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You See, I See, We All See UC

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Introduction

A reported 1.3% of the adult US population carry a diagnosis of Inflammatory Bowel Disease. (IBD) (1) While the majority of patients suffer from ulcerative colitis or Crohn's disease, a significant minority carry a diagnosis of indeterminate colitis. Age (45 or older), race/ethnicity (Hispanic or non-Hispanic white), education (less than high school diploma), unemployment, US birth, poverty and living in suburban areas made individuals more likely to report this history.

The increased risk of colorectal cancer (CRC) in ulcerative colitis (UC) is well documented. Increased risk begins to increase 8-10 years post-diagnosis, although overall incidence in UC patients has declined significantly since the correlation was first described in 1925. This is likely due to advances in screening and surveillance. Among those who develop CRC, disease duration and degree of colitis are most closely correlated, though family history, pseudopolyps, significant inflammation on histology and primary sclerosing cholangitis also increase a patient's risk. (2)

Most UC patients who develop CRC do so >10 years after initial diagnosis. Although lymphoma accounts for <1% of all colon cancers, there is an association between ulcerative colitis and EBV-positive non-Hodgkin's lymphoma (including diffuse B-cell lymphoma). (3,4) Patients who develop the disease typically have a history of immunosuppressive therapy, EBV+ lymphocytes and prolonged IBD. (5) However, not all patients meet these criteria. (5) It is crucial that neoplastic processes be considered early in the disease course of UC patients, as colorectal non-Hodgkin's lymphoma has been shown to have a 5-year survival rate of <40%. One of the most aggressive forms, diffuse-B cell lymphoma, has a median survival of approximately two years. (7)

Toxic megacolon, perforation and acute hemorrhage are the most worrisome emergencies in patients with UC. Suspicion of such emergencies arise when patients are hemodynamically unstable and may have findings of air on plain films. Other more insidious processes like malignancy may require a CT scan to declare themselves.

Patient Presentation

A 21 year old male with history of biopsy-proven ulcerative colitis diagnosed via colonoscopy (Image 1) six months prior presented to an outside Emergency Department with 5-6 daily episodes of bloody diarrhea, left sided sharp abdominal pain and abdominal mass with "tightness" over a week. These symptoms had recently worsened but had persisted since diagnosis. His review of systems was otherwise negative. Outpatient management with sulfasalazine, balsalazide and prednisone did not provide relief. He had been making monthly outpatient visits and did not receive further imaging.

In the ED he was afebrile and hemodynamically stable. Physical exam was significant for tenderness of the left upper and lower quadrants, palpable mass on the left that crossed midline and positive guaiac test. CBC, BMP, LFT and inflammatory markers were significant for leukocytosis (14.5), mild normocytic anemia (Hgb 12.6), elevated CRP (2.4) and Sedimentation Rate (45). Abdominal plain films (Image 2) showed a non-obstructive bowel gas pattern without evidence of colonic distension. Truelove and Witts score (used for determining UC severity) was mild/severe.(8)

Although initially suspected to be a UC flare, CT revealed significant concentric thickening of the proximal sigmoid colon up to the entire descending colon and splenic flexure with a masslike lesion measuring 24 cm x 10 cm intramurally and mildly enlarged pericolonic lymph nodes (Image 3 and 4) which was concerning for a neoplastic process. Patient was admitted on IV antibiotics with consideration for ulcerative colitis flare but high suspicion for neoplastic process.

Sigmoidoscopy was significant for severe left sided colitis (Mayo Score 3) and a discrete, friable mass. (Image 5, 6, 7) Biopsy confirmed EBV+ diffuse B-cell lymphoma with a high proliferative fraction and MYC translocation without Bcl rearrangement. Initial pathology was concerning for Burkitt lymphoma particularly in the setting of a MYC translocation, though this was eventually ruled out due to gene expression and morphology. (Figure 4 and 5) Genetic cytology determined that patient did not possess a double expressor phenotype. Bone marrow aspirate was hypocellular for age but showed no evidence of dysplasia. CSF was negative for malignant cells.

The patient was initiated on R-EPOCH with plans for possible eventual surgical debulking. On day 13 of his stay, he appeared toxic with acute abdominal pain. Although imaging showed colonic distension without peritoneal gas, pneumatosis intestinalis or obvious perforation, patient was taken to the OR emergently based on clinical exam. He was found to have bowel perforation and purulent peritonitis requiring left colectomy and end-colostomy. He was discharged post-op day nine. R-EPOCH was resumed two weeks post-op. Several months after initial diagnosis and surgical intervention, patient maintains an ostomy and is continuing his course of chemotherapy.

Radiology

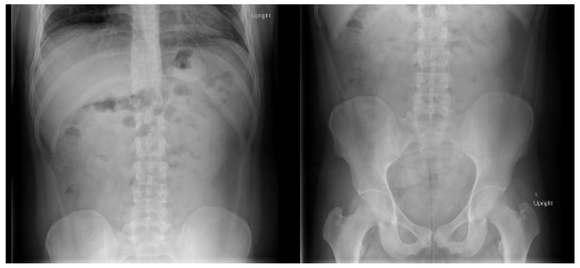
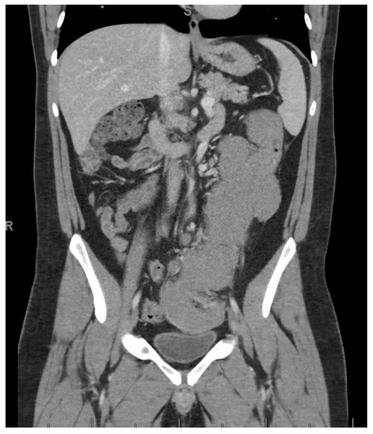


Image 2: Plain abdominal and KUB at time of presentation



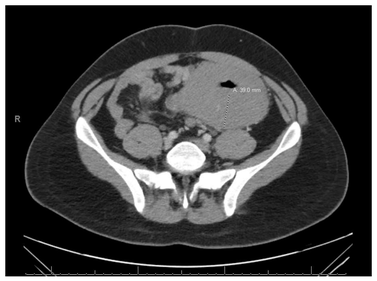


Figure 3 and 4: Abdominal CT at time of presentation

Endoscopic Findings

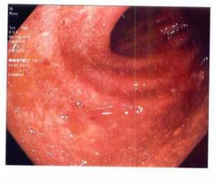
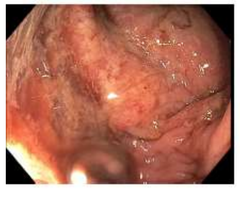
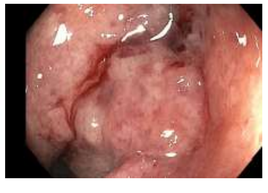
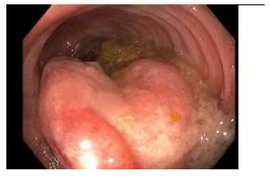


Image 1: Colonoscopy at time of UC diagnosis (outside facility) showing generalized colitis







Images 5-7: Sigmoidoscopy at presentation six months after UC diagnosis. Rectosigmoid junction (5), sigmoid colon (6) and descending colon (7)

Pathology

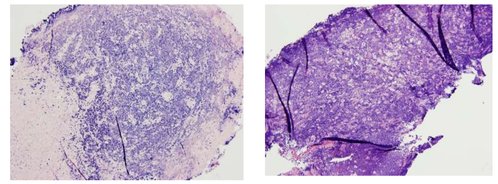


Figure 4 and 5: Sigmoidoscopy biopsy specimens

Discussion

Although increased risk of cancer is well documented in UC patients, development of malignancy is typically not so early in the disease course.

Initial colonoscopy was completed as an outpatient at the time of diagnosis, but no further imaging was completed despite six months of poor response to therapy and development of a mass. Although CT scan is not required to make a diagnosis of UC, it is possible that earlier recognition of this patient's lymphoma could have resulted in improved outcomes. Although bowel perforation is a known complication in patients undergoing chemotherapy for DBCL, earlier initiation of chemotherapy prior to the lymphoma eroding the mucosal wall may have prevented his eventual left-sided colectomy and end-ostomy, which is a significant life-altering procedure. (9)

This patient's initial ED presentation could have reasonably been considered a moderate UC flare with disposition for outpatient follow-up based on UC severity indices, labs and plain film that made perforation or mega-colon unlikely. However, use of CT based on physical exam findings and patient's history of symptoms refractory to multiple resulted in almost diagnosis of an aggressive lymphoma that perforated this patient's colon less than two weeks later. Although providers must avoid over-exposing patients to radiation, complications diagnosed by CT are often serious. In a retrospective review of 354 IBD patients presenting to the ED with new or worsening GI symptoms, the yield of abdominal CT for clinically actionable findings (eg abscess, tumor, perforation, obstruction, fistulae, diverticulitis, choledocholithiasis, or appendicitis) was 32.1% for Crohn's Disease and 12.8% for UC ($p<0.01$). (10) CT imaging in the ED or outpatient setting should be considered due to the seriousness of potential underlying processes.

In contrast, clinical judgement was crucial at the time of the patient's bowel perforation. This patient's abdominal imaging (plain film and CT) showed some evidence of abdominal distension but perforation was not evident. This case reminds providers that they should not be afraid to rely on clinical findings despite lack of evidence in radiographic findings.

This case highlights the need to be vigilant in considering UC complications, optimizing imaging in patients whose UC symptoms are refractive to multiple courses of treatment and the importance of trusting clinical exam findings despite lack of radiographic evidence.

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