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Carcinomatous Encephalitis (Miliary Metastases): Lack of Contrast Enhancement

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Summary: Carcinomatous encephalitis is a rare form of brain metastasis in which there is diffuse miliary spread of punctate tumor nodules in a perivascular distribution. In this case, these tiny tumor nodules were seen throughout the cortical and basal gangliar gray matter only on T2-weighted images. Contrast-enhanced CT and T1-weighted MR images did not demonstrate these tumor nodules.

Index terms: Encephalitis; Brain neoplasms, metastatic; Brain neoplasms, magnetic resonance; Brain neoplasms, computed tomography

Case Report

This 59-year-old woman had been in good health, when she presented with a persistent cough. Chest films revealed a right hilar mass that proved to be a small cell carcinoma of the lung at bronchoscopy. Multiple liver metastases were demonstrated on computed tomography (CT) examination. A bone scan showed increased uptake in the skull, the 10th thoracic vertebral body, and the left posterior ribs.

Chemotherapy protocol was begun consisting of cisplatin, VP16, cytoxan, adriamycin, and vincristine. Three weeks after its completion, the hilar mass and the liver lesions were no longer evident on CT scan.

Five weeks after chemotherapy, the patient developed lethargy and fatigue that was so severe that she could no longer walk. On admission to the hospital, her neurologic examination was unremarkable except for slow speech. She was completely oriented. Over the next several days her mental status deteriorated to the point that she appeared catatonic with marked motor retardation. She was unable to follow simple commands and was thought to have either a metabolic encephalopathy, a paraneoplastic brain syndrome, or an acute depressive psychosis. Two days before her death, she developed generalized seizures controlled with phenobarbital and diazepam. She demonstrated occasional right-sided seizures thereafter. Lumbar puncture revealed a slightly elevated opening pressure of 25 cm of water. There were 0 white cells and 2 red blood cells per cubic mm. Glucose was 72, protein 33, and central nervous system (CNS) lactate was 1.7. VDRL was negative.

Cerebrospinal fluid cultures and cytology were negative. She became progressively less responsive and died on the 14th hospital day.

Admission CT brain scan with intravenous contrast was normal (Fig. 1A). T1-weighted magnetic resonance (MR) images without and with gadolinium enhancement revealed no abnormalities (Figs. 1B and 1C). However, T2-weighted images reveal innumerable punctate areas of increased signal diffuse throughout the gray matter of the basal ganglia and cerebral cortex (Figs. 2A–2C).

At autopsy, the lungs and liver were free of tumor. There was no viable tumor in the 10th thoracic vertebral body or in the left posterior ribs. On gross brain examination, there were diffuse pebblelike foci of tumor metastasis studding the gray matter of the cortex and basal ganglia (Fig. 3A). On microscopic examination, there were nests of loosely cohesive small cells with scant cytoplasm and enlarged angulated hyperchromatic nuclei (Fig. 3B). The miliary tumor nodules were noted throughout the gray matter and at the gray-white matter junction, in a predominate perivascular distribution. The white matter itself was spared. There was neither edema nor glial reaction. The leptomeninges were entirely free of tumor metastasis.

Discussion

Up to 40% of brain neoplasms in adults are metastatic (1). The primary malignancies usually implicated are lung, breast, melanoma, kidney, stomach, and prostate. Most brain metastases are macroscopic parenchymal masses with surrounding edema, and occur at the gray-white matter junction. Carcinomatous encephalitis is a term that was originated by Madow and Alpers in 1951 (2) to describe a diffuse perivascular distribution of tumor cells producing innumerable tiny tumor nodules. Carcinomatous encephalitis is usually associated with lung carcinoma. The patients may present with disorientation and confusion. The lack of focal neurologic signs may lead the clinician to search for a metabolic or toxic en-

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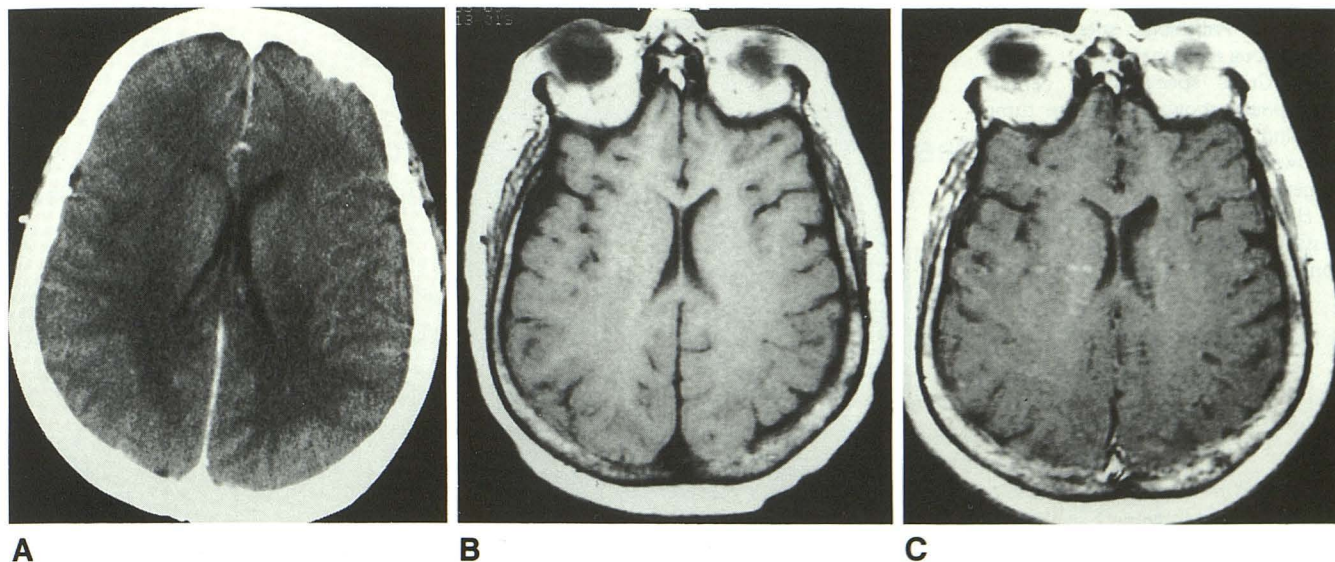


Fig. 1. A, CT scan with contrast enhancement is normal.

B and C, Axial T1-weighted (700/120/1) (TR/TE/excitations) images with and without gadolinium enhancement are unremarkable.

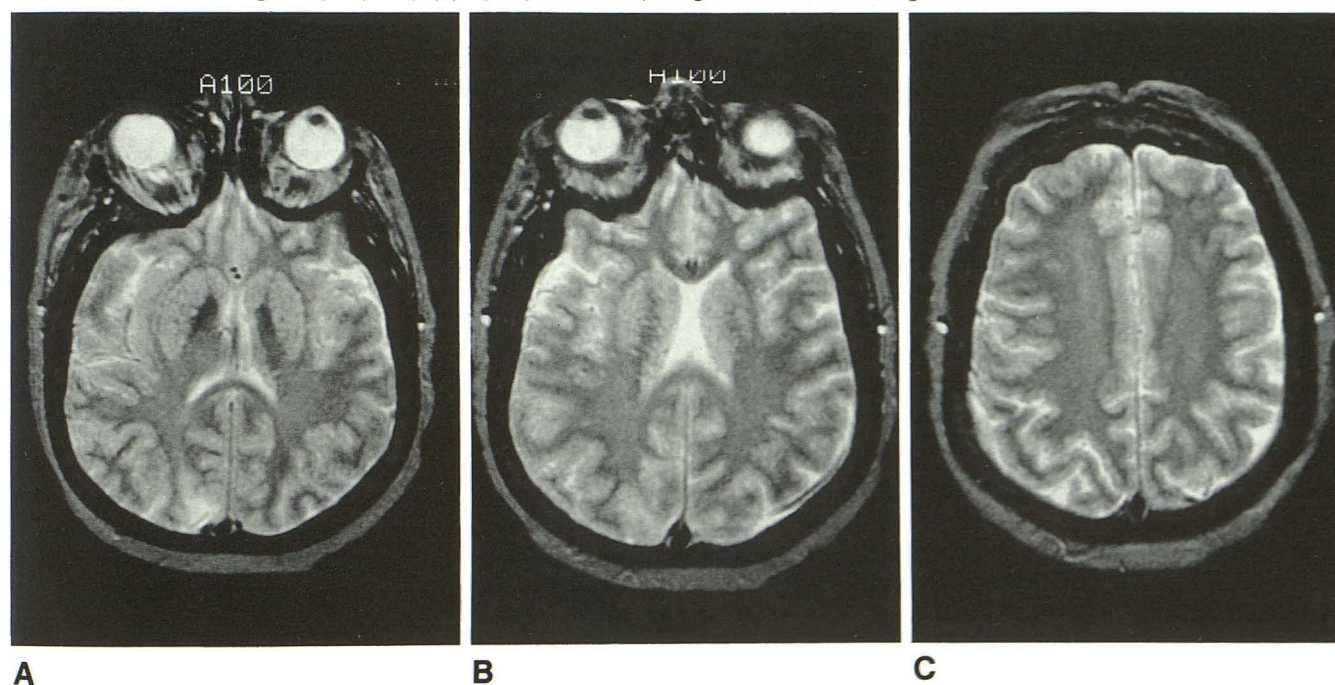


Fig. 2. Axial T2-weighted images (2800/70/1) demonstrate a diffuse military pattern of T2 prolongation involving gray matter of the basal ganglia and cortex.

cephalopathy (3). MR imaging in this case demonstrated throughout the central gray matter a unique military pattern of T2 prolongation that initially was thought to be artifact. On close inspection, nodules are seen throughout the cortical and subcortical gray matter. The findings are atypical for any other disease process and may be specific for carcinomatous encephalitis. This case is unique also because there was no leptomeningeal involvement. A similar case has been previously described in the imaging litera-

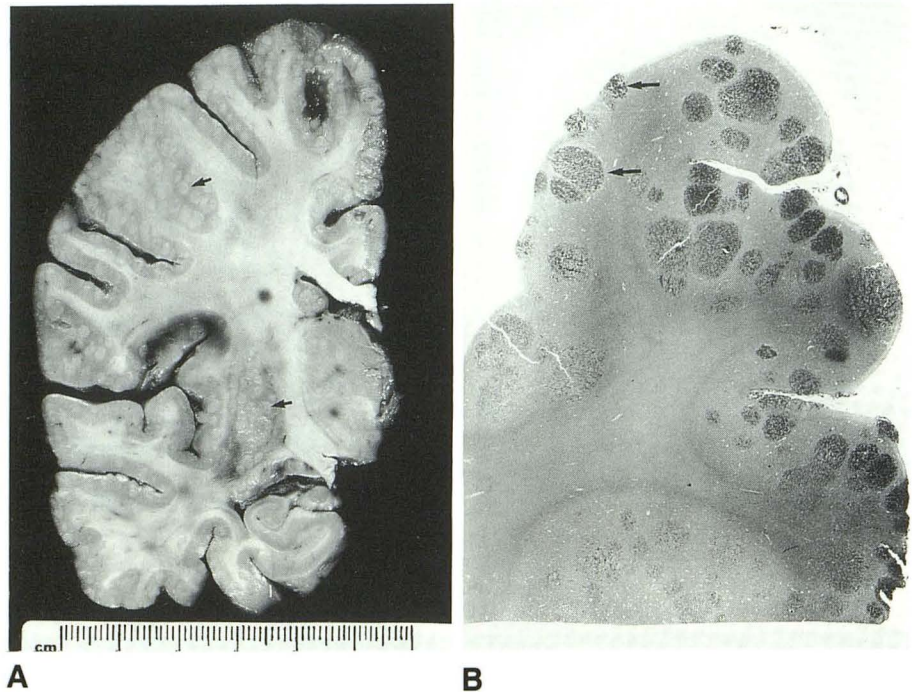
ture (4). That case demonstrated contrast enhancement on CT scanning and a diffuse military pattern of increased signal on T2-weighted images similar to our case. Gadolinium was not available.

Prior to MR imaging, delayed double-dose contrast-enhanced CT scanning was considered to be the optimal method for evaluation of CNS metastatic disease (5). MR has proven to be more sensitive than CT in the detection of CNS pathology (6). MR with gadolinium enhancement

Fig. 3. Pathologic specimen carcinomatous encephalitis.

A, Gross specimen of cerebral hemisphere shows pebblelike tumor studding throughout the gray matter (arrows). White matter and leptomeninges are spared.

B, Microscopic section reveals nests of metastatic small cell carcinoma in the gray matter (arrows).



has further improved lesion detection especially for metastatic disease (7–10).

Our case is more unusual in that there was no contrast enhancement on either CT or MR. The lack of enhancement and the absence of residual neoplasm in the lung, liver, and skeleton at autopsy suggest that both the chemotherapeutic agent and gadolinium failed to cross an intact blood-brain barrier. Besides demonstrating a rare form of intracranial metastatic carcinoma, this case also reemphasizes the need for careful scrutiny of T2-weighted images to exclude brain metastases in patients presenting with confusional states.

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