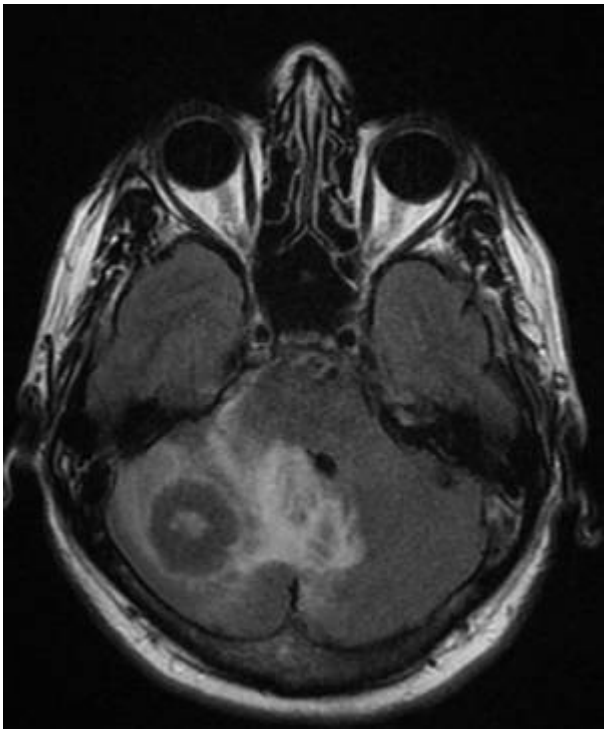
Colorectal cancer intracranial metastases



- Clinicogenomic predictors of survival and intracranial progression after stereotactic radiosurgery for colorectal cancer brain metastases
- HER2 exon 20 mutant non-small cell lung cancer with complete remission of intracranial metastases with trastuzumab deruxtecan: a case report
- Enhanced anti-tumor effects by combination of tucatinib and radiation in HER2-overexpressing human cancer cell lines
- The Impact of Local Control on Overall Survival after Y-90 Selective Internal Radiotherapy of Liver Metastases in Oligometastatic Cancer: A Retrospective Analysis
- HER2 expression and genOmic characterization of rESected brain metastases from colorectal cancer: the HEROES study
- Management of Brain Metastases: A Review of Novel Therapies
- The Role of Stereotactic Radiosurgery in Patients With Brain Metastases From Colorectal Cancers
- Deciphering Brain Metastasis Stem Cell Properties From Colorectal Cancer Highlights Specific Stemness Signature and Shared Molecular Features

---

Epidemiology

Colorectal cancer intracranial metastases epidemiology.

Treatment

Colorectal cancer intracranial metastases treatment.

Outcome

Colorectal cancer intracranial metastases outcome.

Systematic reviews

A systematic review of CRC BMs was performed using the Medline database from 1983 to 2015. The search was limited to studies published in English. Review articles, not relevant case reports or studies or studies relating to animal and in vitro experiments were excluded.

Results: BMs occurred in 0.06-4% of patients with CRC. Most BMs were metachronous and were associated with lung (27-92%) and liver (12-80%) metastases. Treatment options depended on the number of BMs, the general conditions of the patient and the presence of other metastases. The most frequent treatment was whole-brain radiotherapy (WBRT) alone (36%), with median overall survival comprised between 2 and 9 months. Median overall survival was better after surgery alone (from 3 to 16.2 months), or combined with WBRT (from 7.6 to 14 months). After stereotactic radiosurgery alone, overall survival could reach 9.5 months. Many favourable prognostic factors were identified, such as high Karnofsky performance status, low recursive partitioning analysis classes, lack of extracranial disease, low number of BMs, and the possibility to perform surgical treatment.

Conclusion: BMs from CRC are rare. In the presence of favorable prognostic factors, aggressive management including surgical resection with or without WBRT or stereotactic radiosurgery can improve overall survival [1].

Christensen et al. showed that the incidence of BM in CRC patients ranges from 0.6 to 3.2%. BM is a late-stage phenomenon, and a young age, rectal primary and lung metastases are associated with increased risk of developing BM. Molecular markers such as KRAS, BRAF, NRAS mutation as well as an increase in CEA and CA19.9 levels are suggested predictors of brain involvement. However, only KRAS mutations are reasonably well investigated and associated with an increased risk of BM.

The incidence of BM from CRC is 0.6 to 3.2% and did not seem to increase over time. Development of BM is associated with young age, lung metastases, rectal primary and KRAS mutation. Increased awareness of brain involvement in patients with these characteristics is necessary [2]

Case series

A total of 228 patients (134 male [59%], 94 female [41%]) with histologically proven CRC and BM were classified into different groups according to extracranial metastatic patterns. Time intervals to metastatic events and survival times from initial CRC diagnosis, extracranial and intracranial metastasis were analyzed. Extracranial organs mostly affected were the liver (102 of 228 [44.7%]) and the lung (96 of 228 [42.1%]). Liver and lung metastases were detected in 31 patients (13.6%). Calculated over the entire course of the disease, patients with lung metastasis showed longer overall survival (OS) than patients with liver metastasis or patients without lung metastasis (43.9 vs 34.6 [P

= .002] vs 35.0 months [P = .002]). From the date of initial CRC diagnosis, lung metastasis occurred later in CRC history than liver metastasis (24.3 vs 7.5 months). Once lung metastasis was diagnosed, BM occurred faster than in patients with liver metastasis (15.8 vs 26.0 months; Δ 10.2 months). Accordingly, OS from the diagnosis of liver metastasis was longer than from lung metastasis (27.1 vs 19.6 months [P = .08]). Once BM was present, patients with lung metastasis lived longer than patients with liver metastasis (3.8 vs 1.1 months [P = .028]). The shortest survival times in all survival categories analyzed revealed patients with concurrent liver and lung metastasis. Patients with CRC and BM form a heterogeneous cohort where extracranial metastasis to the liver or lungs predicts survival [3].

2019

A retrospective cohort study was conducted at a tertiary care cancer center. Subjects were patients with brain metastases from CRC among all patients who received initial treatment for CRC at the National Cancer Center Hospital from 1997 to 2015 (n = 7147). Prognostic clinicopathological variables for overall survival (OS) were investigated.

There were 68 consecutive patients with brain metastases from CRC, corresponding to 1.0% of all patients with CRC during the study period. The median survival time was 6.8 months. One-year and 3-year OS rates were 28.0 and 10.1%, respectively. Among the six covariates tested (age, KPS, presence of extracranial metastases, control of primary lesion, number of brain metastases, and history of chemotherapy), multivariate analysis revealed KPS (score ≥ 70), number of brain metastases (1-3), and no history of chemotherapy to be independent factors associated with better prognosis.

In addition to KPS, the number of brain lesions and history of chemotherapy was independent prognostic factors for OS in patients with brain metastases from CRC. An awareness of these factors may help gastrointestinal surgeons make appropriate choices in the treatment of these patients [4].

2017

Nozawa et al. retrospectively reviewed data on a total of 2,238 patients with primary CRC who underwent surgical resection at our hospital between 1999 and 2014. Predictive factors for BM and prognostic factors after the diagnosis of BM were examined by univariate and multivariate analyses using Cox proportional hazards models.

Three patients (0.1%) had BM at the initial diagnosis, and 23 patients (1.2%) developed metachronous BM during the median follow-up period of 44.6 months. Lung and bone metastases were identified as independent predictive factors for BM. Median survival after the diagnosis of BM was 7.4 months. Stereotactic radiosurgery, administered to 41% of the patients with BM, was associated with a better postdiagnostic survival.

CRC patients with metastasis to the lung or bone were at a higher risk of BM. Because the survival is still limited, it is crucial to determine the treatment strategy in consideration of the characteristics of each therapy and quality of life in CRC patients with BM [5].

---

56 consecutive colorectal cancer patients who underwent neurosurgical resection of BM. Tumor

samples were tested for KRAS, NRAS, BRAF and PIK3CA. The molecular profile of the brain lesion was compared with the corresponding primary tumor.

The molecular profile concordance rate was 95.1%. Median survival after neurosurgery was 5.5 months (95% CI: 4.7-6.3); median overall survival was 24.0 months (95% CI: 15.6-32.4).

In this cohort, Aprile et al. report a high frequency of KRAS mutations and a very high concordance rate between the molecular status of BM and that of matched primary tumors [6].

---

44 patients with colorectal and one patient with anal canal primary. The median marginal dose to the radiosurgery volume was 17 Gy (range 10-24 Gy). Thirteen patients were treated with whole-brain radiotherapy (WBRT) prior to GKS.

The median dose delivered to the margin of the tumour was 17 Gy (range: 10-24 Gy). The median largest tumour diameter was 2.7 cm (range: 0.60-6.1 cm).

Colorectal cancer metastases tend to have a higher rate of leptomeningeal failure than other types of GI cancer metastases [7].

Case reports

A 57-year-old man who visited the department for headache and lightheadedness. He was admitted with a diagnosis of brain tumor based on imaging findings. Severe brain dysfunction and mild ataxia were observed, and craniotomy tumor resection was performed 5 days after admission. He was diagnosed with brain metastasis of colorectal cancer based on histopathological examination and endoscopic findings, and was therefore referred. No extracranial metastases were observed, laparoscopic-assisted low anterior resection was performed 1 month after the craniotomy. The final diagnosis was rectal cancer(Ra), pT3N0M1a(BRA), Stage IVa. Three months after the craniotomy, subsequent MRI examination revealed a new metastatic lesion inferior to the tumor excision cavity, and gamma knife radiosurgery was performed. However, because an increasing tendency was noted, craniotomy was performed again 7 months after the first craniotomy. Following operative treatment, follow up has been performed without adjuvant chemotherapy or prophylactic irradiation, the patient has survived without recurrence at 34 months postoperatively. A valuable rare case of solitary brain metastasis of colorectal cancer in which prognosis could be expected by radical resections [8].

2021

A rare case of a 49-year-old patient presenting with headaches and left-sided weakness found to have a solitary brain metastasis from primary rectal cancer. Primary rectal cancer, young age, lung and liver metastases, and KRAS mutation are risk factors associated with brain metastases in patients with colorectal cancer. Intracranial imaging should be considered as part of the workup in the staging of colorectal cancer in patients who are at high risk of brain metastasis [9].

2006

A 52-year-old woman in whom the first manifestation of the disease was metastasis to brain [10].

1998

Erten et al. report a patient with rectum adenocarcinoma which metastasized into the cerebellum and mimicked a stroke, and discuss the clinical features and diagnostic problems of this uncommon condition [11].

References

1)
Mege D, Sans A, Ouaissi M, Iannelli A, Sielezneff I. Brain metastases from colorectal cancer: characteristics and management. ANZ J Surg. 2018 Mar;88(3):140-145. doi: 10.1111/ans.14107. Epub 2017 Jul 7. PMID: 28687024.

2)
Christensen TD, Spindler KL, Palshof JA, Nielsen DL. Systematic review: brain metastases from colorectal cancer–Incidence and patient characteristics. BMC Cancer. 2016 Apr 1;16:260. doi: 10.1186/s12885-016-2290-5. Review. PubMed PMID: 27037031; PubMed Central PMCID: PMC4818396.

3)
Thurmaier J, Heinemann V, Engel J, Schubert-Fritschle G, Wiedemann M, Nüssler NC, Ruppert R, Kleeff J, Schepp W, Löhe F, Karthaus M, Neumann J, Kumbrink J, Taverna F, Stahler A, Heinrich K, Westphalen CB, Holch JW, Kirchner T, Michl M. Patients with colorectal cancer and brain metastasis: The relevance of extracranial metastatic patterns predicting time intervals to first occurrence of intracranial metastasis and survival. Int J Cancer. 2021 Apr 15;148(8):1919-1927. doi: 10.1002/ijc.33364. Epub 2020 Dec 2. PMID: 33113215.

4)
Imaizumi J, Shida D, Narita Y, Miyakita Y, Tanabe T, Takashima A, Boku N, Igaki H, Itami J, Kanemitsu Y. Prognostic factors of brain metastases from colorectal cancer. BMC Cancer. 2019 Jul 31;19(1):755. doi: 10.1186/s12885-019-5973-x. PubMed PMID: 31366387; PubMed Central PMCID: PMC6670227.

5)
Nozawa H, Ishihara S, Kawai K, Sasaki K, Murono K, Otani K, Nishikawa T, Tanaka T, Kiyomatsu T, Hata K, Watanabe T. Brain Metastasis from Colorectal Cancer: Predictors and Treatment Outcomes. Oncology. 2017;93(5):309-314. doi: 10.1159/000478661. Epub 2017 Jul 13. PubMed PMID: 28700994.

6)
Aprile G, Casagrande M, De Maglio G, Fontanella C, Rihawi K, Bonotto M, Pisa FE, Tuniz F, Pizzolitto S, Fasola G. Comparison of the molecular profile of brain metastases from colorectal cancer and corresponding primary tumors. Future Oncol. 2017 Jan;13(2):135-144. PubMed PMID: 27578453.

7)
Page BR, Wang EC, White L, McTyre E, Peiffer A, Alistar A, Mu F, Loganathan A, Bourland JD, Laxton AW, Tatter SB, Chan MD. Gamma Knife radiosurgery for brain metastases from gastrointestinal primary. J Med Imaging Radiat Oncol. 2017 Jan 31. doi: 10.1111/1754-9485.12584. [Epub ahead of print] PubMed PMID: 28139076.

8)
Ida A, Yokomizo H, Okayama S, Yamada Y, Maeda H, Asaka S, Usui T, Shimakawa T, Katsube T, Kato H, Yoshimatsu K, Shiozawa S. [A Case of Rectal Cancer Diagnosed Based on Brain Metastasis and Had a Long-Term Prognosis by Radical Resections]. Gan To Kagaku Ryoho. 2022 Feb;49(2):223-225. Japanese. PMID: 35249068.

9)
Shaikh AS, Pavurala R, Gou E. Brain Metastasis in a Young Patient: Consider the Rectum. Cureus. 2021 Nov 30;13(11):e20055. doi: 10.7759/cureus.20055. PMID: 34987931; PMCID: PMC8718300.
10)
Mazur I, Rudnicki P, Kozłowski A, Pardela M. [Metastasis to brain from rectal cancer as the first manifestation of neoplasmatic disease]. Wiad Lek. 2006;59(5-6):422-3. Polish. PubMed PMID: 17017496.
11)
Erten SF, Ertaş E, Duygulu C, Aydin EN, Colak A. An unusual presentation of metastatic adenocarcinoma in the cerebellum associated with intratumoral hemorrhage mimicking a stroke. A case report. Neurosurg Rev. 1998;21(1):69-71. PubMed PMID: 9584291.