

# Cutaneous metastases of colorectal tumors: Report of two cases

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## ABSTRACT

Colorectal cancer metastases to the skin are rare and associated with a poor prognosis. We present two cases, a patient with high-grade B-cell lymphoma in multiple locations of the colon and rectum, with synchronous metastases to the skin, liver and stomach, and a patient with a signet ring cell adenocarcinoma of the cecum that developed metachronous lesions on the skin, colon and rectum.

**Keywords:** colorectal cancer, high-grade B-cell lymphoma, signet ring cell carcinoma, skin metastasis

## INTRODUCTION

Colorectal neoplasms can develop metastases in different locations and are related to the prognosis of the disease. The liver is the most frequent organ of presentation, followed by the lungs, peritoneal cavity and bone.<sup>1</sup> Cutaneous metastases are rare, constituting 3% of cases.<sup>2</sup> On the other hand, signet ring cell carcinoma and lymphoma are rare histological types of colorectal cancer and represent less than 1% of

cases.<sup>3,4</sup>

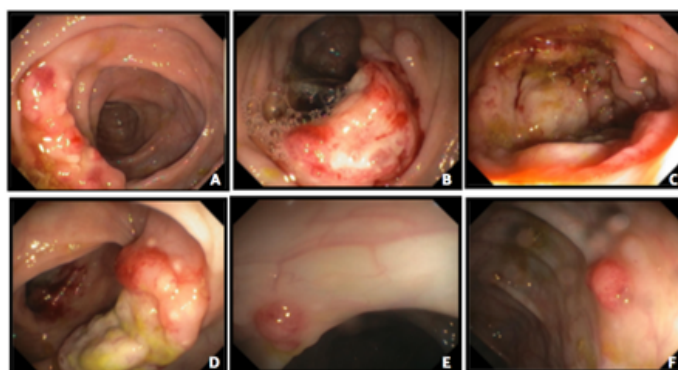
We present a signet ring cell carcinoma and a high-grade B-cell lymphoma of colorectal origin that developed synchronous and metachronous metastases, respectively, in multiple locations, including the skin.

## CASE 1

A 42-year-old female patient was admitted with diffuse abdominal pain and diarrhea of one month's duration with a weight loss of 10 kg.

Abdominal ultrasound on admission reported multiple focal anechoic lesions in the liver, spleen, peritoneum and adnexa, suggesting pseudomyxoma peritonei as the first diagnosis, followed by peritoneal carcinomatosis.

Colonoscopy revealed multiple exophytic masses with areas of ischemic excavation occupying  $\frac{3}{4}$  of the circumference in different locations of the colon (Fig. 1).

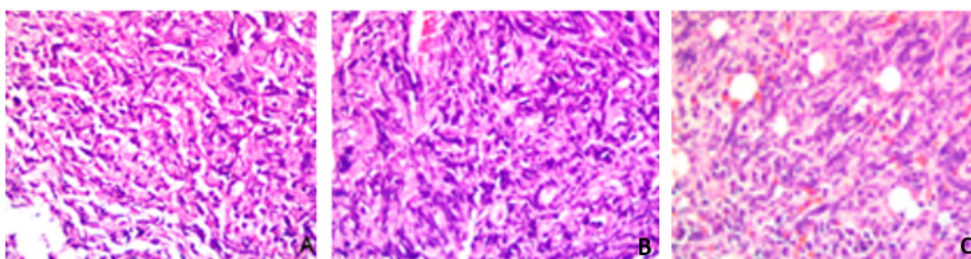


**Figure 1.** Colonoscopy. *A-D.* Ulcerated exophytic tumor lesions in the transverse, descending, sigmoid colon, and rectum. *E-F.* Satellite nodules.

The biopsy showed intermediate to large-sized cells, with angled, hyperchromatic nuclei, dense chromatin, discrete nucleoli and scant eosinophilic cytoplasm, whose immunophenotype in immunohistochemical studies was compatible with high-grade B-cell lymphoma. This diagnosis was confirmed in liver tissue samples (Fig. 2) and in a painless,

euchromic, indurated skin nodule located on the scalp (Fig. 3). Genetic mutations were found in c-MYC, BCL2 and BCL6.

The patient received a single cycle of R-CHOP chemotherapy, however, she died one month after diagnosis



**Figure 2.** Histopathology. *H&E, 40X.* High-grade B-cell lymphoid neoplasia in the transverse colon (*A*), rectum (*B*), and liver (*C*).

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**Figure 3.** A 3x3 cm metastatic skin nodule can be seen on the scalp.

## CASE 2

A 33-year-old male patient was admitted for diffuse abdominal pain of two months' duration associated with constipation, nausea, and weight loss of approximately 25 kg.

Abdominal CT showed inflammatory changes in the cecum and thickening of the colonic wall. Colonoscopy revealed an exophytic inflammatory mass occupying 100% of the circumference and 90% of the lumen of the cecum with involvement of the ileocecal valve.

The biopsy reported a malignant neoplasm composed of discohesive cells with a signet ring appearance, floating among amorphous amphophilic material with a mucinous appearance, which dissect the stromal fibers and compromise the entire thickness of the colonic wall. These findings were compatible with high-grade, poorly differentiated signet ring cell adenocarcinoma (Fig. 4).

A laparoscopic right colectomy with ileotransverse anastomosis was performed, removing an exophytic mass of approximately 5x7 cm that occluded 75% of the intestinal lumen.

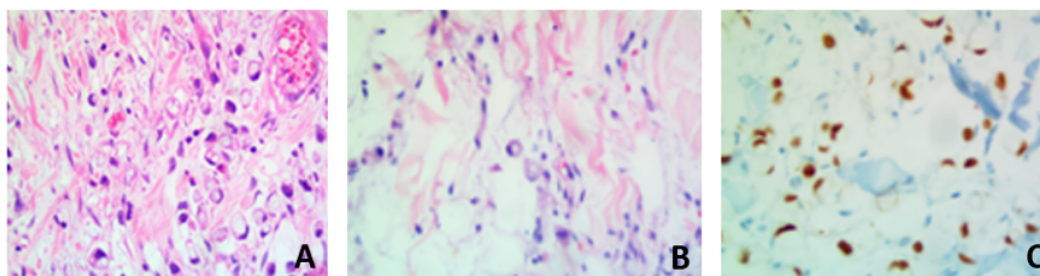
The patient subsequently received a cycle of FOLFOX.

In the control colonoscopy 19 months after the initial diagnosis, multiple metachronous lesions were found in all segments of the colon and rectum.

Computed tomography showed multiple sessile polyps in the transverse colon and anorectal junction and findings suggestive of peritoneal carcinomatosis.

In addition, two painless, firm, erythematous-based skin nodules were found in the interscapular and subscapular regions, whose biopsy reported metastatic adenocarcinoma with signet ring cells and positive immunohistochemical markers for colonic histogenesis (Fig. 4).

The patient refused further interventions despite the poor short-term prognosis and had no follow-up.



**Figure 4.** Histopathology. H&E, 40X. Discohesive cells with a signet ring appearance are evident in the colonic subepithelial stroma (A) and in the reticular dermis (B). C. Immunohistochemistry shows intense and diffuse nuclear reactivity for the CDX2 marker, an immunophenotype compatible with colonic histogenesis.

## DISCUSSION

Approximately 20% of patients with colorectal cancer have synchronous metastatic tumors and 30% develop them during follow-up.<sup>5</sup> Metastases are associated with a more aggressive nature of the tumor and indicate a worse prognosis. In this regard, a study showed that tumors without metastases had an overall survival rate twice as high as tumors with synchronous metastases (HR: 2.1; 95% CI: 1.2-3.7;  $p=0.01$ ).<sup>2</sup> The liver is the most frequent site of secondary lesions, followed by the lungs and peritoneum.<sup>6</sup>

Cutaneous metastases are rare, both in signet ring cell adenocarcinoma and lymphoma.<sup>3</sup> Mandzheva et al.<sup>2</sup> found only 5 cases published in PubMed of cutaneous metastases of signet ring cell adenocarcinoma, while Dehal et al.<sup>7</sup> reviewed 28 cases of cutaneous metastases of rectal cancer, in which adenocarcinoma was the underlying histology in all cases, although only 4 presented signet ring cells.

Regarding high-grade B-cell lymphoma, it has been described to comprise 0.66% of colorectal malignancies,<sup>8</sup> with no findings of synchronous or metachronous cutaneous metastases in the reviewed literature.

In most cases, it has been hypothesized that dissemination of colorectal adenocarcinoma to the skin occurs via the lymphatic route when lesions are adjacent to the primary tumor, whereas the development of lesions in distant locations is secondary to hematogenous dissemination.<sup>2</sup> In particular, the behavior of signet ring cell adenocarcinoma of the rectum is unpredictable, because anaplastic and undifferentiated cells have the capacity for diffuse infiltration and rapid dissemination to surrounding structures.<sup>3</sup>

A familial and environmental predisposition to develop synchronous and metachronous metastases has been identified. Kattan, et. al<sup>9</sup> detected gene expressions of miR-497 and BCL2 by RT-PCR in 106 patients with high-grade B-cell lymphomas, finding an up-regulation of BCL2 in metastatic samples (median = 1.16; 95% CI 1.09–1.60) compared to non-metastatic samples (median = 1.02; 95% CI 0.89–1.25; p<0.001). In patients with colorectal cancer, this has been associated with pathological grade, clinical stage, overall survival, and disease-free survival. In our patient, genetic mutations were found in c-MYC, BCL2, and BCL6.

## CONCLUSIONS

Metastases in colorectal cancer occur in a significant number of patients and are associated with poor short-term survival. Although the most frequently affected organ is the liver, metastases in uncommon locations such as the skin are often associated with rapid clinical deterioration and high mortality, as they are usually associated with secondary lesions in other locations.

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