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Curative Intent Treatment for Colorectal Cancer with Isolated Brain Metastases: A Case Report

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Abstract

Introduction: Brain metastases (BM) are a rare complication of colorectal cancer (CRC), typically presenting late in the course of the disease and are associated with other systemic metastases. Management of solitary brain metastases in colorectal cancer is still not well established.

Case presentation: We describe the case of a 65 year-old man presenting with a solitary brain metastasis as the first sign of colon cancer. The treatment approach included surgical resection of the brain lesion followed by resection of the primary tumor, systemic chemotherapy and local radiation therapy to the BM.

Conclusion: This curative intent approach has resulted in dramatically prolonged patient's survival compared to the average reported in the literature, now nearly 2.5 years after presentation. Our case describes the feasibility of a multidisciplinary curative intent approach to solitary BM in CRC.

Keywords: Brain metastases; Colorectal cancer; Chemotherapy; Radiation therapy

Introduction

Brain metastases (BM) are a rare complication of colorectal cancer (CRC) reported in only 4% of patients [1]. Their prevalence is expected to increase with the incorporation of new therapies for colorectal cancer which prolong patients' survival [2]. BM typically appear late in the course of the disease and coexist with lung metastases in 55 to 85% of cases [3], and with liver metastases in 75% of cases [4]. Very few cases of CRC presenting with solitary BM have been described [5-7]. We report our experience with a patient who presented with a BM as the first sign of colon cancer.

Case Presentation

Our patient is a 65-year-old man who presented initially to the neurosurgery clinic in 8/2011 after noticing difficulty with his vision. His past-medical history was positive only for hypertension. He had no previous surgical history, no prior colonoscopies and no family history of colon cancer. His only gastrointestinal complaint was chronic mild constipation, and he denied any melena, hematochezia, changes in bowel pattern or weight loss. On exam, he was noted to have a left lower quadrant visual field loss (left inferior quadrantanopsia). A brain MRI showed an enhancing lesion in the right occipital lobe. Three days after his clinic visit he underwent a right occipital craniotomy with resection of the tumor, with intraoperative concern for incomplete resection. Pathology results were positive for adenocarcinoma with signet ring features. Tumor cells were positive for CK20 and negative for CK7 and TTF1, suggestive of a colorectal primary lesion.

A CT of the chest, abdomen and pelvis, PET and MRI of the liver were obtained, showing a mass in the proximal ascending colon and pericolonic adenopathy but no other evidence of metastatic disease. A colonoscopy demonstrated an ascending colon mass and biopsies of the lesion revealed poorly differentiated adenocarcinoma with signet ring features. CEA was markedly elevated at 140.8 ng/mL. Three weeks after the brain metastasis resection, he underwent a laparoscopic right hemi-colectomy. Pathology confirmed moderately differentiated adenocarcinoma extending into the pericolonic fat. The surgical margins were negative for tumor, and one of thirty-one lymph nodes was involved by adenocarcinoma. The cancer was classified as stage IV disease by virtue of the central nervous system (CNS) metastases (T3 N1a M1a). The patient underwent stereotactic radiosurgery (SRS) targeted to the postoperative intracranial tumor bed (5 isocenter plan to dose of 17 Gy) 6 weeks after the initial neurosurgical operation. This was followed by 12 cycles of systemic chemotherapy (FOLFOX).

Brain MRI at three months after SRS was negative, but at six months from SRS and eight months from initial presentation, there was evidence of tumor recurrence at the occipital surgical site on MRI accompanied by a rise in CEA. He was treated with partial brain fractioned radiation to the operative bed (30 Gy in 10 fractions). Continued surveillance MRI imaging subsequently has shown no evidence of persistent or recurrent disease in the brain.

Following fractionated radiotherapy, pt was offered additional chemotherapy or a watch and wait approach, and elected to defer additional chemotherapy at that time. Surveillance CT imaging of the abdomen was normal until 12 months after presentation when there was evidence of local recurrence at the ileocolonic anastomosis and at two abdominal port sites, again accompanied by a rise in CEA to 828.1 ng/mL. These were treated with surgical excision and a new ileocolic anastomosis created. After recovery, he was treated with FOLFIRI with

Cetuximab. The patient recovered and is doing well without evidence of any additional recurrence. Continued surveillance is necessary however as there remains a significant risk of local site recurrence (3-15% [8]) and intracranial recurrence (up to 50%) in patients with similar treatments. He continues to be followed closely with serial surveillance imaging (body CT and brain MRI), colonoscopy and laboratory studies including CEA, now 29 months after presentation (Dec 2013). He has no neurologic deficits including no sensory, motor, visual or cognitive impairments.

Discussion

Metastatic colon cancer to the liver or the lung traditionally carried a poor prognosis with a median survival of 12 months. The incorporation of surgical resection of the metastases, neoadjuvant and adjuvant chemotherapy, ablative and targeted radiotherapies have transformed the management in such patients from a palliative to a curative approach [9]. Management of liver and lung metastases with CRC is now well established, with surgical resection for curative intent being the treatment of choice in selected patients with distant metastases and recurrences in whom the primary tumor is well controlled [10,11]. Complete resection can increase 5-year survival to 30-50% in liver metastases and 40% in lung metastases [8]. In contrast, BM in patients with CRC still carries a dismal prognosis, with a median survival of two months from the date of diagnosis [12,13] that extends up to 5.4 months with treatment. This is in part secondary to their late presentation, and presence of concomitant lung and liver metastases when discovered. Management of BM is still unclear and is usually determined by the extracranial disease progression and response to chemotherapy, since most of the patients die from their extracranial disease [14,15]. The management of locoregional recurrent colon cancer is more clearly defined, with surgical resection in appropriate candidates offering an opportunity for curative therapy [16,10].

Treatment goals in presence of BM range from a conservative/palliative approach to an aggressive/curative one. In such cases where few or no randomized trials are available, it is reasonable to make clinical decisions based on the patient's life expectancy, treatment options currently available, and on the main prognostic factors identified in the literature. Among those, are the Karnofsky performance status (KPS) (≥70), age (≤65 years), control of primary tumor, absence of extracranial metastases and number of brain lesions [17]. Recursive partitioning analysis (RPA) has been used to evaluate patient survival when patients were classified in three prognostic classes. RPA Class I patients with KPS of 70 or greater, age 65 years or younger, controlled primary tumor and absence of systemic metastases, had a median survival of 7.1 months [14,18]. Considering these prognostic factors, our patient would be classified as RPA class I and was a good candidate for a curative treatment regimen.

Multiple approaches have been tried to manage BM. Surgical resection has the benefit of providing tissue for diagnosis and prolonging survival in patients with BM from CRC, with the main drawback being neurologic deficits [11]. Initial treatment strategies combined surgery with whole brain radiation therapy (WBRT) in efforts to decrease recurrence rates, however studies did not improve overall survival [10,19,20]. In addition, the complications incurred by WBRT included an increase in long-term neurotoxicity and decrease quality of life [21]. These complications of WBRT and advancement in the field of radiation therapy have led to alternative radiation treatment modalities such as stereotactic radiosurgery (SRS) and hypofractionated stereotactic radiotherapy (hfSRT) that focus therapy on the tumor bed and spare normal brain tissue from potential toxicity.

In our case, SRS was chosen as an adjuvant therapy due to concern for initial incomplete resection, obtaining the local control benefit of combined radiation and surgery, but avoiding the toxicity of WBRT. To our knowledge, no randomized controlled trials have compared surgery with WBRT to surgery with SRS in patients with BM from CRC. However, several retrospective studies on patients BM and varying primary malignancies treated with surgery and adjuvant SRS are available, and have demonstrated similar outcomes in survival and local intracranial recurrence similar to WBRT although with higher rates of distant brain recurrences [22-24]. In patients who do develop intracranial recurrence, studies showed that salvage SRS provided an extended survival in selected patients in whom the major prognostic factors such as RPA class are favorable [25].

Hypofractionated stereotactic radiotherapy can be an alternative to SRS in large or anatomically challenging lesions allowing higher cumulative radiation doses to the tumor. Although the use of hypofractionated radiation as a salvage therapy has not been rigorously evaluated, there have been similar results between use of SRS and hfSRT as adjuvant therapies in terms of local and distant control, survival and recurrences, and need for salvage therapy [26,27].

Chemotherapy is indicated for patients with CRC and high-risk features, local or distant metastatic spread [28-30]. Although its benefit in BM was initially thought to be limited because of the anatomic barriers: the blood-tumor and blood-brain barriers, a recent retrospective study showed that administration of chemotherapy after local control of BM in patients with CRC was associated with a statistically significant increase in overall survival, and was the most powerful independent prognostic factor for survival after BM [31]. These results are encouraging, and will hopefully prompt additional studies with a prospective design to further clarify the role of chemotherapy in relation to brain metastases beyond the well documented benefit for reduction in risk of systemic metastases.

Conclusion

Significant progress has been made over the last two decades in management of patients with metastatic colon cancer, leading to curative treatment of patients previously resigned to palliative therapies. This has largely been restricted to patients with limited metastatic disease of the abdomen, liver or lungs, however our case demonstrates that with some patients more aggressive therapy can be extended to include patients with brain metastases with excellent outcomes. Prospective studies are still needed to unify the management of BM in CRC patients, particularly in patients with early and isolated BM, and well-controlled primary tumor site. Unfortunately, these studies will be limited by the small number of cases available. For now, the management should be individualized to each patient, considering prognostic factors and patient's preferences. The best patient care will be achieved by a good communication between the multidisciplinary groups involved in the treatment including the gastroenterologist, neurosurgeon, colorectal surgeon, radiation oncologist and medical oncologist, with the goal to achieve control of the primary tumor, any additional systemic disease and the local brain tumor. It is clear however that the diagnosis of isolated brain metastases is no longer a contraindication to curative intent therapy in selected patients.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing Interests

The authors declare that they have no competing interests.

Authors' Contributions

See accompanying contributions page.

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