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

Cynthia Cherfane1, Muneera R Kapadia2, Ron Schey3 and Adrian Holm4
1Department of Internal Medicine, University of Iowa Roy J. and Lucille A. Carver College of Medicine, 200 Hawkins Drive, Iowa City, USA
2Department of Surgery, University of Iowa Roy J. and Lucille A. Carver College of Medicine, 200 Hawkins Drive, Iowa City, USA
3Corresponding author: Adrian Holm, Department of Internal Medicine, University of Iowa Roy J. and Lucille A. Carver College of Medicine, 200 Hawkins Drive, Iowa City, IA 52242, USA, Tel: 319-356-2742, E-mail: adrian-holm@uiowa.edu

Received date: Jan 10, 2014, Accepted date: Feb 18, 2014, Published date: Feb 25, 2013

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 quadrant anastomosis). A brain MRI showed an enhancing lesion in the right occipital lobe. Three days after his clinic visit he underwent a left 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 pericolic 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 1408.8 ng/mL. Three weeks after the brain metastasis resection, he underwent a laparoscopic right hemicolectomy. Pathology confirmed moderately differentiated adenocarcinoma extending into the pericolic 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, preoperative and postoperative 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 (hSRT) 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].

Hypo fractionated 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 hypo fractionated radiation as a salvage therapy has not been rigorously evaluated, there have been similar results between use of SRS and hSRT 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.

Acknowledgements

We are grateful to our patient, who agreed to the publication of this case report and provided all information needed.

References

1. Cascino TL, Leavengood JM, Kemeny N, Posner JB (1983) Brain metastases from colon cancer. J Neurooncol 1: 203-209.
2. Sundermeyer ML, Meropol NJ, Rogatko A, Wang H, Cohen SJ (2005) Changing patterns of bone and brain metastases in patients with colorectal cancer. Clin Colorectal Cancer 5: 108-113.
3. Morgan JP, Fadul CE, Cole BF, Zaki BI, Suriawinata AA, et al. (2009). Prognostic factors for survival after salvage surgery for locoregional recurrence of colon cancer. J Surg Oncol 101: 49-55.
4. Gómez Raposo C, Mora Rillo M, Gómez Senent S, Robles Maruhenda A, Succi L, Urrico GS, Prumeri S, Politi A, Latteri F (2000) Brain metastasis: first sign of colorectal carcinoma. Chir Ital 52: 419-420.
5. Ruiz-Tovar J, Tartas A, Ramos JL, Miramón J, Limones M (2010) Cranial metastases: first sign of colorectal cancer. Is the resection of the primary non-complicated tumour indicated when the metastases have been resected? Clin Transl Oncol 12: 154-156.
6. Gómez Raposo C, Mora Rillo M, Gómez Senent S, Robles Maruhenda A, Montoya F, et al. (2007) Brain metastases as the first sign of colon cancer. Clin Transl Oncol 9: 742-743.
7. Suzic L, Urdin-GS, Prumeri S, Politi A, Latteri F (2000) Brain metastasis: first sign of colorectal carcinoma. Chir Ital 52: 419-420.
8. Akiyoshi T, Fujimoto Y, Konishi T, Kuroyanagi H, Ueno M, et al. (2011) Prognostic factors for survival after salvage surgery for locoregional recurrence of colon cancer. Am J Surg 201: 726-733.
9. Ku G, Tan IB, Yau T, Boku N, Laohavinij S, et al. (2012) Management of colon cancer: resource-stratified guidelines from the Asian Oncology Summit 2012. Lancet Oncol 13: e70-e81.
10. Garden OJ, Rees M, Poston GJ, Mirza D, Saunders M, et al. (2006) Guidelines for resection of colorectal liver metastases. Gut 55: ii3-8.
11. National Comprehensive Cancer Network (NCCN) (2014) Guidelines for Colon cancer v3.
12. Patchell RA, Tibbs PA, Regine WF, Dempsey RJ, Mohiuddin M, et al. (1998) Postoperative radiotherapy in the treatment of single metastases to the brain: a randomized trial. JAMA 280: 1485-1489.
13. Farnell GF, Buckner JC, Cascino TL, O’Connell MJ, Schomberg PJ, et al. (1996) Brain metastases from colorectal carcinoma. The long term survivors. Cancer 78: 711-716.
14. Jung M, Ahn JB, Chang JH, Sub CO, Hong S, et al. (2011) Brain metastases from colorectal carcinoma: prognostic factors and outcome. J Neurooncol 101: 49-55.
15. Noordijk EM, Veicht CJ, Haaxma-Reiche H, Padberg GW, Voormolen JH, et al. (1994) The choice of treatment of single brain metastasis should be based on extracranial tumor activity and age. Int J Radiat Oncol Biol Phys 29: 711-717.
16. Harji DP, Sagar PM, Boyle K, Griffiths B, McArthur DR, et al. (2013). Surgical resection of recurrent colon cancer. Br J Surg 100: 950-958.
17. Gaspar L, Scott C, Rotman M, Asbell S, Phillips T, et al. (1997). Recursive partitioning analysis (RPA) of prognostic factors in three Radiation Therapy Oncology Group (RTOG) brain metastases trials. Int J Radiat Oncol Biol Phys 37: 745-751.
18. Gaspar LE, Scott C, Murray K, Curran W (2000) Validation of the RTOG recursive partitioning analysis (RPA) classification for brain metastases. Int J Radiat Oncol Biol Phys 47: 1001-1006.
19. Bradley KA, Mehta MP (2004) Management of brain metastases. Semin Oncol 31: 693-701.
20. Kocher M, Soffietti R, Abacioglu U, Villa S, Fauchon F, et al. (2011). Adjuvant whole-brain radiotherapy versus observation after radiosurgery or surgical resection of 1-3 cerebral metastases: results of the EORTC 22952-26001 study. J Clin Oncol 2011: 134:141.
21. Sun A, Bae K, Gore EM, Movsas B, Wong SJ, et al. (2011) Phase III trial of prophylactic cranial irradiation compared with observation in patients with locally advanced non-small-cell lung cancer: neurocognitive and quality-of-life analysis. J Clin Oncol 29: 279-286.
22. Rwigema JC, Wegner RE, Mintz AH, Paravati AJ, Burton SA, et al. (2011) Stereotactic radiosurgery to the resection cavity of brain metastases: a retrospective analysis and literature review. Stereotact Funct Neurosurg 89: 329-337.
23. Karlovits BJ, Quigley MR, Karlovits SM, Miller L, Johnson M, et al. (2009). Stereotactic radiosurgery boost to the resection bed for oligometastatic brain disease: challenging the tradition of adjuvant whole-brain radiotherapy. Neurosurg Focus 27: E7.
24. Jagannathan J, Yen CP, Ray DK, Schlesinger D, Oskouian RJ, et al. (2009) Gamma Knife radiosurgery to the surgical cavity following resection of brain metastases. J Neurosurg 111: 431-438.
25. Kwon KY, Kong DS, Lee JI, Nam DH, Park K, et al. (2007) Outcome of repeated radiosurgery for recurrent metastatic brain tumors. Clin Neuroradiol 109: 132-137.
26. Steinmann D, Maertens B, Janssen S, Werner M, Frühauß J, et al. (2012). Hypofractionated stereotactic radiotherapy (hsSRT) after tumour resection of a single brain metastasis: report of a single-centre individualized treatment approach J Cancer Res Clin Oncol: 1523-1529.
27. Fokas E, Henzel M, Surber G, Kleinert G, Hamm K, et al. (2012) Stereotactic radiosurgery and fractionated stereotactic radiotherapy: comparison of efficacy and toxicity in 260 patients with brain metastases J Neurooncol 109: 91-98.
28. Benson AB, Bekaii-Saab T, Chan E, Chen YJ, Choti MA, et al. (2012) Rectal cancer. J Natl Compr Canc Netw 10: 1528-1564.
29. Nordlinger B, Sorbye H, Gilmeleus B, Poston GJ, Schlag PM, et al. (2008). Perioperative chemotherapy with FOLFIRI4 and surgery versus surgery alone for resectable liver metastases from colorectal cancer (EORTC Intergroup trial 40983): a randomised controlled trial. Lancet 1007-1016.
30. Riquet M, Foucault C, Cazes A, Mitry E, Dujon A, et al. (2010) Pulmonary resection for metastases of colorectal adenocarcinoma. Ann Thorac Surg 89: 373-380.
31. Back JY, Kang MH, Hong YS, Kim TW, Kim DY, et al. (2011) Characteristics and prognosis of patients with colorectal cancer-associated brain metastases in the era of modern systemic chemotherapy. J Neurooncol 104: 745-753.