

Hidden in Plain Sight: Isolated Right Upper Quadrant Pain Revealing Triple Synchronous Primary Colorectal Carcinomas Including Aggressive Signet Ring Cell Adenocarcinoma - A Case Report

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Abstract

Background: Synchronous colorectal carcinoma (SCRC), defined as two or more distinct primary colorectal malignancies diagnosed simultaneously or within six months is rare in patients with colorectal cancer. The coexistence of multiple synchronous tumors with signet ring cell differentiation is exceedingly rare and presents significant diagnostic and therapeutic challenges because of its aggressive biology and poor prognosis.

Case Presentation: A 75-year-old woman with remote breast cancer, a previously identified tubulovillous adenoma lost to surveillance, and other comorbidities presented with isolated right upper quadrant abdominal (RUQ) pain and nausea. Labs and imaging of the abdomen and pelvis were unremarkable. Esophagogastroduodenoscopy (EGD) was normal. Colonoscopy identified three benign polyps and three separate malignant-appearing colonic masses involving the distal transverse colon, hepatic flexure, and transverse colon. Histopathology revealed poorly differentiated invasive adenocarcinoma with prominent signet ring cell features in two lesions, while the third demonstrated a distinctly different morphology consistent with a separate synchronous primary colorectal carcinoma.

Conclusion: This case underscores that isolated abdominal pain with nondiagnostic imaging does not exclude colorectal malignancy, particularly in patients with previously identified advanced adenomas who have been lost to surveillance. Complete colonoscopic evaluation remains essential for detecting synchronous colorectal cancers, establishing the diagnosis, and guiding definitive multidisciplinary management.

Keywords: *Colorectal cancer; Synchronous colorectal carcinoma; Signet ring cell carcinoma; Colonoscopy; Advanced adenoma; Right upper quadrant pain; Anemia; Colonoscopy; Endoscopy; Melena*

1. Introduction

Colorectal cancer (CRC) remains a major public health challenge worldwide [1]. According to GLOBOCAN 2022, CRC represents the third most frequently diagnosed malignancy and the second leading cause of cancer-related mortality, accounting for nearly two million new cases and approximately one million deaths annually [1]. In the United States, CRC remains the second leading cause of cancer-related death despite improvements in screening and treatment [2]. Most colorectal cancers arise through the adenoma-carcinoma sequence, a multistep process driven by cumulative genetic and epigenetic alterations over many years [3]. Colonoscopic surveillance with removal of advanced adenomas significantly reduces both colorectal cancer incidence and mortality [4]. Unfortunately, patients lost to surveillance remain at increased risk for progression to invasive carcinoma [5].

Synchronous colorectal carcinoma (SCRC), defined as two or more distinct primary colorectal cancers diagnosed simultaneously or within six months of each other, occurs in approximately 2%-8% of colorectal cancer patients [6]. Recognition is clinically important because additional lesions frequently alter operative strategy, lymph node dissection, pathologic staging, postoperative surveillance, and prognosis [7].

Signet ring cell adenocarcinoma represents one of the rarest histologic subtypes of colorectal cancer, accounting for fewer than 1% of all colorectal malignancies [8]. Compared with conventional adenocarcinoma, signet ring tumors are characterized by diffuse infiltration, poor differentiation, advanced stage at diagnosis, increased lymphovascular invasion, higher rates of peritoneal dissemination, and substantially worse survival [9]. The coexistence of multiple synchronous colorectal carcinomas containing signet ring cell histology is exceptionally uncommon [10].

Furthermore, presentation with isolated right upper quadrant pain and relatively normal laboratory findings may delay diagnosis. We report an unusual case of triple synchronous primary colorectal carcinomas, including poorly differentiated signet ring cell adenocarcinoma, presenting with isolated right upper quadrant (RUQ) abdominal pain despite nondiagnostic computed tomography and minimal laboratory abnormalities.

2. Case Presentation

A 75-year-old woman presented to the emergency department with a three-day history of RUQ abdominal pain associated with nausea. The pain was described as constant, throbbing, localized, and rated 5/10 in severity. Acetaminophen partially relieved her symptoms, while meals did not influence the pain.

Her medical history included a 35-pack-year smoking history, COPD requiring 2 L/min supplemental oxygen, hypertension (HTN), hyperlipidemia (HLD), atrial fibrillation treated with apixaban and clopidogrel, T2DM, gastroesophageal reflux disease (GERD), and remote right breast cancer treated with lumpectomy and radiation therapy. She also reported chronic constipation for approximately four years, managed with intermittent bisacodyl and recently polyethylene glycol with symptomatic improvement. Three years earlier, colonoscopy demonstrated multiple benign adenomatous polyps and a 1 cm × 2 cm tubulovillous adenoma. She was referred for surgical evaluation but was subsequently lost to follow-up.

On admission, she denied hematochezia, melena, hematemesis, fever, chills, weight loss, early satiety, altered stool caliber, family history of colorectal cancer, or recent illness. On examination, vital signs were normal. Abdominal examination demonstrated mild RUQ tenderness without rebound or guarding.

Initial laboratory evaluation demonstrated mild chronic anemia with hemoglobin in the 10 g/dL range and hematocrit in the low 30% range. Mean corpuscular volume (MCV) measured approximately 96 fL. White blood cell count, platelet count, comprehensive metabolic panel, liver function tests, lipase, and urinalysis were unremarkable. CT of the abdomen and pelvis demonstrated constipation and nonspecific hypoattenuation involving the pancreatic head but failed to identify an obvious colorectal lesion or metastatic disease.

TABLE 1. Complete Blood Count (CBC) shows normocytic anemia.

Test / Reference Range	07/09/26 06:00	07/10/26 08:00	07/12/26 06:30	07/13/26 05:00	07/14/26 05:00	07/15/26 05:00	07/16/26 06:00
WBC (4.5-11.0 th/uL)	5.2	3.7 L	4.0 L	4.4 L	4.8	4.3 L	5.4
RBC (4.20-5.40 mil/uL)	3.47 L	3.55 L	3.25 L	3.26 L	3.11 L	3.18 L	3.32 L
Hgb (12.0-16.0 g/dL)	10.5 L	10.6 L	9.9 L	9.8 L	9.5 L	9.6 L	10.0 L
Hct (37.0%-47.0 %)	33.2 L	33.5 L	30.4 L	31.0 L	29.4 L	30.0 L	31.6 L
MCV (81-99 fL)	95.7	94.4	93.5	95.1	94.5	94.3	95.2
MCH (27.0-31.0 pg)	30.3	29.9	30.5	30.1	30.5	30.2	30.1
MCHC (33.0-37.0 g/dL)	31.6 L	31.6 L	32.6 L	31.6 L	32.3	32.0 L	31.6 L
RDW (11.5%-14.5 %)	13.3	13.2	13.3	13.2	13.6	13.5	13.5
Platelet Count (150-450 th/uL)	122 L	118 L	131 L	116 L	121 L	114 L	119 L
MPV (7.4-10.4 fL)	12.2 H	12.1 H	11.9 H	11.8 H	12.0 H	12.0 H	12.0 H

Immature Gran % (Auto) (0.0%-1.0 %)	0.4		0.3				
Neut % (Auto) (40.0%-80.0 %)	54.4		60.4				
Lymph % (Auto) (20.0%-40.0 %)	34.6		32.0				
Mono % (Auto) (0.0%-10.0 %)	7.9		4.8				
Eos % (Auto)	1.9		1.5				

TABLE 2. Basic Metabolic Panel (BMP) is grossly unremarkable.

Test / Reference Range	07/13/ 26 15:55	07/14/ 26 05:00	07/14/ 26 05:38	07/14/ 26 20:39	07/15/ 26 05:00	07/15/ 26 05:21	07/15/ 26 10:29	07/15/ 26 16:34	07/15/ 26 20:20	07/16/ 26 05:49	07/16/ 26 06:00
Sodium (137-145 mmol/L)		143			142						142
Potassium (3.5-5.0 mmol/L)		4.4 A			4.1						4.1
Chloride (98-107 mmol/L)		113 H			109 H						109 H
Carbon Dioxide (22-30 mmol/L)		24			26						27
Anion Gap (5-15 mmol/L)		6			7						6
BUN (7.0-17.0 mg/dL)		8.0			12.0						21.0 H
Creatinine (0.7-1.2 mg/dL)		1.4 H			1.6 H						1.3 H
Estimated GFR		38.5			32.8						42.1

(>59 mL/min/1.73 m ²)											
Glucose (65-105 mg/dL)		96			104						96
POC Glucose (75-110 mg/dL)	80		105	131 H	109	143 H	129 H	137 H	106		8
Calcium (8.4-10.2 mg/dL)		7.8 L			8.3 L						8.2 L
Magnesium											



FIG. 1. Abdominal/ pelvic CT: unremarkable, no enlarged lymph nodes, no colonic obstructions. Given persistent symptoms and the history of an unresected advanced adenoma, gastroenterology was consulted. EGD was normal.

Colonoscopy revealed three benign polyps measuring less than 8 mm in addition to three distinct malignant-appearing masses involving the distal transverse colon (part 2), hepatic flexure (part 3), and transverse colon.



FIG. 2. Distal transverse colon mass.

Histopathologic examination demonstrated benign adenomatous polyps in all three small polyps. The distal transverse colon demonstrated poorly differentiated invasive adenocarcinoma with prominent signet ring cell morphology; the hepatic flexure showed poorly differentiated invasive adenocarcinoma with signet ring cell differentiation involving; the third lesion within the transverse colon exhibited markedly different histologic morphology compatible with an independent synchronous primary colorectal carcinoma.

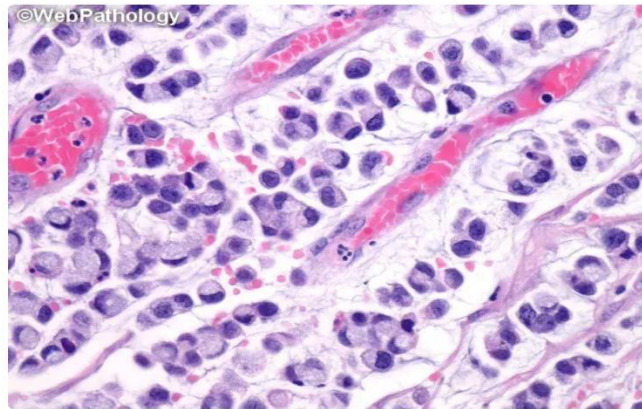


FIG. 3. Signet ring cell carcinoma of colon.

Signet ring cell carcinoma of colon showing **classic histologic pattern**. The tumor cells are arranged singly, in clusters, and anastomosing cords. The **intracellular mucin blob** pushes the nucleus to one side, flattening it against the cytoplasmic membrane, and creates a signet ring appearance. This case shows both intracellular mucin as well as **extracellular mucin lakes**.

<https://www.webpathology.com/images/gastrointestinal/large-bowel/colo-rectal-adenocarcinoma/42744>

CT of the chest and head demonstrated no evidence of distant metastatic disease. The patient was discharged in stable condition with urgent referral to colorectal surgery and oncology for definitive management.

3. Discussion

Colorectal cancer is responsible for approximately 10% of all newly diagnosed cancers worldwide [11,13]. More than 150,000 Americans are diagnosed annually, with nearly 53,000 deaths expected each year [12,13]. Despite declining incidence among older adults because of screening, incidence continues to rise among younger individuals [14]. Most colorectal cancers develop from adenomatous polyps over 10-15 years [15]. Advanced adenomas, including tubulovillous adenomas, villous adenomas, lesions ≥ 10 mm, or those with high-grade dysplasia, carry substantially greater malignant potential than conventional tubular adenomas [16,17]. Our patient previously had an advanced tubulovillous adenoma but failed surveillance, illustrating the importance of guideline-directed follow-up.

Synchronous colorectal carcinoma represents an uncommon but clinically important entity occurring in approximately 2%-8% of colorectal cancer patients [18]. The diagnosis requires anatomically distinct tumors, separate pathologic origins, exclusion of local extension or metastatic spread [19]. Failure to identify additional synchronous lesions may lead to incomplete resection and worse oncologic outcomes [20]. Complete colonoscopy before surgery is therefore strongly recommended whenever technically feasible [21].

Signet ring cell adenocarcinoma is defined by the World Health Organization as tumors containing more than 50% signet ring cells [22]. Compared with conventional adenocarcinoma, these tumors demonstrate: younger age at presentation, diffuse bowel wall infiltration, advanced T stage, higher nodal involvement, increased peritoneal metastases, lower resectability, poorer response to therapy, significantly reduced overall survival [23,24]. Reported five-year survival rates remain below 30% compared with more than 60% for conventional adenocarcinoma [25].

This case is a unique presentation as there are several distinguished features such as isolated right upper quadrant pain without classic colorectal symptoms, non-diagnostic CT imaging, previous advanced adenoma lost to surveillance, three independent primary colorectal malignancies, two demonstrating aggressive signet ring histology, and absence of metastatic disease despite multifocal cancers. Only a few published reports describe triple synchronous colorectal carcinomas containing signet ring cell differentiation [26,27].

Current U.S. Multi-Society Task Force guidelines recommend surveillance colonoscopy approximately three years following removal of advanced adenomas [28]. Loss to surveillance remains one of the strongest modifiable risk factors for interval colorectal cancer [29]. This patient's delayed follow-up likely allowed progression from advanced adenoma to invasive multifocal carcinoma [30].

Clinicians should maintain suspicion for colorectal malignancy in elderly patients with persistent abdominal pain despite negative cross-sectional imaging [31]. A normal CT scan does not exclude colorectal cancer, particularly early mucosal lesions or synchronous tumors [32]. Complete colonoscopic evaluation remains the diagnostic gold standard. Multidisciplinary management involving gastroenterology, colorectal surgery, oncology, radiology, and pathology is essential because treatment strategies differ substantially depending on the number and location of primary tumors.

4. Conclusion

This case demonstrates an exceptionally rare presentation of triple synchronous primary colorectal carcinomas, including poorly differentiated signet ring cell adenocarcinoma, presenting solely with right upper quadrant abdominal pain. Despite reassuring laboratory studies and non-diagnostic CT, colonoscopy identified multiple independent primary malignancies that substantially altered clinical management. The case reinforces the critical importance of surveillance colonoscopy after advanced adenomas and emphasizes that persistent abdominal symptoms should not be dismissed solely because cross-sectional imaging is unrevealing. Early recognition of synchronous colorectal carcinoma allows appropriate staging, surgical planning, and improved oncologic outcomes.

5. Contributors

All authors contributed to the conception, literature review, manuscript preparation, critical revision, and final approval of the manuscript. All authors accept responsibility for the integrity and accuracy of the work.

6. Competing Interests

The authors declare no competing interests.

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