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CASE REPORT

Precocious Brain Metastasis of Colorectal Cancer: A Report of Two Cases

Precocious Beyin Metastazı Olan Kolorektal Kanserli İki Olgunun Sunumu

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ABSTRACT

Colorectal cancer is one of the most common causes of death due to cancer. In the majority of patients, diagnosis of brain metastasis (80%) follows diagnosis of the systemic cancer (metachronous presentation). However, brain metastases can be diagnosed before primary tumour diagnosis (precocious presentation) or simultaneously (synchronous presentation). With this case report, we aim to share the experience we gained with these two cases of precocious brain metastasis. These cases demonstrate that tumour biology is one of the most important of the widely recognized prognostic factors of colorectal cancer.

Keywords: Colorectal, precocious brain metastasis, cancer

ÖZ

Kolorektal kanserler halen en önemli kanser ölüm nedenlerinden biridir. Beyin metastazlı hastaların çoğunda (%80) metastaz sistemik kanserin tanısı konulduktan sonra (metakron prezentasyon) ortaya çıkar. Ancak, bazı hastalarda beyin metastazı primer tümör saptanmadan önce (precocious prezentasyon) ya da aynı zamanda (senkronize prezentasyon) teşhis edilebilir. Biz de bu olgu sunumumuzda precocious beyin metastazı ile başvuran iki olgumuzda kazanmış olduğumuz deneyimi paylaşmayı amaçladık. Bu iki olgudaki deneyimimiz, kolorektal kanserlerin yaygın olarak kabul edilen prognostik faktörleri arasında, tümör biyolojisinin önemli faktörlerden birisi olduğudur.

Anahtar Kelimeler: Kolorektal, precocious beyin metastazı, kanser

Introduction

Colorectal cancer is currently one of the main causes of cancer mortality. Synchronized metastatic cancer is found at initial diagnosis in 10-15% of primary colorectal carcinoma patients. In adults, primary tumors responsible for brain metastases are pulmonary in 50%, breast in 15-30% and colon in 5% of cases, while no primary focus can be detected in 10-15%. The incidence of colorectal cancer with brain metastasis (0.4-2.3%) is low compared to the rates of colorectal cancer with liver (20-30%) and lung (10-20%) metastasis. However, there has been an increase in reported cases due to advances of magnetic resonance imaging (MRI) and systemic colorectal cancer therapy. For most patients with brain metastasis (80%), metastasis appears after the systemic cancer is diagnosed (metachronous presentation).[1] However, in some cases, brain metastasis may be diagnosed before (precocious presentation) or at the same time (synchronized presentation) as the primary tumor.[2,3,4] Brain metastases are the most common intracranial malignancies and occur at 10 times the frequency of primary brain tumors.[5,6]

The average survival after diagnosis of colorectal cancer with brain metastasis has been reported as 2.7-8.3 months.[7] In patients with no detectable primary focus and brain metastasis as the sole finding, those with the best prognosis have an average survival of 13.4 months. Patients with brain metastasis of breast cancer have a better prognosis than patients with brain metastases of other primary tumors. In contrast, patients with brain metastasis of colorectal cancer tend to have a worse prognosis. This may be attributable to the higher prevalence of cerebellar metastasis in these patients, which has poor prognosis among intracranial tumors.[8]

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In this study, we present two cases of colon cancer patients presenting with precocious brain metastasis and discuss their treatment and follow-up.

Case Reports

Case 1

A 55-year-old male patient presented in January 1989 due to sudden-onset epileptic seizures. Two different masses were observed on brain MRI. One was located in the right temporo-parietal region and measured 1.5 cm; the other was located in the left frontal lobe and was 1 cm in size. The patient had right visual field scotoma. The brain lesions were surgically removed. Pathologic diagnosis was reported as poorly differentiated adenocarcinoma metastasis. The pathology report suggested the gastrointestinal system (GIS) as a possible primary focus; therefore, the GIS and other systems were investigated.

No primary focus was found during radiologic, endoscopic or biochemical tests. The patient underwent fractionated cranial radiotherapy and was followed closely at 3-month intervals. In July 1989, during tests conducted 7 months after brain metastasis diagnosis, the patient had a positive fecal occult blood (FOB) test. Subsequent colonoscopy revealed a 7x8x8 cm mass located in the cecum and invading the terminal ileum and mezoileum. In July 1989, the patient underwent complete excision of the tumor and extended right hemicolectomy with lymph node dissection. Pathologic diagnosis was reported as colon adenocarcinoma. The patient was treated with 6 courses of adjuvant chemotherapy consisting of a combination of 5-fluorouracil (FU) and folinic acid (FA).

Following adjuvant chemotherapy, the patient was followed at regular intervals for 13 years starting in 1990. In April 2002, the patient was determined to be anemic and FOB test was positive. Colonoscopy revealed an ulcerovegetating mass at the junction of the descending colon and sigmoid colons, and a biopsy of the mass was reported as adenocarcinoma. The lesion was excised with clean surgical margins in a subtotal colectomy surgery. The pathology report indicated poorly differentiated adenocarcinoma, Dukes C. Because the patient's first colon tumor originated from the cecum and the second originated from the descending colon-sigmoid junction, the latter was considered a new primary focus unrelated to the first tumor. The patient had no distant organ metastasis. Recurrence was not detected on repeat brain MRI examination. The patient continued to be followed at 6-month intervals and survived for a total of 15 years after the appearance of brain metastasis. In 2004, he died of cancer-related causes.

Case 2

A 61-year-old male patient presented to an ophthalmologist with the complaint of epiphorea starting in November 2014. His medical history included type 2 diabetes mellitus and hypertension. Ophthalmologic examination revealed papillary edema possibly resulting from an intracranial pathology, so the patient was referred to the neurology clinic for evaluation. On brain MRI, an irregularly shaped 37x45 mm solid mass lesion with surrounding edema was observed in the right occipital lobe and gray parietal lobe. The brain lesion was suspected to be metastasis; colonoscopy conducted to find the primary focus revealed a mass in the rectum. The result of colonoscopic biopsy was reported as adenocarcinoma. Carcinoembryonic antigen and carbohydrate antigen 19-9 values were normal. Between January and June 2015, the patient underwent neoadjuvant chemoradiotherapy for the brain and rectum consisting of fractionated radiotherapy (28 days for the rectal lesion and 18 days for the brain lesion) and 12 rounds of chemotherapy (a triple regimen of FA, 5-FU and irinotecan). Nine to 10 weeks after the patient underwent primary chemotherapy and local radiotherapy, the patient was admitted to the clinic for rectal surgery. Because in this case laparoscopic surgery may have led to elevated intracranial pressure syndrome, the patient underwent open low anterior resection with a coloanal straight anastomosis to 2 cm above the dentate line with a protective loop ileostomy surgery in July 2015. Postoperative pathologic diagnosis was a 3.5 cm diameter, moderately differentiated, mucinous rectal adenocarcinoma (AJCC version 7 2010: T3, N0, M1a, Stage IVa). The patient was discharged and followed at 3-month intervals. Brain MRI conducted in November 2014 revealed a metastatic intracranial mass approximately 4x4 cm in size, which measured 7x8 cm on MRI in August 2015. A craniotomy and metastasectomy was performed using neuronavigation in October 2015. The patient underwent ileostomy closure surgery in December 2015 following adjuvant chemotherapy. The patient survived for a total of 16 months after being diagnosed with brain metastasis, dying in January 2016 due to cancer-related causes.

Discussion

Metastatic brain masses are not common and are usually associated with disease of another region. Although it was previously believed that 10-15% of intracranial tumors were metastatic, this rate has more recently been reported as 20-40%.[1,2,3,4,5,9] Brain metastasis as the initial sign of primary colon cancer, without lung or liver metastasis is extremely rare, and only a few cases can be found in the literature.[10,11,12] The intracranial spread pattern and focus number of a metastatic tumor depends on the origin and

type of the primary tumor. There are several factors that affect the prognosis of central nervous system tumors. These include the size and number of metastatic foci, the extent of peritumoral edema and response to pharmacologic agents, whether the mass can be resected and the possibility of local recurrence on the same side as the metastatic tumor resection, radiosensitivity of the primary tumor, and timing of metastasis diagnosis (precocious vs metachronous presentation).[3,4,8] In adults, the origin of brain metastasis is lung in 41% of cases, breast in 19%, malignant melanoma in 10%, GIS in 7%, colorectal in 4%, and genito-urinary system (kidney) in 3%.[13]

The frequency of intracranial metastasis of colorectal system cancers is 33% for rectum, 23% for sigmoid colon, 15% for cecum and ascending colon, 9% for rectosigmoid colon, 4% for descending colon, and 1% for transverse colon.[14] Brain metastasis is present at diagnosis in 1-3% of colorectal cancer patients, while 10% develop metastasis during the course of disease.[7,15] The management of brain metastasis of colorectal cancer is determined by several factors, including patient performance; location, grade, and type of the primary cancer; number and location of brain lesions, and the presence of leptomeningeal disease.[16] Metastatic tumor cells reach the brain via hematogenous spread. Arterial circulation is the primary route to the brain, though a small proportion of cells from pelvic and retroperitoneal cancers may reach the brain via Batson's plexus (vertebral venous system).[4] Brain metastases are often found in the gray-white junction where the vascular structures narrow and embolism is more likely.[17] Approximately 80% of brain metastases are found in the cerebral hemispheres, 15% in the cerebellum and 5% in the brain stem. In both of our cases, the lesions were located in the cerebral hemispheres. Molecular studies have demonstrated that brain metastases as associated with disruption of the blood-brain-barrier. Colon, breast, and renal cancer metastases are often single (37-50%), whereas malignant melanoma and lung cancer metastases are usually multifocal (63%).[18,19] The most common presenting symptom for these patients is headache. The focal weakness, papillary edema, and focal and generalized seizures exhibited in our two cases are also common signs.[20] Rarely, as in the two cases reported here, brain metastases may be detected incidentally while investigating other symptoms.

The best diagnostic method for brain metastases is contrast MRI and computed tomography examination. These methods allow metastasis to be differentiated from primary brain tumors, abscesses, cerebral infarcts, and hemorrhage. Angiography and/or biopsy are generally requried for definitive diagnosis. Stereotactic biopsy is a safe and appropriate approach for obtaining brain tissue.[21] Untreated brain metastases have a poor prognosis, with an average survival of about 4 weeks.[22]

The best treatment approach for patients whose brain metastasis consists of a single focus is full brain radiotherapy, surgery and stereotactic radiosurgery.[23,24] Surgical removal of metastatic brain lesions extends survival.[25,26] Increased awareness, early diagnosis and aggressive treatment of brain metastases may increase survival in colorectal cancer patients with brain metastasis to 3.5-7.13 months. Although the development of brain metastasis usually indicates poor prognosis, it is now possible to alleviate most symptoms associated with brain metastasis and substantially improve patients' quality of life. In a case series reported by Vagn-Hansen and Rafaelsen[9], they reported that operated patients lived 1 month longer than patients who were not operated. Malafosse et al.[3] reported that the survival of patients who underwent chemoradiotherapy and aggressive surgery with craniectomy was significantly longer than in those who did not undergo surgery (86.6±17.35 days or 2.9±0.59 months). Metastasectomy is a common practice in oncologic surgery.[4,8] In rare cases, a metastatic lesion may be detected in the brain in the absence of any signs of disease. In these cases, metastasectomy (craniotomy of the metastatic lesions) is necessary to extend survival.[5,27] Our first case survived for 15 years after the diagnosis of metastatic cancer. This period is remarkably long when compared to the literature. We attribute this to the biological behavior of the patient's tumor. Another interesting aspect of this case is the secondary colon malignancy which appeared after 13 years. Our second case survived for 16 years after metastatic cancer diagnosis, which is consistent with the best prognosis reported in the literature.

In conclusion, although there are few case series of this kind and our own series comprises only two patients, several points must be kept in mind: albeit rare, the brain is a metastasis zone for colorectal cancers; during treatment, priority should be given to symptom-producing brain metastases and complete surgical resection is required; following neoadjuvant chemoradiotherapy, primary focus resection should be performed with reliable surgical margins and oncologic principles; and patients should be followed using a multidisciplinary approach.

On the other hand, we are rapidly acquiring new information about molecular oncogenetics and how malignant cells behave. Our experience with these two cases shows that, of the widely accepted prognostic factors for colon cancer, tumor biology is an important factor.

Ethics

Informed Consent: Consent form was filled out by all participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Şahin Kaymak, Sezai Demirbaş, Consept: Şahin Kaymak, Sezai Demirbaş, Design: Şahin Kaymak, Hüseyin Sinan, Data Collection or Processing: Şahin Kaymak, Mehmet İnce, Analysis or Interpretation: Şahin Kaymak, Literature Search: Şahin Kaymak, Oğuz Hançerlioğulları, Writing: Şahin Kaymak.

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References

1. Succi L, Urrico GS, Prumeri S, Politi A, Latteri F. Brain metastases: first sign of colorectal carcinoma. Chir Ital 2000;52:419-420.
2. Wen PY, Black PM. Metastatic brain cancer. In: De Vita VT. Cancer, principles and Practice of oncology. Philadelphia: Lippincott-Williams, 2001;2655-2670.
3. Malafosse R, Penna C, Sa Cunha A. Surgical management of hepatic metastases from colorectal malignancies. Ann Oncol 2001;12:887-894.
4. Skibber MD. Spread of colon cancer. In: De Vita. Cancer, principles and practice of oncology. Philadelphia: Lippincott-Williams, 2001;1229-1238.
5. Arnold SM, Patchell RA. Diagnosis and management of brain metastases. Hem Oncol Clin N Am 2001;15:1085-1107.
6. Jenkinson MD, Haylock B, Shenoy A, Husband D, Javadpour M. Management of cerebral metastasis: evidence-based approach for surgery, stereotactic radiosurgery and radiotherapy. Eur J Cancer 2011;47:649-655.
7. Kruser TJ, Chao ST, Elson P, Barnett GH, Vogelbaum MA, Angelov L, Weil RJ, Pelley R, Suh JH. Multidisciplinary management of colorectal brain metastases: A retrospective study. Cancer 2008;113:158-165.
8. Greco FA. Cancer of unknown primary site. In: De Vita. Cancer, principles and practice of oncology. Philadelphia: Lippincott-Williams, 2001;2001-2038.
9. Vagn-Hansen CA, Rafaelsen SR. Brain metastases from colorectal cancer. Ugeskr Laeger 2001;163;1864-1865.
10. Succi L, Urrico GS, Prumeri S, Politi A, Latteri F. Brain metastasis: first sign of colorectal carcinoma. Chir Ital 2000;52:419-420.
11. Gomez Raposo C, Mora Rillo M, Gomez Senent S, Robles Maruhenda A, Montoya F, Garcia Puig J, Gonzalez Baron M. Brain metastases as the first sign of colon cancer. Clin Transl Oncol 2007;9:742-743.
12. Ruiz-Tovar J, Tartas A, Ramos JL, Miramón J, Limones M. 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 2010;12:154-156.
13. Nayak L, Lee EQ, Wen PY. Epidemiology of brain metastases. Curr Oncol Rep 2012;14:48-54.
14. Balasingam V, McCutcheon IE. Metastatic colorectal carcinoma, chapter 16. In: Sawaya R, ed. Intracranial Metastases, Current Management Strategies. Malden, MA: Blackwell, 2004:279-291.
15. Schouten LJ, Rutten J, Huveneers HA, Twijnstra A. Incidence of brain metastases in a cohort of patients with carcinoma of the breast, colon, kidney, and lung and melanoma. Cancer 2002;15:2698-2705.
16. Vogelbaum MA, Suh JH. Resectable brain metastases. J Clin Oncol 2006;24:1289-1294.
17. Hwang T, Close TP, Grego JM. Predilection of brain metastases in gray and white matter junction and vascular border zones. Cancer 1996;77:1551-1555.
18. Delattre JY, Krol G, Thaler HT. Distribution of brain metastases. Arch Neurol 1998;45:741-744.
19. Linskey ME, Andrews DW, Asher AL, Burri SH, Kondziolka D, Robinson PD, Ammirati M, Cobbs CS, Gaspar LE, Loeffler JS, McDermott M, Mehta MP, Mikkelsen T, Olson JJ, Paleologos NA, Patchell RA, Ryken TC, Kalkanis SN. "The role of stereotactic radiosurgery in the management of patients with newly diagnosed brain metastases: a systematic review and evidence-based clinical practice guideline," J Neurooncol 2010;96:45-68.
20. Bartelt S, Lutterbach J. Brain metastases in patients with cancer of unknown primary. J Neurooncol 2003;64:249-253.
21. Postner JB. Clinical manifestation of brain metastases. In: Weiss L, Gilbert HA, Posner JB, editors. Brain metastases. Boston: GK Hall, 1980;189-207.
22. Succi L, Urrico GS, Prumeri S, Politi A, Latteri F. Brain metastasis: first sign of colorectal carcinoma. Chir Ital 2000;52:419-420.
23. Nieder C, Pawinski A, Molls M. Prediction of short survival in patients with brain metastases based on three different scores: a role for 'triple-negative' status? Clin Oncol (R Coll Radiol) 2010;22:65-69.
24. Siu TL, Jeffree RL, Fuller JW. Current strategies in the surgical management of cerebral metastases: an evidence-based review. J Clin Neurosci 2011;18:1429-1434.
25. Ko FC, Liu JM, Chen WS, Chiang JK, Lin TC, Lin JK. Risk and patterns of brain metastases in colorectal cancer. Dis Colon Rectum 1999;42:1467-1471.
26. Zorrilla M, Alonso V, Herrero A, Corral M, Puertolas T, Trufero JM, Artal A, Anton A. Brain metastases from colorectal carcinoma. Tumori 2001;87:332-324.
27. Wrensk M, Arbit E. Resection of brain metastases from colorectal carcinoma in 73 patients. Cancer 1999;85:1677-1685.