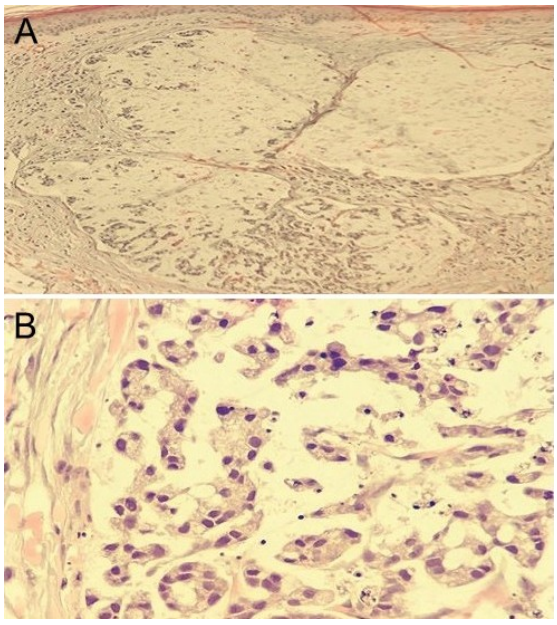

Figure 2. *Histopathology of the cutaneous lesion.* ***A.*** *Preserved epidermis with dermal infiltration by neoplastic cells associated with abundant extracellular mucin, consistent with mucinous adenocarcinoma (H&E, 40×).* ***B.*** *Tumor cells arranged in clusters within extracellular mucin pools, showing vesicular nuclei and prominent nucleoli (H&E, 400×).*

While nodular lesions are the most common clinical presentation, atypical variants that may mimic infectious or inflammatory conditions, including zosteriform patterns, have also been described.[4,8] This phenomenon may lead to diagnostic delays, particularly in immunocompromised patients, in whom cutaneous infections are more prevalent. In the present case, the initial suspicion of herpes zoster in a renal transplant recipient illustrates this diagnostic challenge.

Immunosuppression is a relevant factor in this context, not only due to the increased risk of de novo malignancies in transplant recipients, but also because of the potential for atypical and more aggressive clinical presentations.[10] This underscores the importance of maintaining a high index of suspicion for persistent or atypically evolving cutaneous lesions in this population.

Histopathology and immunohistochemistry play a central role in determining tumor origin, particularly when the primary tumor has not been previously identified. The presence of mucin lakes containing floating neoplastic cells, together with an immunoprofile characterized by CK20 and CDX2 positivity and CK7 negativity, supports a colorectal origin and helps exclude other common primary sites such as lung, breast, kidney, or gynecologic tumors.

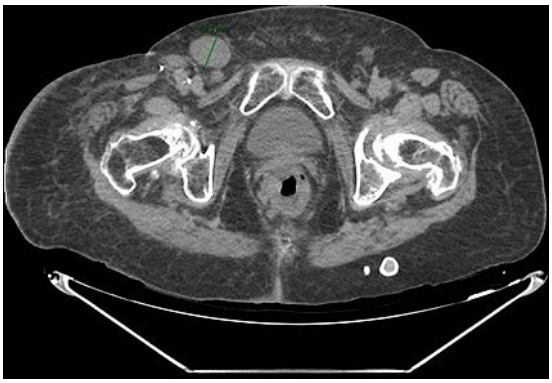

Figure 3. *CT scan of the abdomen and pelvis showing irregular mural thickening of the lower rectum with associated inguinal lymphadenopathy.*

Regarding prognosis, the development of cutaneous metastases in colorectal cancer is associated with limited survival, with reported medians ranging from 5 to 12 months from diagnosis.[4,5] Although treatment of colorectal cutaneous metastases is predominantly palliative, a multidisciplinary approach may contribute to improved symptom control and quality of life. In the present case, systemic chemotherapy with capecitabine initially achieved disease stabilization; however, tumor progression was subsequently observed at 8 months after diagnosis, with an overall survival of 11 months, consistent with the published literature.

This case adds several clinically relevant aspects to the existing literature, including metastatic involvement of an extremity, a pseudozosteriform clinical presentation, and the context of immunosuppression in a renal transplant recipient. It also highlights the importance of integrating clinical, histopathological, and imaging findings to achieve an accurate diagnosis and guide appropriate therapeutic management.

CONCLUSIONS

The presence of atypical, persistent, or unusually evolving cutaneous lesions, particularly in immunocompromised patients, should raise suspicion for metastatic involvement, even when the clinical presentation mimics common infectious entities such as herpes zoster.

Skin biopsy, complemented by histopathologic and immunohistochemical analysis, represents the key diagnostic tool for determining tumor origin in neoplasms with an initially unknown primary site.

This case underscores the importance of a comprehensive multidisciplinary diagnostic approach and the consideration of uncommon differential diagnoses in atypical clinical presentations. The integration of clinical, histopathological, and imaging findings is essential to guide therapeutic decision-

making and optimize the management of patients with advanced malignancy.

Author Contributions
AAA: conceptualization, methodology, research, drafting of the original manuscript, revision, and editing of the manuscript. IM: conceptualization, methodology, research, drafting of the original manuscript. JAP: supervision, project management, and manuscript revision. TFFQ: research, resources, and collection and curation of material. All authors approved the final version of the manuscript.

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