

Survival from the precocious brain metastasis of the colon cancer

NECDET ÜSKENT¹, SEZAI DEMİRBAŞ², ORHAN TÜRKEN³, ŞÜKRÜ YILDIRIM⁴, COŞKUN TECİMER¹, GÖKHAN KANDEMİR³, MUSTAFA YAYLACI³

¹Metropolitan Florence Nightingale Hospital, Department of Medical Oncology, GATA Haydarpaşa Training Hospital, Departments of ²General Surgery, ³Medical Oncology and ⁴Pathology, İstanbul - Turkey

ABSTRACT

Brain metastases frequently occur after the diagnosis of systemic cancer. However some patients with brain metastasis may be diagnosed before the primary tumor is found (precocious presentation). Colorectal cancer patients with brain metastasis have a poor prognosis due to the tendency of these patients to have a higher frequency of cerebellar metastases. Two different masses on the brain was found by MRI in a fifty-five year old man in January 1989. Pathologic examination revealed poorly differentiated adenocarcinoma. An extensive investigation failed to reveal the primary site. After 7 months, a mass in the caecum was found by colonoscopy. Complete surgical resection of the tumor and lymph nodes was performed. Pathologic specimen was reported as adenocarcinoma. In April 2002, 13 years after the diagnosis of colon cancer, colonoscopy revealed an ulcerovegetative mass in ascending colon and biopsy disclosed adenocarcinoma in low grade differentiation. This case is a survivor of inevitable death from the metastatic colon cancer and the second colonic malignancy has appeared 13 years later. [Turk J Cancer 2003;33(3):154-157]

KEY WORDS:

Colon, cancer, brain, metastasis

INTRODUCTION

Colorectal cancer is one of the most cancers leading causes of death from cancer in the industrialized countries. There is no curative treatment for unresectable or metastatic colon cancer and survival is about 9 months. Cure for colorectal cancer depends on its resectability. From 10%-15% of patients with primary colorectal cancer will present with synchronous metastatic cancer disease. Patients with synchronous metastases that are potentially resectable should undergo definitive surgical resection of the primary tumor. Brain metastases develop in approximately 10% to 30% of adults and 6% to 10% of children with cancer. In adults, the most common primary tumors responsible for brain metastasis are lung (50%), breast (15-30%), unknown primary (10-15%) and colon (5%). In the majority of patients (80%), brain metastases develop after the diagnosis of systemic cancer (metachronous presentation) (1). However in some patients, brain metastases may be diagnosed before the primary tumor is found (precocious presentation) or at the same time (synchronous presentation) (2-4). Besides, metastases to the brain are the most common intracranial tumor outnumbering ten times as much as primary brain tumors (5).

Patients with brain metastasis as the only manifestation of an undetected primary tumor have a favorable prognosis

with an overall median survival of 13.4 months. Breast cancer patients with brain metastasis generally have more favorable prognosis than brain metastases from other types of primary tumors. On the other hand, patients with colorectal carcinoma tend to have a poorer prognosis. This may be due to the tendency of these patients to have a higher frequency of cerebellar metastases, which are associated with an adverse prognosis (6).

A patient presenting with brain metastasis and precocious presentation of colorectal primary has a very poor prognosis with no long-term survival expectancy. The patient reported here has been a survivor of brain metastasis with precocious presentation (7 months before the diagnosis of colorectal cancer) for 13 years. However, he has been recently diagnosed to have a second primary in the descending colon.

CASE REPORT

Fifty-five year old male patient was admitted to the hospital for the evaluation of sudden onset seizures on 13th of January 1989. An magnetic resonance imaging (MRI) of the whole brain revealed two different masses. One was in the right temporo-parietal region measured 1.5 cm in size and the second in the left side of the frontal lobe of the brain that was 1 cm in size. He experienced scotomas in his right visual area. Surgical resection was performed and brain lesions were successfully removed. Pathologic diagnosis was poorly differentiated adenocarcinoma. After it was suggested by the pathologist that the primary might be gastrointestinal tract in origin, special care was given to find any lesion in the gastrointestinal tract.

An extensive investigation for the primary site including CT scans of the thorax and abdomen, bronchoscopy, bone scintigraphy, thyroid ultrasonography, some biochemical markers, and colonoscopy as well as gastroduodenoscopy failed to reveal the primary site. A total of 30 gray (Gy) the fractionated regimen of cranial radiotherapy (RT) was given and the patient was followed closely with 3 month intervals. In July 1989, seven months after the diagnosis of brain metastases, the patient was found to have positive occult blood in his stool. Colonoscopy revealed a 7x8x8 cm mass in the caecum invading terminal ileum and mesentery. Complete resection of the tumor and lymph node

dissection by surgical procedure with ileocolostomy was successfully performed on July 1989. Pathologic specimen was reported as adenocarcinoma. The patient received adjuvant treatment consisted of 5-fluorouracil (FU) 425 mg/m² and folinic acid (FA) 20 mg/m² for 6 cycles.

Following the adjuvant treatment with FU+FA regimen, the patient was followed up for 13 years with 6 months intervals since 1990. In April 2002, the patient was found to be anemic. Stool occult blood test was positive. Colonoscopy this time revealed an ulcerovegetative mass in ascending colon near to sigmoid junction and biopsy revealed adenocarcinoma (Figure1). Then this lesion was resected with clear surgical margins. Pathology disclosed adenocarcinoma in low grade differentiation (second primary) and the case was staged as Dukes C. This was accepted as a second primary having no relation with the first lesion, because of the differences in the origins of the two tumoral masses. There was no visceral organ metastasis including the liver and the lung. A repeat MRI of the brain did not show any recurrence.

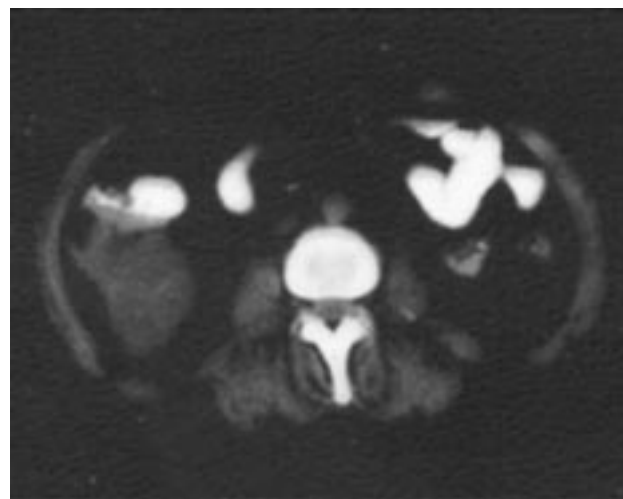


Fig 1. An ulcerovegetative mass in ascending colon near to sigmoid junction

DISCUSSION

Metastatic brain mass is uncommon and frequently associated with metastatic disease elsewhere. Older estimates suggested that metastases constituted 10% to 15% of all intracranial tumors. However, current events estimate their frequency at 20% to 40% (1-5,7). The origin of the primary

tumor is associated with the frequency and pattern of intracranial spread. Some factors that apply specifically to central nervous system involvement include; 1.) The number and size of metastatic foci, 2.) The extent of peritumoral edema and its responsiveness to pharmacologic agents, 3.) Resectability of a solitary focus and the rare possibility of local recurrence at the site of the metastatic tumor resection, 4.) Radiosensitivity of the primary tumor, 5.) The time of the diagnosis of the metastatic tumor whether it is found before the diagnosis of the primary (precocious presentation) or after the diagnosis of the primary (metachronous presentation) (3,4,6). In adults, the commonest sources of brain metastases are the lung, breast, gastrointestinal tract, genitourinary tract and malignant melanoma (Table 1) (4). Tumor cells metastasize to the brain by hematogenous spread. The arterial circulation provides the primary conduit to the brain, although a small proportion of tumor cells from pelvic and retroperitoneal cancers may reach the brain by Batson's plexus (the vertebral venous system) (4). Within the brain, metastases are found most commonly in the gray-white junction area, where the decreased size of blood vessels act as a trap for emboli (8). About 80% of brain metastases are located in the cerebral hemispheres, 15% in the cerebellum and 5% in the brainstem. The molecular investigation showed that brain metastases are undoubtedly related to the breakdown of the blood-brain barrier. Metastases from colon, breast and renal cell carcinoma are often single, whereas malignant melanoma and lung cancer

produce multiple cerebral lesions (9). Headache is the commonest presenting symptom (Table 2). Focal weakness, papil edema, focal generalized seizures, as our patient had, are common (10). The best diagnostic test for brain metastases are contrast-enhanced MR imaging and CT. It is important that metastases should be distinguished from primary brain tumors, abscesses, cerebral infarction and hemorrhages. Other diagnostic measures being needed to establish the diagnosis firmly are angiography and/or biopsy. Stereotactic biopsy has become the most convenient and safe approach to obtain a tissue diagnosis (11). Untreated brain metastases are associated with a median survival time of about 4 weeks and poor prognosis (12). At the time of diagnosis of colorectal carcinoma, 2-3% of patients are likely to be harboring brain metastases and another 10% of patients will develop brain lesions during the course of their disease. Surgical removal of colorectal metastatic brain lesions in selected cases may result in a longer survival time. Increased awareness of the possibility of brain metastases, early diagnosis and aggressive therapy can provide increased survival time for patients with colorectal cancer with brain metastases (3,5-7,13). Although the development of brain metastases usually indicates a poor prognosis for each patient, it is now possible to reverse most of the symptoms of brain metastases and improve significantly a patient's quality of life (QoL) as well. Vagn-Hansen and Rafaelsen (7) noticed in their particular series that surgical procedures made survival time longer than that was 1 month.

Table 1
Frequency of brain metastases by primary tumor type

Primary Tumor	Number of Patients (n)	(%)
Lung	270	48
Breast	82	15
Melanoma	50	9
Colon	26	5
Other known primary	72	13
Unkown primary	61	11
Total	561	100

Malafosse et al. (3) stated that aggressive surgical treatment with chemo-radiotherapy can provide significantly augmented survival time in patients undergoing craniectomy than those with no surgical intervention (86.6 ± 17.35 vs 2.9 ± 0.59 months). Metastatectomy is widely practiced in surgical oncology (4,6). Rarely the metastatic lesion may present in brain with no other evidence of disease. In that situation, metastatectomy (craniotomy for metastatic lesion) is the need to get more survival benefit (5,14). Fey et al. (15) in their particular series have the largest series of resected brain metastases from colorectal carcinoma published to date.

This patient is alive for more than 13 years after the diagnosis of the metastatic disease. Another interesting aspect of the case is the second colonic malignancy which appeared 13 years later. He is a survivor of almost inevitable death from metastatic colon cancer, most probably from the second primary. Information on the molecular basis of oncogenesis and how oncogens determine the behavior of malignant cells is increasing at a rapid pace. Among all widely accepted prognostic factors of colon cancer, our experience presented herein also confirms the hypothesis that the biology of tumor is one of the important prognostic factors.

References

1. Succi L, Urrico GS, Prumeri S, et al. Brain metastases: first sign of colorectal carcinoma. *Chir Ital* 2000;52:419-20.
2. Wen PY, Black PM. Metastatic brain cancer. In: De Vita VT. *Cancer, principles and practice of oncology*. Philadelphia: Lippincott-Williams, 2001; 2655-70.
3. Malafosse R, Penna C, Sa Cunha A. Surgical management of hepatic metastases from colorectal malignancies. *Ann Oncol* 2001;12:887-94.
4. Skibber MD. Spread of colon cancer. In: De Vita. *Cancer, principles and practice of oncology*. Philadelphia: Lippincott-Williams, 2001; 1229-38.
5. Arnold SM, Patchell RA. Diagnosis and management of brain metastases. *Hem Oncol Clin N Am* 2001;15:1085-107.
6. Greco FA. Cancer of unknown primary site. In: De Vita. *Cancer, principles and practice of oncology*. Philadelphia: Lippincott-Williams, 2001; 2001-38.
7. Vagn-Hansen CA, Rafaelsen SR. Brain metastases from colorectal cancer. *Ugeskr Laeger* 2001;163:1864-5.
8. Hwang T, Close TP, Grego JM. Predilection of brain metastases in gray and white matter junction and vascular border zones. *Cancer* 1996;77:1551-5.
9. Delattre JY, Krol G, Thaler HT. Distribution of brain metastases. *Arch Neurol* 1998;45:741-4.
10. Postner JB. Clinical manifestation of brain metastases. In: Weiss L, Gilbert HA, Posner JB, editors. *Brain metastases*. Boston: GK Hall, 1980; 189-207.
11. Sze G, Milano E, Johnson C. Detection of brain metastases: comparison of contrast-enhanced MR with unenhanced MR and enhanced CT. *Am J Neuroradiol* 1990;11:785-91.
12. Markesbery WR, Brooks WH, Gupta GT. Treatment for patients with cerebral metastases. *Arch Neurol* 1978;35:754-6.
13. Zorilla M, Alonso V, Herrero A, et al. Brain metastases from colorectal carcinoma. *Tumori* 2001;87:332-4.
14. Wrensk M, Arbit E. Resection of brain metastases from colorectal carcinoma in 73 patients. *Cancer* 1999;85:1677-85.
15. Fey MF. Metastatectomy: a direct therapeutic effect or an illusion due to patient selection? *Ther Umsch* 2001;58:726-31.