

# Infarct Like Necrosis of Colorectal Liver Metastasis Without Chemotherapy: A Rare Phenomenon

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**ABSTRACT:** Usual type necrosis (UN) and infarct like necrosis (ILN) occur in CRLMs. ILN is a rare form of necrosis in colorectal liver metastases which is usually seen following chemotherapy. De novo occurrence of ILN is a very rare phenomenon. ILN in CRLM without adjuvant chemotherapy following colorectal resection was not described previously. We describe the presence of complete ILN in a solitary metachronous liver metastasis from right colonic adenocarcinoma without prior chemotherapy.

**KEYWORDS:** Infarct like necrosis, Adenocarcinoma, Colorectal liver metastases

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## Introduction

Surgery and chemotherapy are the mainstay of treatment in colorectal liver metastases (CRLM). Necrosis observed in solid tumors may result from chronic ischemic injury. Two patterns of tumor necrosis have been described in CRLM<sup>1</sup>; the usual type (UN) or “dirty” necrosis and the infarct like necrosis (ILN) consisting of larger zonal areas of necrosis with surrounding fibrosis.<sup>1</sup> Though ILN has been described<sup>2</sup> after perioperative chemotherapy, de novo occurrence is rare. ILN in CRLM without adjuvant chemotherapy following colorectal resection was not described previously. This report describes the presence of complete ILN in a solitary metachronous CRLM without prior chemotherapy.

## Case Presentation

A 53-year-old male was referred with a solitary liver metastasis detected on surveillance ultrasonography 1 year after laparoscopic extended right hemicolectomy for a pT2pN0 moderately differentiated adenocarcinoma. He had not received adjuvant chemotherapy. On presentation with CRLM serum CEA level was 3.5 ng/dl. Abdominal CT and MRI (Figure 1) confirmed a solitary lesion of 2.1 cm in segment VIII. Liver biopsy confirmed the presence of a metastatic deposit of an adenocarcinoma. The morphological features were in keeping with a metastatic deposit of a colorectal adenocarcinoma (Figure 2). He underwent a non-anatomical resection of the lesion (Figure 3) and had an uneventful recovery. Histopathology showed complete infarct like tumor necrosis (ILN) with microscopically

negative resection margins (Figure 4). The background liver showed moderate steatohepatitis. He proceeded to oncology for adjuvant therapy.

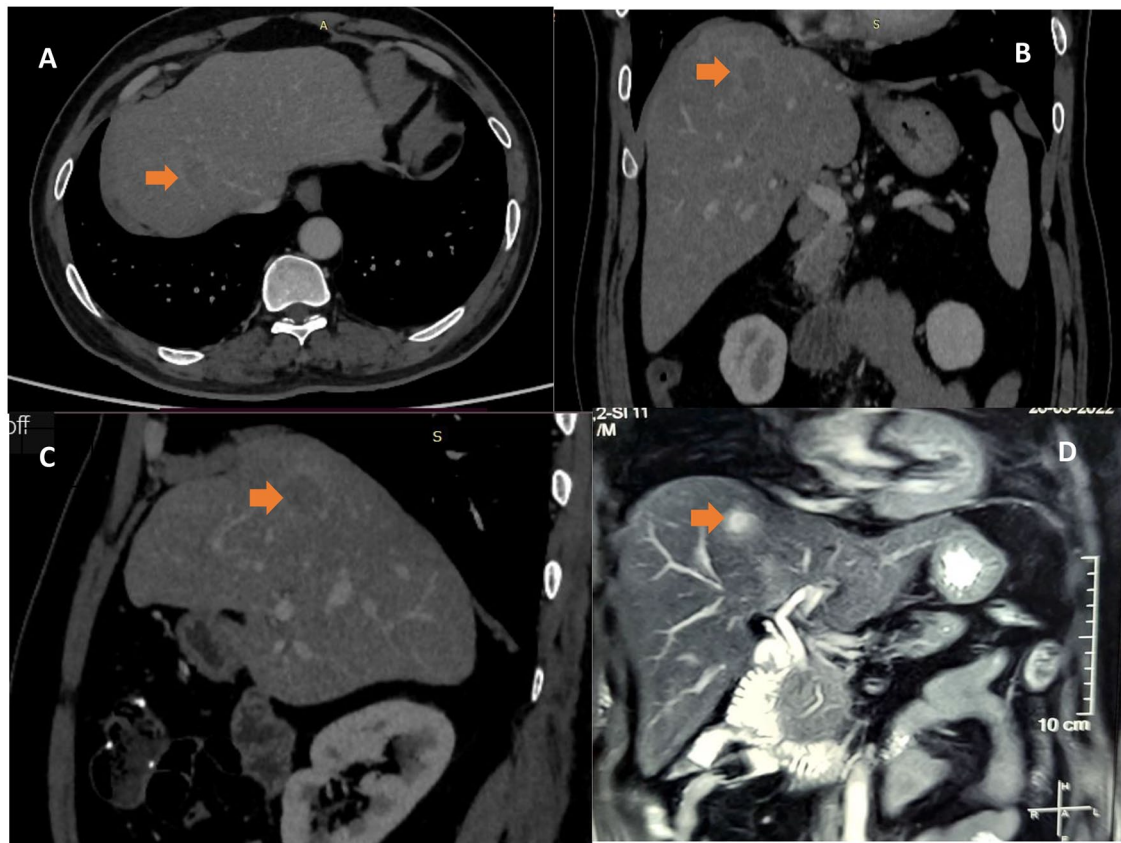
## Discussion

Usual type necrosis (UN) and infarct like necrosis (ILN) occur in CRLMs.<sup>1</sup> UN, the common variant, shows patchy distribution of nuclear debris with necrosis admixed and bordered by viable cells. ILN seen following preoperative chemotherapy, is characterized by confluent areas of eosinophilic cytoplasmic remnants with absent or minimal admixed nuclear debris and is associated with superior disease-free survival<sup>1</sup> compared to UN. Studies show that ILN accounts for 11% to 30% of necrosis in CRLMs and occurs almost exclusively in the context of chemotherapy.<sup>1,3</sup> UN is believed to occur secondary to hypoxia as the tumor outgrows its vascular supply<sup>1,4</sup> while ILN is attributed to the cytotoxic effects of chemotherapy.<sup>1,3</sup> The absence of residual viable tumor in ILN may result in a sharper tumor-liver interface on CT scan.<sup>5</sup>

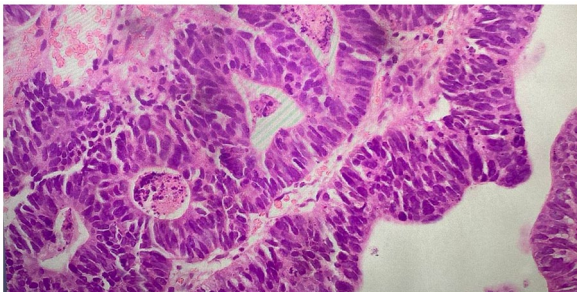
Of interest was the characteristic histopathological features of complete ILN seen in the resected CRLM despite him not having received cytotoxic chemotherapy or alternative native therapy.

The zone of necrosis surrounded by fibrosis and a chronic inflammatory cell infiltrate of lymphocytes and histiocytes and focal granuloma formation seen here are like those described by Chang et al who suggested that ILN represents an intermediate stage in the evolution from viable tumor to fibrosis during chemotherapy.<sup>1</sup>





**Figure 1.** CT/MRI Liver showing solitary segment VIII metastasis (CT (A) axial, (B) coronal, (C) sagittal views, and (D) liver MRI).



**Figure 2.** Liver biopsy showed an adenocarcinoma that was morphologically in keeping with a metastatic deposit of a colorectal adenocarcinoma (Hematoxylin and eosin x 400).

Complete tumor necrosis could represent spontaneous regression. Spontaneous regression of CRLMs have been documented<sup>6</sup> though histopathological confirmation is rarely available. A systematic review identified 9 cases of spontaneous CRLM regression between 1900 and 2005.<sup>6</sup> The presence of liver metastasis had been confirmed by histology in 3 of the 9 cases.<sup>7-9</sup> Histological assessment of the regressed tumor was performed in only one of the 3 cases, and showed marked chronic inflammation and coagulative necrosis with a few viable tumor cells.<sup>8</sup> Though not described as such, the histological features described by Matsuki et al were compatible with ILN.<sup>10</sup>

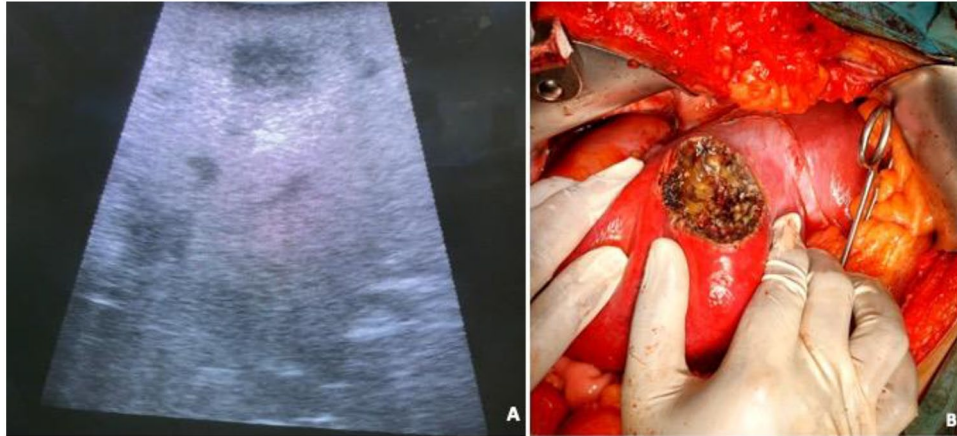
The details of these cases are summarized in Table 1

Immunological, genetic, metabolic, hormonal and psychological factors may play a role in spontaneous tumor

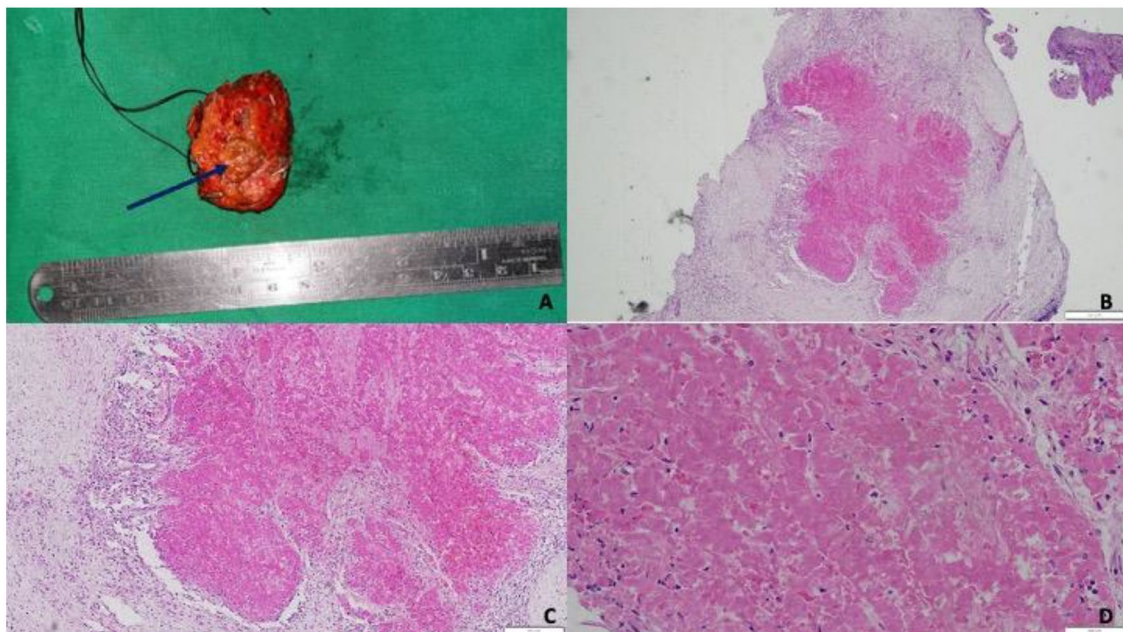
regression.<sup>6</sup> Epigenetic mechanisms and repression of telomerase activity have been considered as possible mechanisms of spontaneous regression, with a few cases of colorectal carcinoma with evidence of regression being associated with family history for both the development of cancer and its spontaneous regression.<sup>6,11</sup>

A medullary variant of colonic cancer characterized by prominent lymphocytic infiltrates has shown complete nodal tumor regression,<sup>12</sup> suggesting immunological mediated tumor regression. Interestingly the primary tumor in this case showed a moderate lymphocytic infiltrate, though this was not seen in the metastatic deposit. Some cases have shown regression following surgery. The dissemination of tumor cells via the blood, lymphatics or trans-coelomically during resection is postulated to result in a tumor-antigen load of sufficient magnitude to stimulate a substantial anti-tumor immune response.<sup>6,13</sup> However, in this case the liver metastasis was identified several months after surgery for the primary tumor.

This patient had a previous liver biopsy that confirmed the presence of a metastatic deposit in the liver. Three of the cases described above also had a previous liver biopsy.<sup>7-9</sup> The effects brought about by the biopsy may have contributed to regression of this tumor. Cases of tumor regression following biopsy have been reported in cancer at other sites<sup>14</sup> and is thought to be brought about by activation of the immune response due to the injury brought about by the biopsy or destruction or emboli of the feeding artery of the tumor by the core needle biopsy.



**Figure 3.** (A) Intraoperative ultrasound (IOUS) depicting segment VIII lesion and (B) intraoperative view of segment VIII non anatomical resection.



**Figure 4.** (A) The macroscopic examination of the liver showed a 15 mm nodule (blue arrow), (B) microscopic examination showed large confluent areas of eosinophilic cytoplasmic remnants surrounded by fibrosis (Hematoxylin and eosin x 40), (C) the areas of necrosis were surrounded by a chronic inflammatory cell infiltrate comprising lymphocytes and histiocytes (Hematoxylin and eosin x 100), and (D) the necrotic areas showed ghost outlines of the tumor cells. Nuclear debris was not prominent.

**Table 1.** Details of histologically confirmed colorectal liver metastasis with clinical/histological evidence of regression.

AUTHOR (REFERENCE)	AGE/SEX	INITIAL PRESENTATION	HISTOLOGICAL TYPE/GRADE OF PRIMARY CARCINOMA	HISTOLOGICAL FEATURES OF LIVER METASTASIS	HISTOLOGICAL FEATURES OF REGRESSED TUMOR IN LIVER	DURATION OF FOLLOW UP
Francis et al <sup>7</sup>	69, M	Synchronous rectosigmoid junction tumor and liver metastasis	Moderate to poorly differentiated adenocarcinoma	Adenocarcinoma	Not confirmed histologically.	11 years
Ikuta et al <sup>8</sup>	60, M	Synchronous lower rectal tumor and liver metastasis	Adenosquamous carcinoma	Adenosquamous carcinoma	Chronic inflammation and coagulative necrosis with a few nodules of residual tumor.	18 months Died due to peritoneal carcinomatosis.

(Continued)

Table 1. (Continued)

AUTHOR (REFERENCE)	AGE/SEX	INITIAL PRESENTATION	HISTOLOGICAL TYPE/GRADE OF PRIMARY CARCINOMA	HISTOLOGICAL FEATURES OF LIVER METASTASIS	HISTOLOGICAL FEATURES OF REGRESSED TUMOR IN LIVER	DURATION OF FOLLOW UP
Rankin et al <sup>9</sup>	44, M	Synchronous lower rectal tumor and liver metastasis in a patient with familial polyposis	Grade 4 dedifferentiated adenocarcinoma	Poorly differentiated carcinoma	Not confirmed histologically.	10 years
Matsuki et al <sup>10</sup>	72, F	Metachronous liver metastasis detected after surgery for ascending colon tumor.	Moderately differentiated adenocarcinoma	Not assessed	Necrotic columnar epithelial cells surrounded by histiocytes, inflammatory cells and fibrosis.	13 months
Index case	53, M	Metachronous liver metastasis detected after surgery for tumor in hepatic flexure.	Moderately differentiated adenocarcinoma	Moderately differentiated adenocarcinoma	Necrotic columnar epithelial cells surrounded by chronic inflammation and fibrosis.	12 months

Spontaneous tumor regression has also been reported in hepatocellular carcinoma and metastatic renal cell carcinoma.<sup>15,16</sup> Sepsis induced immune enhancement has been postulated to contribute to spontaneous cancer regression<sup>6</sup> though evidence for this is scanty. The presence of ILN which is typically seen in response to chemotherapy supports the presence of regression in this case. However, a definite explanation for this cannot be given.

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### Author Contributions

DS involved in conceptualization of the manuscript. DS, HW prepared the initial draft of the manuscript. DS, VD and SS were involved in the surgical care of the patient. US involved in oncological management of the patient. HW and PA were involved in the pathological diagnosis. SS reviewed and critically revised the manuscript. All authors read and approved the final manuscript.

### Availability of Data and Material

Data used in this analysis is available from the corresponding author on reasonable request.

### Consent

Informed written consent was obtained from patient for publication of this case report and accompanying images.

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