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Metastatic Adenocarcinoma to the Brain: MR with Pathologic Correlation

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PURPOSE: To describe the appearance on T2-weighted scans of metastatic adenocarcinoma to the brain and to show that the hypointensity frequently associated with these lesions is not related to the presence of mucin, blood products, iron, or calcium. **METHODS:** The MR scans of 14 patients with metastatic adenocarcinoma to the brain were reviewed retrospectively. The signal intensity on T2-weighted scans of the solid enhancing portion of the tumors was compared with white matter. Histologic examination of the surgical specimens included special stains to search for calcium, mucin, and iron. **RESULTS:** Eight of nine surgical and all six nonsurgical lesions were either iso- or hypointense to white matter on T2-weighted scans. There was no correlation with tumor histology or the presence of mucin, blood products, iron, or calcium. **CONCLUSIONS:** The presence of a hypointense intraaxial mass on T2-weighted scans strongly suggests the possibility of metastatic adenocarcinoma. The MR appearance is not explained by the presence of mucin, blood products, iron, or calcium. This phenomenon most likely reflects the relaxation parameters of the tissue from which the metastasis arose.

Index terms: Brain, neoplasms; Brain, diseases; Brain, magnetic resonance; Neoplasms, metastasis

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The hypointensity on T2-weighted scans of metastatic disease of the brain, metastatic adenocarcinoma in particular, has been documented in a few scattered reports (1–6). Hinshaw DB, et al (MRI of metastatic adenocarcinoma to brain. Presented at the 26th annual meeting of the American Society of Neuroradiology, Chicago, IL, May 17, 1988) suggested that this appearance was caused by magnetic susceptibility produced by blood products. Yock (2) and Egelhoff et al (3) believed that it might be caused by the presence of mucin. Over the past 5 years, we have observed several cases of metastatic adenocarcinoma that were iso- or hypointense to white matter on T2-weighted scans. Because these le-

sions occurred in the absence of demonstrable blood products on unenhanced T1-weighted scans, we hypothesized that the magnetic resonance (MR) appearance might be related to proteinaceous mucin. The purpose of this report is to correlate the MR appearance of cerebral metastatic adenocarcinoma with the histopathology of surgical specimens to attempt to explain the mechanism of hypointensity on T2-weighted scans.

Methods

The MR scans of nine patients with surgically resected metastatic adenocarcinoma to the brain (three colon, three lung, two breast, one unknown primary) were reviewed. An additional five patients with known primary adenocarcinomas and presumed metastatic intracranial lesions (three colon, one lung, one breast) were also reviewed. One of the surgical patients had an additional lesion that was not removed, for a total of 15 lesions. Cases were not included if they demonstrated hyperintensity on unenhanced T1-weighted scans, which would suggest the presence of gross blood products. When computed tomography (CT) scans were available, they were reviewed for calcification. The solid enhancing portion of the tumors was analyzed on MR scans by two neuroradiologists and was classified as hypo-, iso-, or hyperintense to white matter.

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All nine surgically removed metastases were stained with hematoxylineosin and for mucin with mucicarmine and/or Alcine blue. Six of the specimens were also stained for iron with Prussian blue. The material was examined by a neuropathologist and carefully analyzed for the presence of mucin, blood products, iron, and calcium. The mucin content was rated as 0, 1+, or 2+. Although a few lesions demonstrated a slight degree of signal heterogeneity on T2-weighted scans (Fig. 1B), no attempt was made to correlate the pathology material with specific areas within a lesion.

Scans were performed using standard T1-weighted 450–700/15–17/2 (repetition time/echo time/excitations) and T2-weighted 2000/80 spin-echo sequences. A gradient-echo scan, fast imaging with steady precession 400/12 (30° flip angle), was done in one case to identify regions of magnetic susceptibility. Twelve patients received gadopentetate dimeglumine and the other two had enhanced CT scans available.

Results

In 14 of the 15 (93%) metastatic lesions included in this study, the solid enhancing portion of the tumor was iso- or hypointense on T2-weighted scans to white matter (Figs. 1 and 2). Only one of the 15 metastases (lung carcinoma) was hyperintense to white matter on the T2-weighted scans (Fig. 3). The true incidence of the hypointense appearance of cerebral metastatic adenocarcinoma cannot be determined from this

study because an indeterminate number of cases were not included if they demonstrated calcium on CT scan or blood products on the T1-weighted images. There was no correlation between signal intensity and the presence or amount of mucin (Table 1). One lesion was minimally positive for iron on the Prussian blue stain and one was minimally positive for hemosiderin on the hematoxylineosin stain. These histologic findings were very focal and were not believed to explain the diffuse hypointensity demonstrated on the T2-weighted scans. Neither of these lesions was evaluated with the gradient-echo scan. No other blood products and no calcifications were demonstrated. No magnetic susceptibility was demonstrated on the gradient-echo scan (Fig. 1C).

Discussion

It is generally accepted that primary intraaxial brain neoplasms are hyperintense to normal parenchyma on T2-weighted scans and, indeed, this has been confirmed in many reports (7–15). In several of these reports, T2 relaxation times were measured for tumor and normal white and gray matter. The T2 relaxation time of primary neoplasm was consistently higher than the time for white matter, thus accounting for the hyperintense appearance on T2-weighted scans of pri-

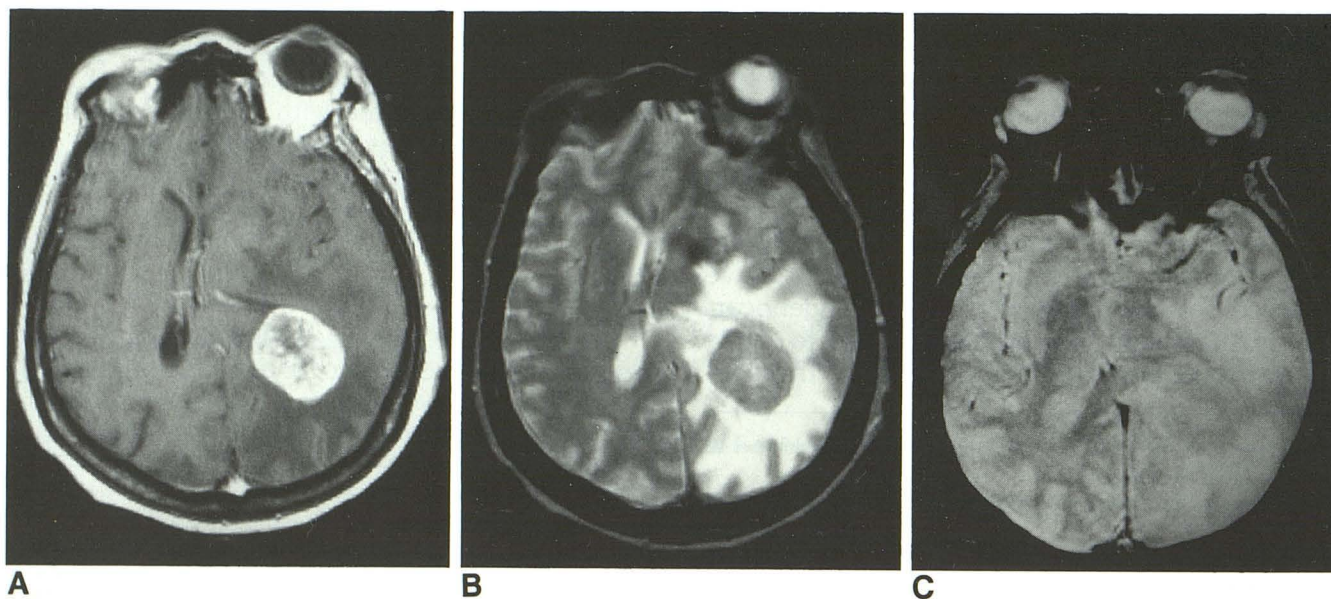


Fig. 1. Isointense breast metastasis.

A, The postgadolinium T1-weighted scan demonstrates a generally solid enhancing left parietal mass with central area of nonenhancement. B, On the T2-weighted scan, the viable solid outer rim of the mass is isointense to white matter. The inner portion is higher signal and corresponds to areas of nonenhancement on the T1-weighted image, which probably represents areas of necrosis. C, The gradient echo scan does not demonstrate any magnetic susceptibility, as might be expected in the presence of blood products, iron, or calcium.

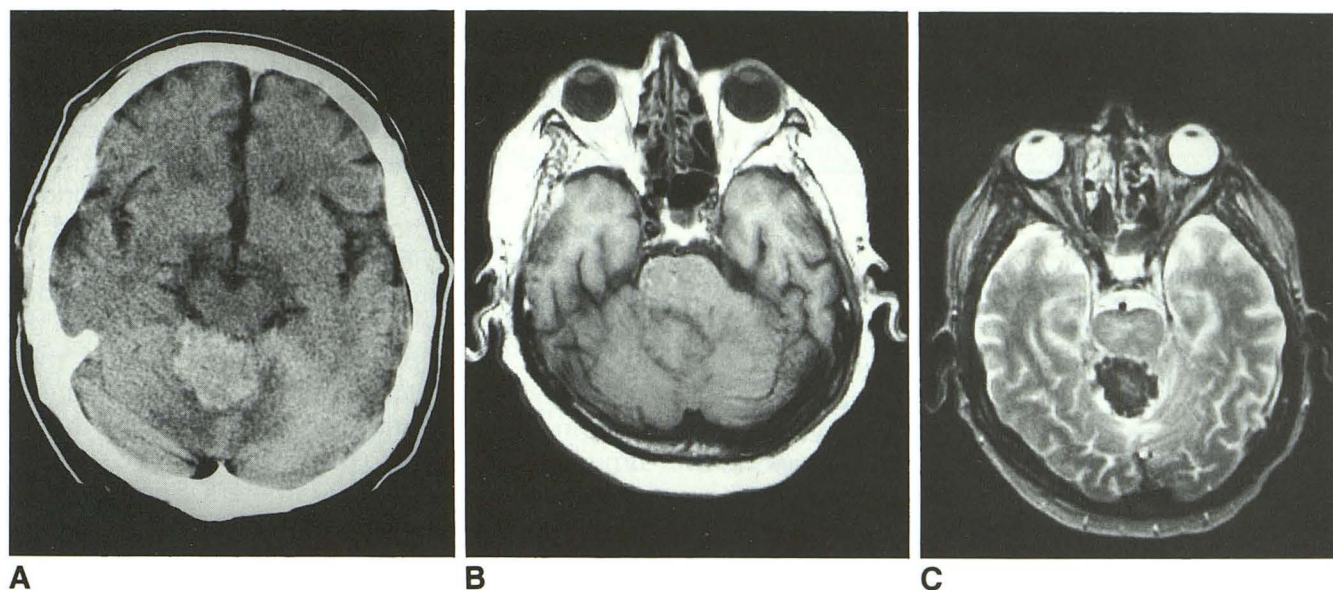


Fig. 2. Hypointense colon metastasis.

A, The unenhanced CT scan demonstrates a dense mass within the cerebellar vermis. B, The unenhanced T1-weighted scan shows an isointense mass, without evidence of blood products. C, On the T2-weighted scan, the mass is slightly heterogeneous but generally hypointense to white matter.

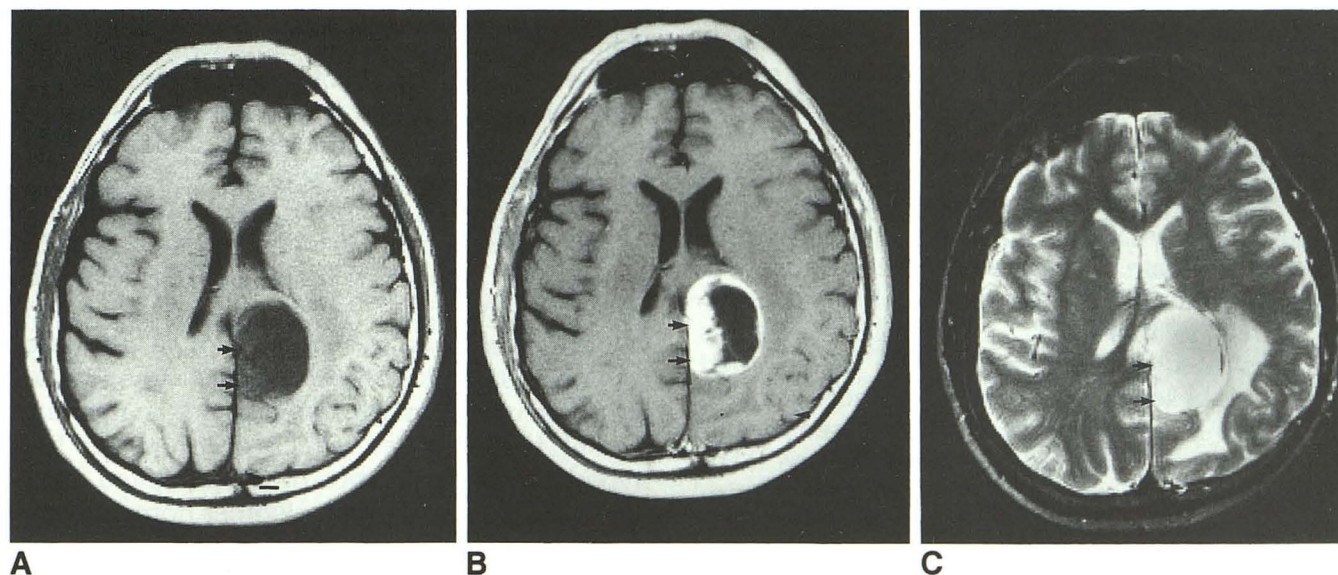


Fig. 3. Hyperintense lung metastasis.

A, B, The pre- and postgadolinium T1-weighted scans show a ring-enhancing mass with central necrosis. The medial aspect contains the thickest portion of viable tumor (arrows). C, On the T2-weighted scan, the area corresponding to the thick medial enhancement is hyperintense to white matter.

mary gliomas. In reports in which T2 relaxation times were measured for metastatic disease and primary tumors (6, 10–12), relaxation times for metastases were relatively shorter than those for primary tumors. Specifically, Komiyoma et al (12) found that the T2 relaxation time of two of three metastatic adenocarcinomas was equal to or less

than the T2 relaxation time of normal white matter.

MacKay et al (4) reported a rectal metastasis with a very hypointense appearance on the T2-weighted scan but could find no histologic feature to explain the appearance. In their series of metastatic lesions, Tsuchiya (5) believed that an iso-

TABLE 1: *Mucin content versus signal intensity*

Mucin Content	T2-Weighted Scan Signal Intensity Relative to White Matter		
	Hypo	Iso	Hyper
2+	x	xx	x
1+		xx	
		xx	
0		x	

The signal intensity of metastatic adenocarcinoma on T2-weighted scans does not correlate with mucin content

or hypointense appearance on T2-weighted scans suggested metastatic disease. Yock (2) reports a case of hypointense metastatic adenocarcinoma. He believes that this finding frequently correlates with high density on CT and may be related to the presence of mucin. Egelhoff et al (3) reported 12 of 16 metastatic adenocarcinomas to brain with areas of hypointensity on T2-weighted images. They hypothesized this was caused by the presence of mucin, a complex macromolecule that causes changes in the state of bound and unbound water. However, only four lesions were examined histologically. These had "increased protein concentration," but it is not stated whether this protein actually represented mucin and the amount was not quantified. Hinshaw reported a series of 10 pathologically proved and two presumed metastatic adenocarcinomas to brain (Hinshaw DB, MRI of metastatic adenocarcinoma to brain. Presented at the 26th annual meeting of the American Society of Neuroradiology, Chicago, IL, May 17, 1988). All these lesions demonstrated hypointensity on T2-weighted scans. He believed that this appearance was secondary to magnetic susceptibility caused by underlying blood products. Hemosiderin was identified for some of the cases, but the exact pattern (ie, focal or diffuse) was not reported. In addition, some of these cases demonstrated areas of hyperintensity on unenhanced T1-weighted scans, indicating subacute hemorrhage.

Our series also demonstrates the very frequent hypointense appearance on T2-weighted scans of metastatic adenocarcinoma: 14 of 15 lesions were hypo- or isointense to white matter. However, we did not include any case that demonstrated hyperintensity on gadolinium T1-weighted scans, which would suggest the presence of blood products. No significant amounts of hemosiderin or other forms of iron were identified on the hematoxylineosin or Prussian blue stains. Although one case was minimally positive

for hemosiderin on hematoxylineosin stain and one was minimally positive for iron on the Prussian blue stain, these findings were extremely focal and were not considered adequate to explain the diffuse hypointensity of the lesions on the T2-weighted scans. A separate case, which underwent gradient-echo scanning, demonstrated no evidence of magnetic susceptibility. In our study, there was no histologic or MR evidence of blood products or other forms of iron or calcium as the cause of the hypointense appearance of metastatic adenocarcinoma on T2-weighted scans.

Spin-spin relaxation, which determines the T2 time, is a complicated process in biologic systems and depends on many parameters. Some of these are temperature, pH, relative proportion of protein and water, size and type of protein molecules, cell density, and cell size (16-18). The T2 shortening effect of high-protein concentrations has been demonstrated previously in proteinaceous sinus secretions (19, 20). Because mucin is a common product of adenocarcinoma and is similar to sinus secretions, we initially hypothesized that this might be responsible for the T2 shortening observed in metastatic adenocarcinomas. However, there was absolutely no correlation between the presence or amount of mucin demonstrated histologically and lesion signal intensity on T2-weighted scans (Table 1).

Bottomley et al compiled two large reviews of articles reporting nuclear MR relaxation times (T1 and T2) for normal (21) and pathologic tissues (13) in many organ systems. Normal gray and white matter have relatively long T2 relaxation times of 101 and 92 msec, respectively. Primary intraaxial neoplasms are even longer, in the range of 111 to 141 msec, which accounts for their hyperintense appearance on T2-weighted scans. We find it interesting that all other normal tissues in the body have much shorter T2 relaxation times compared with normal brain, averaging 49 to 79 msec. More importantly, the corresponding neoplasms of these extracranial tissues have T2 relaxation times in the range of 68 to 94 msec, which is generally equal to or shorter than the T2 relaxation time of 91 msec for normal white matter. Therefore, we believe that metastatic lesions to the brain tend to be iso- or hypointense to white matter, simply on the basis of their naturally shorter T2 relaxation times compared with the relaxation times for normal white matter. This observation supports our inability to find any specific histologic or theoretical reason to explain

the relative hypointensity of metastatic adenocarcinoma to brain.

Further research is suggested to compare other types of metastases to primary brain tumors and metastatic adenocarcinomas. The specificity of a hypointense intraaxial mass on T2-weighted scans could then be determined.

In conclusion, the hypointense appearance on T2-weighted scans of cerebral metastatic adenocarcinoma is extremely common. This appearance is not attributable the presence of mucin, blood products, iron, or calcium. Rather, it simply reflects the relatively shorter T2 relaxation time of the tissue from which the metastasis arose compared with the T2 relaxation time of normal white matter.

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