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Calcified Brain Metastases from Carcinoma of the Gastrointestinal Tract Correlation between Computed Tomography and Histopathology*

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消化管癌由来の石灰化脳転移

—CT と病理組織像との対比—

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転移性脳腫瘍に石灰沈着を認めることは稀である。消化管癌の脳実質転移の頻度も多くない。過去2年半の期間 Computed tomography (CT) 検査を受けた120例の転移性脳腫瘍の内、消化管癌由来の脳実質転移は10例(8.3%；食道癌2例，胃癌1例，大腸癌4例，直腸癌3例)であった。CT装置はGE CT/T 8800を使用し，スライス幅10mm，間隔10mm でスキャンした。

これら10例全例に造影 CT が行われたが，造影前 CT をも施行されている7例を対象として，造

影前 CT における転移巣の濃度を検討した結果，5例において，転移巣が正常脳組織より明らかに高いX線吸収値を示した。この5症例の原発巣は，大腸癌2例（4例中），直腸癌2例（2例中），胃癌1例（1例中）であった。外科手術又は剖検により，組織学的検索が可能であった4症例で，腫瘍壊死巣に散在する石灰沈着が確認され，出血巣は欠如しているか，又は軽微であった。この石灰沈着がCT上，高X線吸収陰影をもたらす主要因子であると考えられた。

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転移性脳腫瘍の数、大きさ、分布の診断に造影CTが有用であることは周知の如くであるが、造影前CTを省略して造影CTのみを施行すると、石灰沈着又は出血等の重要な所見は見逃される。従来、転移性脳腫瘍のCT診断に関しては、腫瘍濃度と原発巣の組織型との相関、造影剤増強効果、脳浮腫等を検討する報告が数多くみられるが、CT像と病理組織像を対比した検討は殆んどなされて

いない。数多くの依頼検査をこなさなければならぬ日常診療において、転移性脳腫瘍が疑われる場合、造影前CTを省略し当初から造影後CTを実施することもしばしばである。造影前CTは、出血の有無以外に石灰沈着の有無を把握して、石灰沈着が考えられる場合、胃、大腸又は直腸原発の癌を推定することが可能であることに1つの重要な意義がある。

Introduction

Calcification in the metastatic brain tumor is rare. Brain metastases from carcinoma of the gastrointestinal tract is infrequently found. One hundred and twenty cases of metastatic brain tumor have been studied by CT scan in the past two and a half years. Ten of these cases (8.3% of all metastatic brain tumors) were metastases from carcinoma of the gastrointestinal tract.

Precontrast CT scans of seven patients (stomach, 1 case; colon, 4 cases; rectum, 3 cases) were analysed as to tumor density. Metastatic lesions with markedly increased density were found in five cases of metastases from the colon (two cases out of four cases), rectum (two cases out of two cases) and stomach (1 case out of 1 case). Microscopic calcifications were present in the necrotic debris of these surgical or autopsy specimens. We believe that the main causative factor for high density on CT scan is the presence of microscopic calcifications in these cases of metastases from gastrocolorectal carcinomas.

The correlative study has convinced us that precontrast CT is of practical value yielding a relatively specific diagnosis of metastasis in the brain from gastrocolorectal carcinomas.

Liver metastases from carcinoma of the large bowel are frequently calcified¹⁾. Brain metastasis with calcification is rare, however²⁾. Since the installation of a Computed tomography (CT) scanner in Tokyo Metropolitan Komagome Hospital, five of seven cases of brain metastases from the digestive tract showed hyperdense brain metastases on precontrast CT suggesting the presence of calcification. Histopathological analysis of these specimens was made with respect to the presence of calcification and/or hemorrhage. After introduction of CT for diagnosis of brain metastases, there have been few correlative studies on brain metastases with increased density and histological proof of calcium deposits except a report, which has not illustrated any photomicrograph of the specimen, by Deck, et al.³⁾

Materials and Methods

Since the installation of a CT scanner (GE CT/T 8800) in our hospital in April 1979, one hundred and twenty cases of metastatic brain tumors have been diagnosed by CT. Of these cases, ten cases (8.3% of all metastatic brain tumors) were metastases from carcinomas of the digestive tracts (esophagus, 2 cases; stomach, 1 case; colon, 4 cases; rectum, 3 cases). Three cases (esophagus, 2 cases; rectum, 1 case) studied only by postcontrast CT were excluded from the study and seven cases (stomach, 1 case; colon, 4 cases; rectum, 2 cases) scanned before and after intravenous administration of 65% Angiografin were analysed with special reference to tumor density on precontrast CT. The CT findings were correlated with histopathologic findings.

Results

Clinical data and CT findings of these five patients are summarized in Table 1. CT and microscopic photographs are illustrated in Fig. 1—5.

Table 1 Clinical course and CT findings in five patients with calcified brain metastases

Case	Age/Sex	Primary cancer	Interval between diagnosis of primary cancer and brain metastasis on CT	Location of calcified brain metastasis (Size)	Perifocal brain edema	Autopsy (A) Surgery (S)
1 (IH)	51/M	Stomach	6months	Temporal (4.5 x 6cm)	Slight	A
2 (AS)	50/M	Sigmoid colon	2years 6months	Cerebellum (3 x 2.5cm)	None	S
3 (KH)	42/F	Sigmoid colon	2years 10months	Cerebellum (3 x 3.5cm)	Slight	S
4 (HY)	54/F	Rectum	6years	Occipital (6 x 4.7cm)	Moderate	S
5 (MK)	61/F	Rectum	5years 11months	Cerebellum (3 x 2.7cm)	Slight	None

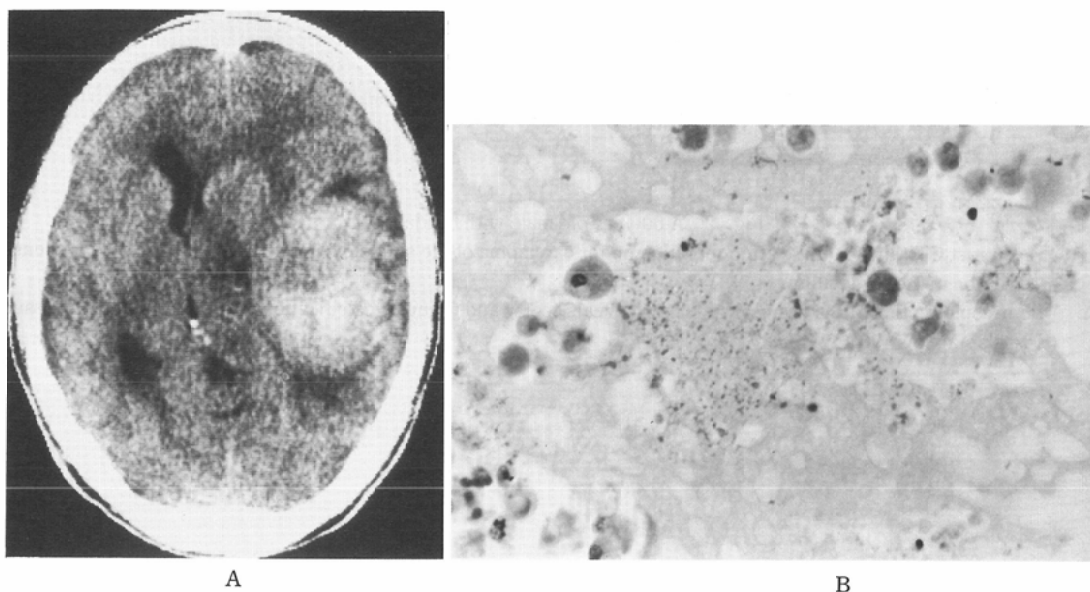


Fig. 1 A 51-year-old male with one month history of progressive disorientation, speech disturbance and right hemiplegia.

A: Precontrast CT six months after subtotal gastrectomy for carcinoma of the stomach. Note a 45 x 60 mm irregularly hyperdense tumor in the left temporal lobe with minimal brain edema.

B Microscopic section of the autopsied specimen shows fine granular calcification in the necrotic tumor tissue (Kossa's staining x384).

Metastatic lesions with increased density suggesting the presence of calcification were found in five cases of metastases. The primary sites of these cases are the stomach (1 case out of 1 case), colon (2 cases out of 4 cases) and the rectum (2 cases out of 2 cases). Perifocal brain edema in these cases appeared to be less prominent than in other types of metastatic or primary brain tumor.

In four cases of brain metastases from gastrointestinal malignancy, scattered and/or conglomerate deposits of calcium were microscopically disclosed in the necrotic debris of surgical or autopsied specimens.

No significant hemorrhage was noted in the metastatic foci.

Discussion

Brain metastasis is one of the most troublesome complications and suggests the preterminal stage of systemic malignant disease. Abrams et al.⁴⁾ found brain metastases in 17.6% (43 cases) of 1000 autopsied

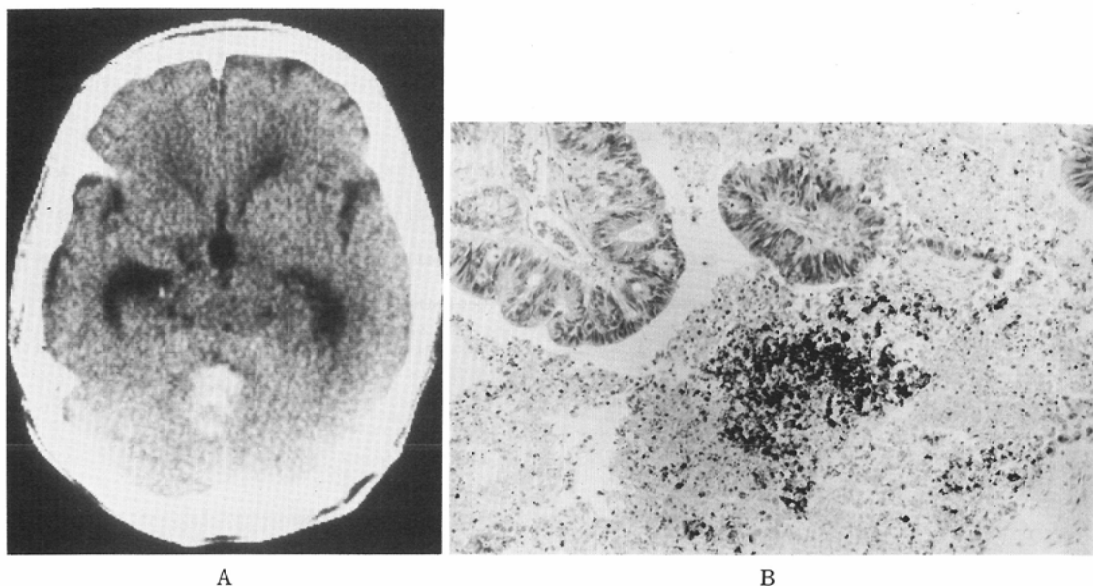


Fig. 2 A 50-year-old male with headache.

- A: Precontrast CT thirty months after operation on for carcinoma of the sigmoid colon shows a markedly hyperdense mass lesion in the cerebellum.
- B: Microscopic section of the surgical specimen reveals spotty and granular calcification in the necrotic tumor tissue (Kossa's staining $\times 96$).

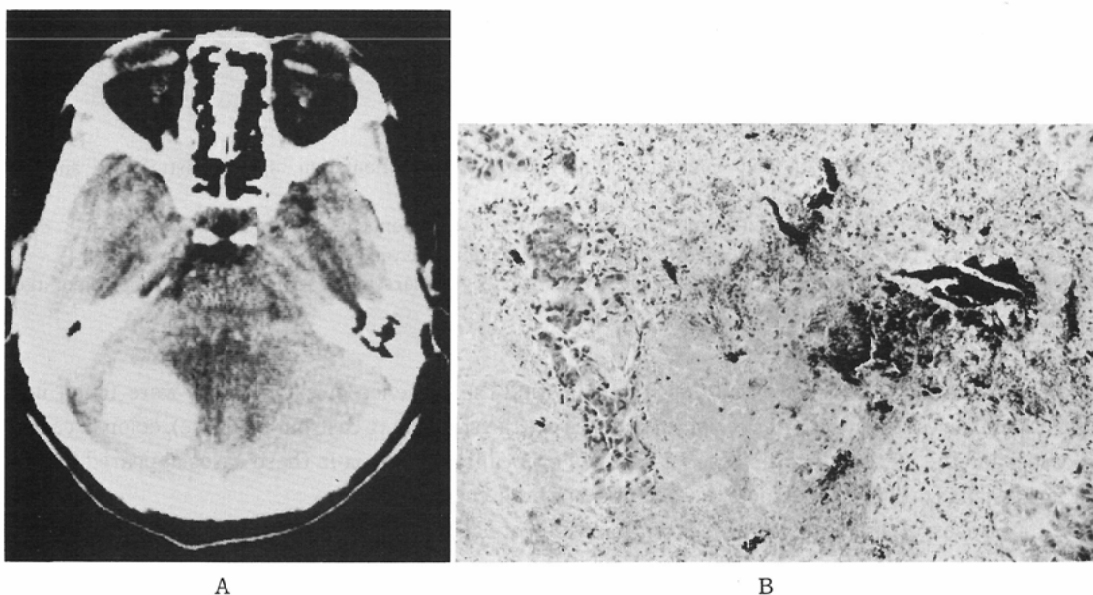


Fig. 3 A 42-year-old female with one month history of headache.

- A: Precontrast CT thirty four months after surgery of carcinoma of the sigmoid colon. A markedly hyperdense mass, measuring about 30×27 mm, is noted in the right cerebellar hemisphere.
- B: Microscopic section of the surgical specimen reveals irregular and massive calcification in the necrotic tumor tissue (Kossa's staining $\times 96$).

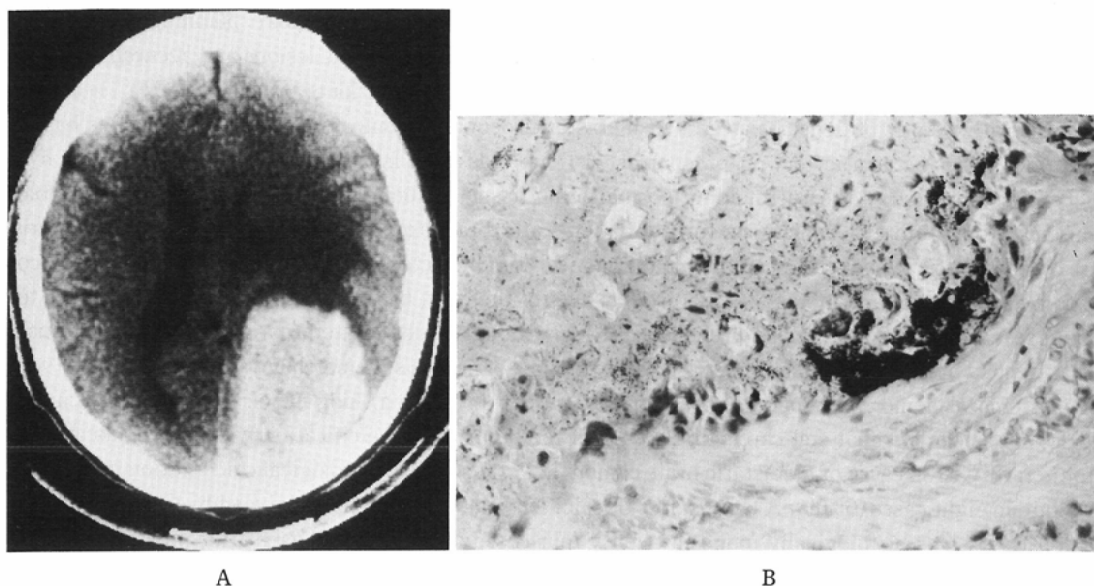


Fig. 4 A 54-year-old female with two months duration of headache and vomiting.

- A: Precontrast CT six years after surgical removal of rectal cancer. A markedly hyperdense mass lesion is seen in the left occipital lobe.
- B: Microscopic section of the surgical specimen demonstrates granular and amorphous calcification in the necrobiotic tumor tissue (Kossa's staining $\times 240$).



Fig. 5 A 61-year-old female who had surgical resection of rectal cancer seventy one months previously. Precontrast CT after two months duration of headache and occasional vomiting shows dense calcified mass lesion, with perifocal edema, in the lateral aspect of the left cerebellar hemisphere. The same findings were noted on the last precontrast CT made in another hospital about one month before coming to our hospital. The patient died six months later. No autopsy was done, but it is presumed with considerable certainty that the hyperdense metastatic focus is from rectal cancer.

cases of carcinoma. Metastases to the brain can occur from any primary sites. The most common primary foci of brain metastases are lung, breast and melanoma⁵⁾⁶⁾. Brain metastases from the gastrointestinal tract are less common; 1.0 to 7.9% of cases of gastrointestinal tract cancer⁵⁾⁷⁾⁸⁾ and 3.8 to 6.4% of cases of colon cancer³⁾⁶⁾⁹⁾¹⁰⁾. In review of autopsy cases of carcinomas, intracerebral metastases were found in two cases (8.3%) of 119 cases of gastric cancer and did not occur in any cases of carcinomas of the colon (118 cases) and rectum (87 cases)⁴⁾.

CT scan is indispensable as a noninvasive screening method and adequate planning of surgical or palliative radiotherapy of brain metastases. For early detection of metastatic lesions and accurate evaluation of their size, extent, locations and numbers, postcontrast CT scan is superior to precontrast CT.

Comparative study of density patterns of metastatic foci on precontrast CT and primary sites has been attempted³⁾. The metastatic foci on precontrast CT are classified into hypodensity, isodensity or hyperdensity in comparison to the surrounding normal brain tissue. Although it is difficult to decide histologic specificity from different density patterns of metastatic brain tumors, there are certain characteristic features; metastatic lesions from melanoma, chorionic carcinoma, colonic carcinoma and osteogenic sarcoma tend to be hyperdense and metastatic foci from cancer of the lung, breast, kidney and lymphoma tend to be hypodense³⁾. These CT features on precontrast CT are thought to be related to a variety of factors such as cellular density of the tumor, tumor neovascularity, degree of necrosis, hemorrhage and calcification³⁾¹¹⁾.

Intratumoral hemorrhage occurs most commonly with melanoma, lung cancer and choriocarcinoma¹²⁾ and also occasionally renal cell carcinoma⁷⁾¹²⁾¹³⁾. On the other hand, calcification within a metastatic brain tumor is rare. Of 136 cases of metastatic brain tumors in Potts's series, histological calcification in the tumors was found in eight cases (6%)¹⁴⁾. A large series of calcified brain tumors were analysed by Gouliamos, et al.²⁾; no calcification was histologically found in twenty four cases of brain metastases after introduction of CT, and histological calcification was seen in only one patient of 253 cases of brain metastases before introduction of CT. A few cases of calcified metastatic brain tumors have been reported; their primary sites are lung¹⁴⁾, breast¹⁴⁾¹⁵⁾, colon³⁾¹⁴⁾ and bone¹⁶⁾.

In our review of brain metastases from gastrointestinal tract, metastasis of hyperdensity on precontrast CT were encountered with high incidence, and calcifications were microscopically confirmed in these specimens. From the result of our study, authors believe that these calcium deposits in the necrotic debris of metastatic lesion are the main causative factor producing hyperdense spots on precontrast CT. Although some etiologic factors such as the presence of mucus, which may stimulate calcification¹⁷⁾, or accumulation of polymorph leucocytes associated with the tumor¹⁾ have been discussed in the cases of calcified liver metastases from the large bowel, the etiology of production of calcium in the tumor has not been well established.

Postcontrast CT provides early and more accurate diagnosis of brain metastases rather than precontrast CT, especially in the case of tiny and/or isodense metastatic lesions. In addition to conventional technique of contrast enhancement, expanded high iodine dose¹⁸⁾ or delayed high iodine dose¹⁹⁾ has been studied and the number of equivocal CT has certainly been reduced. However, hemorrhage or calcification may be obscured after administration of contrast material, and one may miss these important findings if only postcontrast CT is obtained without a precontrast CT.

Although hyperdensity in metastases is more often due to hemorrhage than calcification, it is useful to detect tumor calcification on precontrast CT for yielding a relatively specific diagnosis of metastasis from gastrocolorectal carcinomas, if cancer of breast or lung, or osteogenic sarcoma is excluded.

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