



Not All Cirrhosis is Created Equal: A Rare Case of Regorafenib-induced Pseudocirrhosis

Patrick J. Carey, MD,¹ Nimish Thakral, MD,² Venkata Rajesh Konjeti, MD,² Alla Y. Grigorian, MD, PhD²

¹University of Kentucky COM, Department of Internal Medicine

²University of Kentucky, Division of Digestive Diseases and Nutrition



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INTRODUCTION

- Chemotherapy has been shown to improve survival rates in metastatic colorectal cancer (CRC), but it can be associated with severe side effects.
- Regorafenib, an oral multikinase inhibitor, is commonly used as third- or fourth-line chemotherapy for refractory CRC. Rare reports of pseudocirrhosis with regorafenib have been reported in the literature.
- Pseudocirrhosis = radiological appearance of cirrhotic liver morphology without histological evidence of fibrosis
- We present a case of regorafenib-induced pseudocirrhosis in a patient with advanced metastatic CRC

CASE PRESENTATION

A 39-year-old male with stage IV adenocarcinoma of the colon with metastatic liver lesions presented with a few days of diffuse abdominal pain and mild jaundice. He had started regorafenib 4 months prior after failing 3 prior chemo/immunotherapy regimens. Prior chemo/immunotherapy regimens were FOLFOX + panitumumab, FOLFIRI + panitumumab, and trifluridine/tipiracil + bevacizumab.

Physical exam was notable for jaundice, scleral icterus, and diffuse abdominal tenderness without concern for acute abdomen.

EVALUATION

- Initial labs
 - AST 55 IU/L
 - ALT 39 IU/L
 - Alkaline phosphatase 594 IU/L
 - Total bilirubin 5.5 mg/dL (direct 3.8)
 - GGT 272 IU/L
 - INR 1.4
 - Platelet count 74,000/ μ L
 - IgG 2185, IgG4 102.8 (both elevated)
 - ANA 1:640 (speckled pattern)
 - Anti-mitochondrial Ab, anti-smooth muscle Ab, anti-liver kidney Ab negative
- Imaging
 - CT-abdomen/pelvis: cirrhotic liver morphology, ascites, splenomegaly, non-obstructed biliary tract
 - MRCP: interval increase in hepatic metastases burden with non-obstructed biliary tract
- Infectious workup was negative
- Ascitic fluid studies with SAAG of 2 without evidence of SBP or malignancy

EVALUATION (CONTINUED)

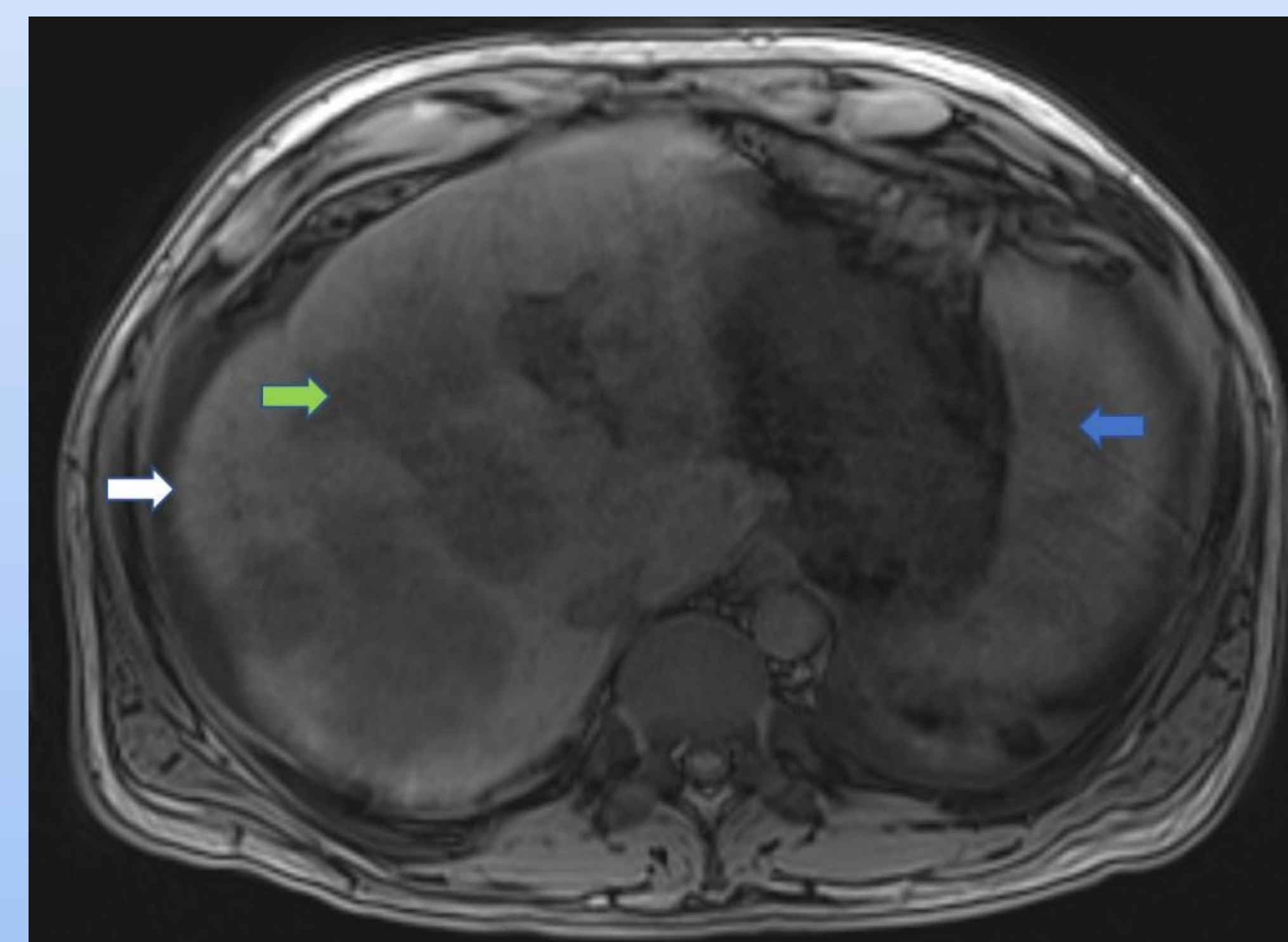


Figure 1: MRI abdomen showing nodular liver contour (white arrow), metastatic disease (green arrow), and splenomegaly (blue arrow)

- Liver biopsy
 - Normal lobular architecture
 - Severe cholestasis
 - Focally prominent sinusoidal dilatation
 - Negative for cirrhosis, bridging fibrosis, sinusoidal obstruction, fatty change, or centrilobular necrosis

CLINICAL COURSE

- The patient's bilirubin continued to increase during admission, so he underwent ERCP with pre-emptive biliary stenting. He was also started on furosemide, spironolactone, and ursodiol.
- The patient was diagnosed with regorafenib-induced pseudocirrhosis.
- Bilirubin was 8.2 the day of discharge and continued to increase to 11.0 two weeks after discharge. Due to his continuously increasing bilirubin, no further chemotherapy options were available.
- He was offered hospice care.

DISCUSSION

- This patient demonstrated cirrhotic liver morphology and portal hypertension without evidence of fibrosis on liver biopsy. Development of these changes 4 months after starting regorafenib leads to the diagnosis of regorafenib-induced pseudocirrhosis.
- Concomitant cholestasis and sinusoidal dilation in this case are indicative of post-sinusoidal pathology.
- Regorafenib-induced pseudocirrhosis is an example of idiosyncratic drug-induced liver injury.
- Some studies postulate that nodular regenerative hyperplasia (NRH) in the setting of progressing liver metastases is the causative pathology. However, no evidence of NRH was found in our case.

CONCLUSION

- This case represents a rare example of regorafenib-induced pseudocirrhosis, which is an idiosyncratic drug-induced liver injury.
- Increased CRC incidence necessitates higher suspicion and awareness about potential adverse effects of chemotherapy drugs.

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