Solitary Cerebellar Metastasis as Herald Symptom of Primary Cecal Adenocarcinoma

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Background	We present a case of a 65-year-old female who initially presented with neurological complaints and was subsequently diagnosed with a solitary cerebellar metastasis of an otherwise asymptomatic cecal carcinoma.
Summary	A 65-year-old female presented to an outlying facility with the complaint of a five-day history of right-sided headache, nausea, and the sensation of drifting to the right upon ambulation. Computed tomography (CT) of the head revealed a left-sided cerebellar mass with associated mass effect. Additional imaging demonstrated small bowel mesenteric, retroperitoneal, periaortic, and periportal adenopathy, which, at the time, was thought to be secondary to lymphoma. CT-guided biopsy of the lymph nodes revealed metastatic adenocarcinoma, with the primary cecal tumor subsequently identified on colonoscopy. Due to concern for the development of obstructive hydrocephalus, the patient underwent craniotomy for gross total resection of the metastatic lesion. Postoperatively, the patient was treated with radiotherapy and FOLFOX/Avastin combination chemotherapy.
Conclusion	Reports on the discovery of metastatic cecal carcinoma revealed by a solitary cerebellar lesion remain a rarity in current medical literature. This case highlights the importance multidisciplinary collaboration when diagnosing and managing late stage malignancies, especially with an unconventional presentation of a primary neoplasm.
Keywords	Cerebellar metastasis, cecal adenocarcinoma, neurosurgery, colorectal

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Case Report

A 65-year-old, right-handed woman presented to an outlying community hospital with a five-day history of right-sided headache and nausea. Upon presentation, the patient denied any changes in vision, weakness, numbness and tingling in her extremities, shortness of breath, chest pain, abdominal pain, hematochezia or melena, bowel or bladder dysfunction. Further questioning revealed that the patient had noted a sensation of drifting to the right while ambulating for several months, though she denied any recent falls. Past medical history was significant for a distant diagnosis of iron-deficiency anemia. Her surgical history included laparoscopic cholecystectomy and three cesarean sections. Social history was significant for a 20-pack-per-year smoking history and occasional alcohol consumption. Review of family history revealed no relatives with bowel, brain, or solid-organ malignancy. Medication included oral iron supplements and a daily baby aspirin. Remarkably, on exam, the patient was neurologically intact, and no abnormalities in gait or coordination were noted. Laboratory results revealed no presence of anemia (hemoglobin 12.4 g/dL, hematocrit 37.8 percent, MCV 91.7 fL) or leukocytosis (WBC 9.4 x 10^3/uL); alkaline phosphatase was found to be only slightly elevated (109 U/L). All other laboratory values were unremarkable. Portable chest radiograph was without significant findings. A non-contrast computed tomography (CT) of the head was ordered, which revealed a 2.2 cm left-sided cerebellar mass with associated mass effect on the fourth ventricle.

Due to these findings, the patient was transferred to our facility, where more comprehensive care could be rendered. Additional imaging was ordered, including magnetic resonance imaging (MRI) of the brain with contrast, which demonstrated a 3 cm contrast-enhancing mass within the left cerebellum, with mild mass effect on the fourth ventricle without hydrocephalus (Figure 1).
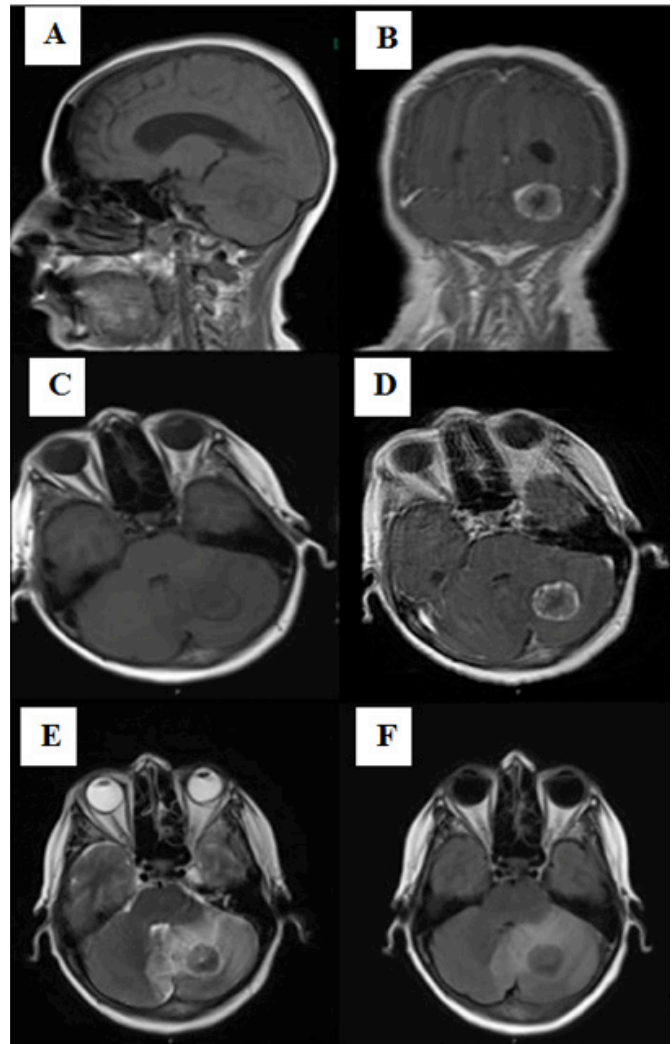

Figure 1. MRI Brain demonstrating contrast-enhancing coin lesion in left cerebellum. **A.** Sagittal T1WI **B.** Coronal T1W1 postcontrast **C.** Axial T1WI **D.** Axial T1W1 postcontrast **E.** Axial T2WI **F.** Axial T2WI FLAIR

CT of the chest, abdomen, and pelvis was performed to evaluate a primary tumor source, revealing soft tissue masses that likely represented adenopathy within the small bowel mesentery and adjacent to the cecum as well as retroperitoneal adenopathy, including an enlarged lymph node between the inferior vena cava and portal vein approximately 2 cm in diameter. Additional enlarged lymph nodes were identified between the aorta and inferior vena cava as well as left periaortic retroperitoneal lymph nodes measuring 1.4 cm, 1.7 cm and 2 cm, in diameter, respectively. Irregular wall thickening of the cecum was also noted (Figure 2).
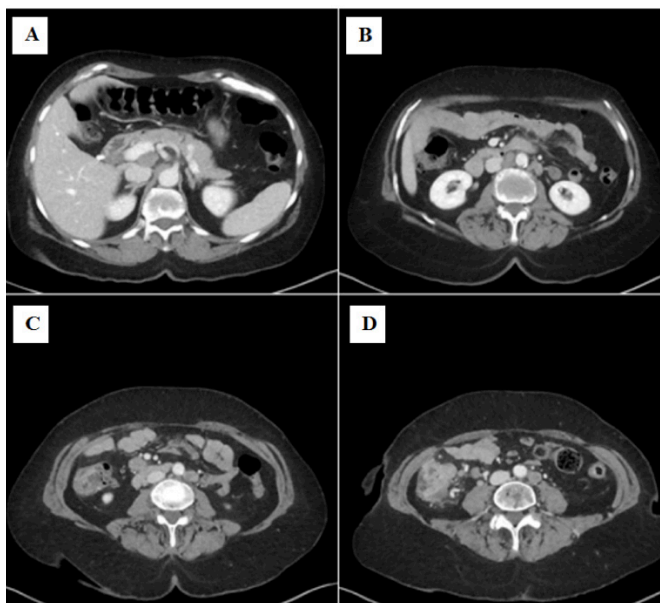

Figure 2. CT chest/abdomen/pelvis with contrast. **A:** Enlarged lymph node present between the inferior vena cava and portal vein, measuring approximately 2 cm in diameter. **B:** Enlarged lymph nodes between the aorta and inferior vena cava, up to 1.4 cm in diameter and a left periaortic retroperitoneal lymph node measuring up to 1.7 cm in diameter, and more inferior left periaortic retroperitoneal lymph node measuring approximately 2 cm in maximal dimension. **C:** Soft tissue masses in the small bowel mesentery, primarily in the right lower quadrant. One of these is seen measuring approximate 2 cm in diameter. **D:** Several other soft tissue masses adjacent to the cecum, measuring up to 2 cm in diameter.

In all, it was felt that such nonspecific retroperitoneal and small bowel mesenteric adenopathy likely represented lymphoma. CT-guided core needle biopsy of the mesenteric and periaortic lymph nodes (Figure 3) was pursued in order to obtain a histopathological diagnosis. This revealed metastatic adenocarcinoma, immunohistochemically consistent with a colorectal primary lesion (tumor cells were positive for cytokeratin 20 and CDX2; negative for cytokeratin 7, TTF-1, Pax 8 and vimentin).
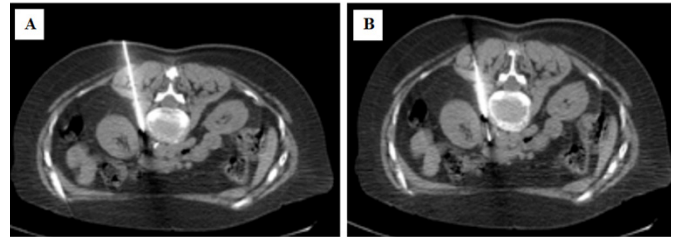

Figure 3. CT-guided biopsy **A.** CT-guided biopsy of enlarged lymph node present between the inferior vena cava and portal vein, measuring approximately 2 cm in diameter. **B.** CT-guided biopsy needle shown sampling enlarged lymph node.

Gastroenterology was consulted, whose work-up yielded findings of a cecal mass and several tubular adenomatous polyps of the distal colon on colonoscopy (Figure 4). Biopsy of these lesions was performed, and surgical pathology of the cecal mass demonstrated invasive, moderately-differentiated adenocarcinoma. Immunohistochemical analysis for microsatellite instability demonstrated preserved DNA-mismatch repair function (positive expression of hMLH-1, hMSH-2, hMSH-6, and PMS2).
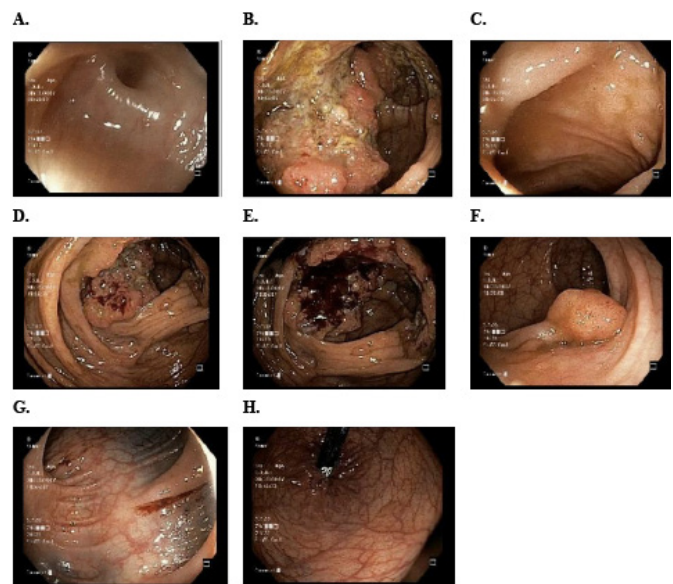

Figure 4. Images captured at colonoscopy. **A:** Diverticuli within sigmoid colon, **B:** Half circumferential mass found in the cecum, multiple biopsies were taken of the lesion and a tattoo was applied. **C:** Sessile polyp found in the descending colon, polypectomy was performed with snare cautery. **D:** Large pedunculated polyp was found in the sigmoid colon **E:** Polypectomies were performed using snare cautery and a tattoo was applied. **F:** Additional large pedunculated polyp was found in the sigmoid colon, polypectomy was performed using snare cautery and the wound site was closed by placing hemoclips. **G:** Otherwise normal sigmoid colon mucosa. **H:** Normal retroflexion view within the rectum.

Colorectal surgery was consulted; however due to the patient's stage IV, TXN2M1 diagnosis, no colonic resection was indicated acutely. The patient's case was discussed at an interdisciplinary tumor board meeting, where it was agreed that, should her cecal mass become obstructing, or her iron deficiency anemia recur, surgical resection or palliative stenting would be discussed at that point in time.

To address the inevitable obstructive hydrocephalus and persistence of the patient's neurological symptoms, stereotactic computer-assisted (navigational) suboccipital craniotomy for gross total resection of the left cerebellar mass, and placement of an external ventricular drain, was performed by neurosurgery. Pathologic frozen sectioning and immunohistochemical analysis of the excised tumor demonstrated metastatic colorectal cancer (tumor cells positive for CK20 and CDX2, negative for CK7, TTF1, GCDFP15, GATA3 and mammaglobin, supporting the aforementioned diagnosis). The patient progressed well during her hospital course and was safely discharged to home on postoperative day five.

The patient was referred to radiation oncology and hematology/oncology for further medical management of her brain lesion and colon cancer (stage IV, TXN2M1), which included radiotherapy, and FOLFOX/Avastin combination chemotherapy, respectively.

The patient is currently seven months out from initial diagnosis and continuing to carry out activities of daily living independently. She recently completed her seventh of 12 cycles of chemotherapy. Surveillance CT has since revealed a marked decrease in the size of the cecal mass and complete resolution of the intraabdominal lymphadenopathy, with no new metastatic lesions noted within the chest, abdomen, or pelvis. Repeat CT head or MRI brain to monitor for metastatic recurrence has yet to occur.

Discussion

Colorectal cancer (CRC) is the third most common cancer in both men and women, and it is the second-leading cause of death in both genders in the United States.[1,2] In 2017, an estimated 135,430 new cases of CRC were diagnosed, contributing to 8 percent of all new cancer diagnoses in the United States.[3] Of these, 21 percent were found to have distant metastasis upon initial diagnosis.[3,4] Sites of metastatic disease are most frequently the lung (10–20 percent) and liver (20–30 percent).[5,6] Brain metastases from CRC are rare, with an estimated incidence of 0.6 to 4 percent.[7-8] Brain metastases are a sign of late-stage metastatic disease,

with 70 and 40 percent of patients having lung and liver metastases, respectively, at diagnosis of brain metastasis.[9] Additionally, postmortem studies have demonstrated that at the time of death, between 2 and 3 percent of patients who die from CRC harbor occult brain metastases.[5,6]

The cerebellum is the involved site in 55 percent of metastatic CRC cases to the brain.[5,6,10] It is hypothesized that pelvic or abdominal primary malignancies are more likely to metastasize specifically to the posterior fossa due to the Batson vertebral venous plexus.[8] Regardless, the prognosis for these patients is dismal, with a reported median survival of less than three months.[11]

Upon our review of current literature, a small number of cases of solitary cerebellar metastasis have been reported; however the vast majority involved the distal colon as the primary site.[12] We hypothesize that differences in vascular anatomy of the proximal versus distal colon result in a higher incidence overall of brain metastases from rectosigmoid primary lesions.[13] Those cases that report more proximal colon cancers are limited to the ascending colon or hepatic flexure; to our knowledge, our case of a cecal carcinoma to present with a solitary cerebellar metastasis is indeed a rarity.[14,15]

Further, the discovery of CRC as heralded by brain metastasis is a rare but reported event, as most patients present with symptoms of mass effect (such as altered mental status or focal weakness), in addition to marked iron deficient anemia.[12,14,16] Unique to our case, the patient presented with an isolated and subtle neurologic symptoms and only a distant history of iron deficient anemia (she was not found to be anemic on exam), for which she had been taking oral iron supplements.

Overall, the prognosis of metastatic CRC to the brain is exceedingly poor. By far, the intervention that prolongs life expectancy significantly is surgical resection of the metastasis, ranging from 6 to 10 months.[5,17,18] Adjuvant whole brain radiation therapy (WBRT) has been shown to substantially improve survival, as opposed to either surgery or radiation alone.[13] However, it must be kept in mind that this survival benefit is obscured by the fact that patients undergoing these treatments are, of course, healthier, and fit to undergo such a rigorous course of treatment.

The patient presented here underwent both surgical resection and WBRT, and continues to do remarkably well seven months from her diagnosis.

Conclusion

Cerebellar metastases from CRC are exceedingly rare, with the vast majority of these cases occurring from distal rectosigmoid primary lesions. Here, we present a case of cecal adenocarcinoma with a solitary distant metastasis to the cerebellum, presenting as headache and subjective gait disturbance. Our case demonstrates an unconventional presentation of CRC, thereby resulting in a seemingly retrograde diagnosis of the primary tumor (i.e., from brain metastasis to primary neoplasm). This highlights the importance of communication between various medical and surgical specialties to arrive at the correct diagnosis and optimize the patient's treatment course.

Lessons Learned

The importance of multidisciplinary collaboration when treating metastatic CRC is invaluable and cannot be understated, particularly in the case of disease metastasizing to the brain. Furthermore, aggressive surgical resection and adjuvant WBRT of isolated metastases can significantly impact the survival of patients with metastatic CRC.

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