An Aggressive Presentation of Colorectal Cancer With an Atypical Lymphoproliferative Pattern of Metastatic Disease: A Case Report and Review of the Literature

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Clinical Practice Points

- Typical metastatic sites in colorectal cancer patients include liver, regional abdominal lymph nodes, peritoneum, and lung. However, colorectal cancer rarely metastasizes to the bone marrow.
- We present a case of a 58-year-old man with a colon cancer of the cecum and an atypical lymphoproliferative pattern of metastatic disease. The patient presented with bone marrow involvement, leukoerythroblastic condition, disseminated intravascular coagulation, and tumor lysis syndrome. Tumor burden and hematologic abnormalities responded swiftly to initiation of chemotherapy (FOLFOX [5-fluorouracil, leucovorin, and oxaliplatin] and bevacizumab). However, a literature review demonstrated that overall prognosis in patients with this pattern of metastatic disease is poor.
- F-18 fluorodeoxyglucose-positron emission tomography (PET) imaging in this patient demonstrated diffusely hypermetabolic disease at the primary site and distant organs such as the liver, lymph nodes, spleen, and bone marrow of the axial and appendicular skeleton. These PET-computed tomography scans appeared radiographically similar to imaging of aggressive lymphomas. Pathologic diagnosis from a bone marrow biopsy and tissue biopsies is necessary for diagnostic clarification when the initial imaging is ambiguous.
- Immunohistochemical (IHC) tissue staining results must be interpreted with caution because atypical staining patterns (eg, Cytokeratin 7+ [CK7+] CK20-) can be observed in metastatic colorectal adenocarcinoma, especially in high-grade tumors arising in the right colon. Discordant IHC staining can be observed in bone marrow biopsies because of artifacts introduced during decalcification, so markers validated for use in decalcified specimens should be used.
- Genetic testing such as BRAF (v-raf murine sarcoma viral oncogene homolog B1) V600E mutational analysis or next-generation sequencing should be pursued on tumor samples to expand possible treatment options.

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The patient is a 58-year-old man with no significant medical history who presented with 3 weeks of lower back pain and left lower quadrant abdominal pain. The pain was associated with anorexia, drenching night sweats, and 15 pounds of unintentional weight loss. He denied constipation, changes in stool caliber, or gastrointestinal bleeding. He had a normal screening colonoscopy at age 50. A computed tomography (CT) scan of the abdomen and pelvis demonstrated focal colonic wall thickening around the
ileocecal valve with extensive bulky periocceal lymphadenopathy, multiple enlarged retroperitoneal and porta hepatitis lymph nodes, and a 1-cm hypodense lesion in the left hepatic lobe, all concerning for metastatic disease. He underwent a colonoscopy that demonstrated an ulcerated nonobstructing, noncircumferential 2-cm mass in the ascending colon. Biopsy of the mass demonstrated a moderately differentiated, invasive adenocarcinoma (Figure 1A) with intact immunohistochemical protein expression for mismatch repair proteins MutL homolog 1 (MLH1), MutS protein homolog 2 and 6 (MSH2 and 6), and postmeiotic segregation increased 2 (PMS2). The tumor was also wild type for the KRAS (Kirsten rat sarcoma viral oncogene homolog) mutation. BRAF (v-raf murine sarcoma viral oncogene homolog B1) mutational analysis demonstrated a V600E mutation. The patient’s carcinoembryonic antigen (CEA) was increased at 153.9. A positron emission tomography (PET)-CT study with F-18 fluorodeoxyglucose (FDG) was performed that demonstrated hypermetabolic activity in the cecum and ileocecal junction, in the ileocecal lymphadenopathy, and in a focal liver lesion. Extensive hypermetabolic uptake was also noted above and below the diaphragm including the left supravacular, left subpectoral, superior mediastinal, upper abdominal, retroperitoneal, and mesenteric lymphadenopathy, splenomegaly, and in the bone marrow of the axial and appendicular skeleton. The maximum standardized uptake values (SUVs) in the enlarged lymph nodes and bone marrow were 8.1 and 8.3, respectively. The PET-CT findings were concerning for a concurrent aggressive lymphoma (Figure 2A).

The patient developed increasing fatigue and lethargy at home and because of the concerning PET-CT findings was admitted for further work-up. His complete blood count demonstrated a white blood cell count of 13,000/µL, hemoglobin of 14 g/dL, hematocrit of 42.1%, and platelet count of 133,000/µL, with a differential of 59% neutrophils, 13% lymphocytes, 9% monocytes, 5% myelocytes, 1% metamyelocytes, 5% bands, and 1% nucleated right blood cells. His coagulation studies demonstrated a prothrombin time (PT) of 14.9 seconds, a partial thromboplastin time (PTT) of 30.2 seconds, and an international normalized ratio (INR) of 1.2. His chemistry was significant for signs of tumor lysis syndrome per Cairo-Bishop clinical criteria—acute renal failure with blood urea nitrogen of 21 mg/dL and an increased creatinine level of 1.3 mg/dL, an increased lactate dehydrogenase (LDH) level of 1968 U/L, an increased uric acid level of 10.4 mg/dL, potassium level of 5.4 mmol/L, calcium level of 10.4 mg/dL, and increased phosphate level of 4.7 mg/dL. He was treated with intravenous (I.V.) fluids and oral allopurinol.

Because of concern for concurrent lymphoma, with the PET-CT findings and clinical tumor lysis syndrome, he underwent bone marrow aspirate and biopsy and whole lymph node excision of a left supravacular lymph node. The bone marrow aspirate demonstrated clumps of malignant cells consistent with a poorly
differentiated metastatic carcinoma, and flow cytometry demonstrated no evidence of lymphoproliferative disorder. The bone marrow core biopsy demonstrated a hypercellular marrow, with 50% of the cellularity comprised of an interstitial infiltrate of dyscohesive epithelioid and polygonal cells with irregular nuclei, dispersed chromatin, prominent nucleoli, and occasional mucinous cytoplasm, which were associated with focal areas of necrosis (Figure 1B). Immunohistochemistry of lesional cells was positive for pan-cytokeratins, including AE1 and 3 and CAM5.2, and focally positive for Cytokeratin 7 (CK7), caudal type homeobox transcription factor 2 (CDX2), and chromogranin. Stains for CK20, synaptophysin, CD3, and CD20 were negative. There was normal maturation of the myeloid and erythroid precursors and slightly increased megakaryocytes. The excisional biopsy of the supraclavicular lymph node showed extensive infiltration by metastatic poorly differentiated adenocarcinoma, which was diffusely positive for CK7, rarely positive for CK20, multifocally positive for CDX2, and negative for thyroid transcription factor-1 (TTF-1), consistent with spread from the patient’s colonic primary tumor (Figure 1C-G).

The patient was discharged from the hospital, but returned to clinic for reevaluation after failing to thrive at home. He also noted...
a significant amount of bruising around a recently placed Port-a-Cath (Smiths Medical). His lab values were significant for an increased LDH of 3600 U/L, hematocrit of 32.1%, platelet count of 146,000/µL, and PT, PTT, and INR increased to 17.3 seconds, 47.2 seconds, and 1.4, respectively. A D-dimer was increased at 4000 ng/mL and a fibrinogen level, which was expected to be increased as an acute phase reactant, was normal at 250 mg/dL. Total bilirubin was 0.9 mg/dL with direct bilirubin 0.4 mg/dL and haptoglobin was elevated at 350 mg/dL. His peripheral blood smear demonstrated multiple early myeloid precursors and scattered nucleated red blood cells consistent with a leukoerythroblastic condition, decreased platelet count, and scattered schistocytes. Because of the hematologic findings concerning for early disseminated intravascular coagulation (DIC), the patient was urgently readmitted for initiation of modified FOLFOX-6 (5-fluorouracil 400 mg/m² I.V. bolus on day 1 followed by 1200 mg/m² daily given via continuous I.V. infusion over 46 hours, leucovorin 400 mg/m² I.V. on day 1, and oxaliplatin 85 mg/m² I.V. on day 1) chemotherapy. The patient was treated with modified FOLFOX-6 given every 2 weeks. Bevacizumab (5 mg/kg) was initially held because of concern for risk of a bleeding event from concurrent early DIC and added after the patient had tolerated 2 cycles of FOLFOX (5-fluorouracil, leucovorin, and oxaliplatin). Before initiation of bevacizumab therapy, he developed a left sided popliteal deep vein thrombosis (DVT) between cycle 2 and cycle 3 of chemotherapy and was given therapeutically dosed dalteparin.

He underwent restaging PET-CT after 4 cycles of treatment (2 months) that demonstrated a partial response to treatment with interval decrease in the wall thickness and decreased FDG uptake in the asymmetric thickening in the cecum and ileocecal junction and a decrease in the extensive pericolonic mesenteric lymphadenopathy, interval mild decrease in the size and uptake of the extensive retroperitoneal, left supraclavicular, left subpectoral, mediastinal, and paracardiac lymphadenopathy, and interval decrease in the avidity of the diffuse uptake in the axial and proximal appendicular skeleton. The maximum SUV in the lymph nodes decreased from 8.1 to 5.3, and the maximum SUV in the bone marrow decreased from 8.3 to 5.3.

The patient underwent 8 cycles of chemotherapy, and responded well with improvement in overall performance status, resolution of all back and abdominal pain, and a significant reduction in use of narcotic pain medication. His complete blood count and white blood cell count normalized with resolution of the presence of early myeloid precursors and nucleated red blood cells in the peripheral blood. His LDH also stabilized to approximately 400 U/L. However, disease progression was noted after 8 cycles with presence of acute gout, return of the leukoerythroblastic condition, increasing adenopathy, and malignant bowel obstruction at the level of the cecal primary. The patient’s bowel obstruction did not improve with bowel rest and nasogastric tube placement, so he underwent an exploratory laparotomy and diverting ileostomy.

The patient was evaluated for several early-phase clinical trials directed at BRAF-mutated tumors, but his poor performance status precluded enrollment. Second-line treatment was started with 1 cycle of dose-reduced FOLFIRI (5-fluorouracil 400 mg/m² I.V. bolus on day 1 followed by 1200 mg/m² daily given via continuous I.V. infusion over 46 hours, irinotecan 120 mg/m² I.V. on day 1) and bevacizumab (5 mg/kg). Unfortunately, the cancer progressed despite chemotherapy and his condition continued to deteriorate. The patient was transitioned to hospice care and passed away 6 months after diagnosis.

**Discussion**

We present a rare case of metastatic colorectal cancer involving bone marrow with diffuse hypermetabolic uptake on FDG-PET. The incidence of metastatic colorectal cancer to the bone marrow has not been studied prospectively, because bone marrow biopsies are not routinely performed as part of a diagnostic work-up. In a retrospective series of 1541 autopsies of patients who died of colon cancer, 24% had bone marrow involvement, 16% of patients had bone marrow and liver metastases and 34% had bone marrow, liver, and lung metastases. Involvement of the bone marrow by solid malignancies resulting in hematologic abnormalities such as a leukemoid neuophilic reaction, microangiopathic hemolytic anemia, erythrocytosis, and thrombocytosis has also been noted in gastric, colon, liver, lung, renal, pancreas, thyroid, bladder, and prostate cancers.

The radiographic differential for the combination of diffuse hypermetabolic bone marrow and systemic adenopathy on FDG-PET that was seen in our patient includes high-grade cancers of unknown primary and myeloid malignancies such as Burkitt lymphoma, diffuse large B-cell lymphoma, double-hit lymphomas, some mantle cell lymphomas, and peripheral T-cell lymphoma. Figure 2B and C show representative examples from patients with diffuse large B-cell lymphoma and mantle cell lymphoma, respectively. The increased bone marrow uptake can also be seen in any marrow stimulation state, including anemia and granulocyte colony stimulating factor administration, and other myeloproliferative disorders like multiple myeloma and leukemia. When this radiographic differential is raised as part of a patient’s initial staging studies, as happened in this case, then clinicopathologic correlation with a tissue biopsy of one of the distant sites is necessary to clarify the diagnosis.

Colorectal cancer patients with a similar atypical metastatic disease pattern of spread are rarely reported in the literature. Since the original retrospective series of autopsies, there have been less than 10 case reports in the literature of living patients that are similar to the presentation of our patient (Table 1). In a case reported in 2001, a 61-year-old man with metastatic sigmoid colon adenocarcinoma presented with a gastrointestinal bleed and later had onset of acute thrombocytopenia and DIC. He was confirmed to have CEA-positive adenocarcinoma according to immunohistochemistry in a bone marrow biopsy. The patient was too ill to receive chemotherapy and died 2 weeks after diagnosis. However, in subsequent case reports, most patients have been able to receive some form of palliative chemotherapy. For example, a 45-year-old man was diagnosed with metastatic poorly differentiated descending colon adenocarcinoma. His PET-CT scan, similar to our patient, also demonstrated diffused FDG-avidity in diffusely lymph nodes, bone marrow, and colonic mass. He was treated with modified FOLFOX-6 with good response.
## Table 1  Clinical Summary of Colorectal Cancer Cases With Metastatic Disease to Bone Marrow Reported in the Literature

<table>
<thead>
<tr>
<th>Reference</th>
<th>Age/Sex</th>
<th>Presenting Symptom(s)</th>
<th>Primary Tumor Location</th>
<th>Involved Metastatic Sites</th>
<th>Hematologic Abnormalities</th>
<th>Imaging</th>
<th>Bone Marrow Biopsy</th>
<th>Treatment Plan</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sema et al⁹</td>
<td>61/M</td>
<td>Abdominal pain, GI bleeding</td>
<td>Sigmoid colon (hepatic flexure)</td>
<td>(+) Bone marrow</td>
<td>DIC</td>
<td>CT: (+) bony metastases</td>
<td>Mucinous adenocarcinoma; CEA⁺, PAS AB⁻⁵</td>
<td>Supportive transfusions</td>
<td>Died 2 weeks after diagnosis</td>
</tr>
<tr>
<td>Lee et al¹⁰</td>
<td>67/M</td>
<td>Abdominal pain, night sweats, weight loss, fever, altered mental status</td>
<td>Ascending colon (hepatic flexure)</td>
<td>(+) Bone marrow (ribs, pelvic bones, whole spine)</td>
<td>TTP (not responsive to plasma exchange)</td>
<td>MRI: (+) bony metastases (multifocal low T2 signal lesions in sacrum, ilium, and spine)</td>
<td>Marrow spaces replaced with coagulative necrotic cells; Grade 1 reticulin</td>
<td>FOLFOX</td>
<td>Alive after 4.5 months after treatment initiation</td>
</tr>
<tr>
<td>Pleyer et al¹¹</td>
<td>48/M</td>
<td>Bowel obstruction, acute abdomen</td>
<td>Not reported</td>
<td>(+) Bone marrow, (+) lymph nodes (mediastinal, mesenteric, retroperitoneal), (+) peritoneal carcinomatosis, (+) pleural/pericardial effusions</td>
<td>Thrombocytopenia, bleeding</td>
<td>CT: (+) diffuse lymph node involvement, (+) bony metastases</td>
<td>Infiltration of metastatic carcinoma cells; EpCAM⁺, CDX⁻²⁺, CEA⁻</td>
<td>FOLFOX with bevacizumab</td>
<td>Died after 5 cycles of chemotherapy of disease progression, peritonitis, and pulmonary embolism</td>
</tr>
<tr>
<td>Wang et al¹²</td>
<td>37/M</td>
<td>GI bleeding</td>
<td>Sigmoid colon</td>
<td>(+) Bone marrow</td>
<td>Anemia, thrombocytopenia, elevated D-dimer</td>
<td>Bone scan: (+) bony metastases</td>
<td>Extensive bone marrow necrosis</td>
<td>FOLFOX with cetuximab</td>
<td>Died after 3 months of disease progression</td>
</tr>
<tr>
<td>Isozaki et al¹³</td>
<td>45/M</td>
<td>Back pain</td>
<td>Descending colon</td>
<td>(+) Bone marrow; (+) lymph nodes</td>
<td>DIC</td>
<td>PET-CT: (+) FDG avid skeleton; (+) FDG avid lymphadenopathy</td>
<td>Not reported</td>
<td>mFOLFOX-6</td>
<td>Symptoms and DIC resolved with 1 cycle of treatment</td>
</tr>
<tr>
<td>Song et al¹⁴</td>
<td>70/M</td>
<td>Back pain</td>
<td>Distal rectum</td>
<td>(+) Bone marrow</td>
<td>Normocytic, normochromic anemia</td>
<td>MAHA</td>
<td>Mucin, groups of colonic type glandular structures, Cytokeratins⁺,CDX⁻²⁺</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Orgel et al¹⁵</td>
<td>65/F</td>
<td>Spontaneous right psoas intramuscular hematoma</td>
<td>Sigmoid colon</td>
<td>(+) Bone marrow, (+) liver, (+) CNS, (+) circulating cells, peripheral flow cytometry</td>
<td>MAHA</td>
<td>CT: (-) bony metastases (+) hepatic metastases</td>
<td>Infiltration of solid tumor cells</td>
<td>FOLFOX with cetuximab</td>
<td>Died after 7 months of CNS metastases</td>
</tr>
<tr>
<td>Present study</td>
<td>58/M</td>
<td>Back pain, abdominal pain, night sweats, weight loss</td>
<td>Ascending colon (cecum)</td>
<td>(+) Lymph nodes, (+) bone marrow, (+) liver</td>
<td>DIC, LEB condition, TLS</td>
<td>PET-CT: (+) FDG-avid bone marrow; (+) FDG-avid diffuse lymphadenopathy</td>
<td>Poorly differentiated carcinoma; focal areas of necrosis and intracellular mucin; CK⁺⁻,CK₂⁺⁻</td>
<td>mFOLFIRI with bevacizumab; FOLFOX with bevacizumab</td>
<td>Disease progression after 8 cycles of chemotherapy with bowel obstruction; died after 6 months</td>
</tr>
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</table>

**Abbreviations:** - negative; + positive; CNS = central nervous system; CT = computed tomography; DIC = disseminated intravascular coagulation; EpCAM = Epithelial Cell Adhesion Molecule; F = female; FDG = F-18 fluorodeoxyglucose; FOLFIRI = chemotherapy with 5-fluorouracil, leucovorin, and irinotecan; FOLFOX = chemotherapy with 5-fluorouracil, leucovorin, and oxaliplatin; GI = gastrointestinal; LEB = leukoerythroblastic; M = male; MAHA = microangiopathic hemolytic anemia; MRI = magnetic resonance imaging; PET-CT = positron emission tomography-computed tomography study; TLS = tumor lysis syndrome; TTP = thrombotic thrombocytopenic purpura.
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CT, bone scan, or blind bone marrow biopsy for detection of bone marrow involvement by other malignancies when no cortical bone lesions are present. 16-18 In 1 study of diffuse large B-cell lymphoma, FDG-PET had significantly greater sensitivity for detection of marrow involvement than iliac bone marrow biopsy alone (94% vs. 24%; P < .001). 16 Although no comparable study has been performed in colorectal cancer, these findings and the 24% rate of marrow involvement by colorectal cancer at autopsy raise the possibility that CT staging alone could underestimate the rate of marrow involvement by colorectal cancer. 2

In addition to PET-CT, bone scans and MRI have also been used to detect bone marrow involvement with colorectal cancer, 10,12,14 including some cases in which CT scans alone did not detect any evidence of bone marrow disease. 21,22 For example, a 37-year-old man with sigmoid colonic adenocarcinoma presented with a gastrointestinal bleed and profound thrombocytopenia. His bone scan showed bony metastases and a bone marrow biopsy demonstrated marrow necrosis. He was treated with oxaliplatin, 5-fluorouracil, leucovorin, and cetuximab. He died of disease progression 3 months after starting treatment. 11 In addition, there are reported cases in the Japanese literature of metastatic colorectal cancer to the bone marrow; in 1 of those cases, the bony metastatic involvement was detectable on MRI. 10 This patient developed thrombotic thrombocytopenic purpura (TTP) not responsive to plasma exchange, but responsive to chemotherapy. 10,19,20 In another case in the German literature, a 65-year-old female patient presented with DIC and metastatic colorectal cancer disseminated to the liver, bone marrow, and circulating tumor cells noted on flow cytometry. This patient’s CT scan demonstrated metastatic disease and a psoas hematoma, but the CT imaging did not detect bone marrow involvement. The cancer and the DIC were responsive for approximately 7 months to FOLFOX and cetuximab, but the patient ultimately died 7 months later after developing central nervous system metastatic disease. 15

Similar to other reports, our patient also demonstrated hematologic abnormalities attributed to malignancy. He showed early signs of a consumptive hemolytic process, DIC, including thrombocytopenia, elevated coagulation studies, elevated D-dimer, a normal level of fibrinogen (normally an increased acute-phase reactant, indicating increased fibrin consumption), slightly increased megakaryocytes on bone marrow biopsy, and increased bruising and bleeding after his Port-a-cath placement. This is consistent with microangiopathic hemolytic anemias such as DIC or TTP that are seen with solid malignancies infiltrating bone marrow. 9 Microangiopathic hemolytic anemia in cancer is related to mechanical shearing of erythrocytes by tumor burden, not by a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13 (ADAMTS13) deficiency, which plasma exchange transfusion replenishes in TTP. 21 Microangiopathic hemolytic anemia caused by solid malignancies is best alleviated with cancer-directed chemotherapy rather than plasma exchange transfusions. 10,20,22 In addition, the peripheral blood smear demonstrated a leukocytodysplastic condition, or the unexpected presence of myeloid precursors and nucleated red blood cells normally present only in bone marrow. This condition is commonly seen with malignant tumor infiltration of bone marrow. A complete blood count (CBC) with differential and peripheral blood smear was regularly monitored in this patient during treatment—resolution of the leukoerythroblastic condition indicated disease response, whereas recurrence heralded disease progression.

No clear molecular pathway explains why patients in this case series presented with a pattern of hematogenously disseminated disease or bone marrow involvement, because in previous case reports genetic testing on tumors was not performed. Administering activated protein C (APC) to a stage III colorectal cancer patient led to physiologic dissemination of disease to the bone marrow and multiple lymph nodes, similar to our patient. 11 It is thought that APC might promote tumor invasion and lead to initiation of hematogenous spread of disease through upregulation of the production of urokinase plasminogen activator, a known oncogenic protein involved in tumor growth, angiogenesis, and metastasis. 11 Our patient’s tumor was KRAS wild-type but did contain a BRAF V600E mutation. BRAF is a member of the Rat Sarcoma/ Rapidly Active Fibrosarcoma/MAPK/ERK Kinase pathway, and activating mutations such as BRAF V600E leads to increased propensity for cellular growth, invasion, and metastasis. 23 In keeping with the prognosis in this case series, BRAF mutations demonstrate poor prognosis in colorectal cancer, 23,24 with a median overall survival of 12.3 months, a 1-year overall survival of 54%, and a 1-year progression-free survival of 56%. 25 BRAF mutations should be investigated in cases of colorectal cancer with aggressive clinical presentation. Although treatment of metastatic melanoma with BRAF inhibitors such as vemurafenib is currently approved by the U.S. Food and Drug Administration, targeting colorectal tumors with BRAF inhibitors remains experimental. 22 Still, clinical trials with BRAF inhibitors (alone or in combination with MEK inhibitors or epidermal growth factor receptor (EGFR) inhibitors such as cetuximab and panitumumab) remain a future treatment option for colorectal cancer patients with BRAF mutations. In addition, whole-exome sequencing (WES), which has been successfully performed on colorectal tumors, 26,27 is currently being performed on the patient’s tumor as part of a clinical trial. WES will provide better understanding of the tumor’s cancer-specific mutations and elucidate clinical trial options for similar patients. Subsequent publication of WES results for this patient’s tumor might be feasible on clinical trial completion.

One potential pitfall in pathologic diagnosis was the lack of CK20 positivity on the bone marrow specimen. CK20 expression is observed in approximately 80% of primary colorectal adenocarcinomas and is used (in conjunction with CK7 and CDX2) to define colorectal origin in patients with metastatic disease. 28,29 Because bone marrow biopsies undergo decalcification before sectioning, there was initial concern that the lack of CK20 staining was due to a false negative interference with the immunohistochemistry process. However, when the supraclavicular lymph node was biopsied, immunohistochemical staining again demonstrated only scattered/rare positivity for CK20. Although more commonly associated with midgut gastrointestinal primary cancers (eg, gastric or pancreatic adenocarcinoma), lack of CK20 expression (with positive CK7) can occur and has been reported in approximately 2% of colorectal adenocarcinomas. 10 In addition, loss of CK20 expression has been reported more commonly in poorly-differentiated and right-sided tumors, and in tumors harboring BRAF mutations. 28-30 Each of these features is consistent with the
patient’s presentation and might help to explain the atypical immunohistochemical staining pattern.

Conclusion

In this case, we presented a case of a 58-year-old man with type B symptoms noted in hematologic malignancies, such as weight loss and night sweats, but was diagnosed instead with metastatic colorectal cancer. He had aggressive atypical metastases to lymph nodes and bone marrow that were hypermetabolic on PET-CT scans, which led to concern for a concurrent aggressive lymphoma that required a bone marrow biopsy for clarification. These types of patients also present with hematologic abnormalities such as leukoerythroblastic conditions and microangiopathic hemolytic anemia syndromes such as DIC and TTP. Bone marrow and tissue biopsies should be pursued in these patients for diagnostic purposes, because of the potential pitfalls associated with immunohistochemical testing on decalcified bone specimens. The patient was treated with chemotherapy consisting of modified FOLFOX-6 and bevacizumab and demonstrated a partial response on PET and CT imaging, but he eventually had disease progression unresponsive to second-line chemotherapy with FOLFIRI and bevacizumab and passed away 6 months after diagnosis. Molecular analysis of the tumor demonstrated a BRAF V600E mutation and WES is currently being performed. Patients who present in a similar aggressive fashion should undergo mutational testing of their tumor samples, which could hold prognostic and therapeutic significance. Review of the literature demonstrated that the overall prognosis in patients who present in this fashion is poor, usually on the order of months. However, treatment should be pursued whenever possible, because the tumor and associated hematologic abnormalities respond to swift initiation of palliative chemotherapy with good improvement in performance status and quality of life.

Disclosure

The authors have stated that they have no conflicts of interest.

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