

Brain metastasis as an initial manifestation of a gallbladder carcinoma

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ABSTRACT

Though autopsy studies demonstrated 5% metastasis to the brain, clinical presentation of a central nervous system metastasis from gallbladder cancer is rare. We report a case of a 72-year-old woman who initially presented with a solitary brain metastasis from an adenocarcinoma of the gallbladder, which was diagnosed pre-operatively as glioblastoma multiforme. This is the second of such a case in the English literature. We emphasize the importance of including metastasis in the differential diagnosis of single intracranial tumor for proper planning of patient management.

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Carcinoma of the gall bladder is the most common biliary tract malignancy and the fifth most common gastrointestinal cancer. Systemic metastasis from gallbladder cancer occur frequently, but involvement of central nervous system is rare.

Case Report. A 72-year-old diabetic woman previously well, presented with confusional state for the past 6 weeks. Neurological examination showed expressive aphasia and sensory agnosia, no other focal deficits. Chest x-ray was normal and MRI of the brain (**Figure 1**) revealed a 5 x 4 x 5 cm heterogenous left frontal lobe mass, with mild effacement of the frontal horn of the left lateral ventricle and midline shift to the right, and possible spread along the left external capsule. Pre-operative diagnosis was glioblastoma multiforme. She had fronto-parietal craniotomy and frozen section was consistent with papillary carcinoma; the tumor was then excised. Postoperative course was uneventful. She improved dramatically. Histopathology reported a highly malignant papillary carcinoma, most likely

metastatic (**Figure 2**). Immunohistochemical stains showed that most of the tumor cells were carcinoembryonic antigen-positive and several of them contained mucin, consistent with a metastatic mucin-producing papillary adenocarcinoma (**Figure 3**). A CT of the abdomen (**Figure 4**) showed a malignant gallbladder mass directly invading the right lobe of the liver with multiple metastatic foci and enlarged porta hepatis lymph nodes with subsequent moderate dilatation of intra-hepatic biliary radicles. She was referred to the Hepatobiliary team for possibility of palliative resection. Laparoscopy revealed an unresectable gallbladder tumor with multiple deposits in both hepatic lobes, no seeding. Liver biopsy (**Figure 5**) confirmed metastatic papillary tumor. Because of the lack of survival benefit with systemic chemotherapy and age of 72 in spite of performance status 2, palliative radiotherapy to the brain and primary tumor was decided to be the best option for this patient.

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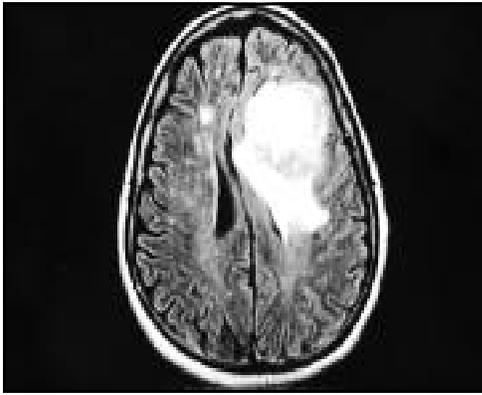


Figure 1 - Gadolinium-enhanced axial T1-weighted MRI showing a left frontal lobe mass of mixed signal intensity with contralateral midline shift.

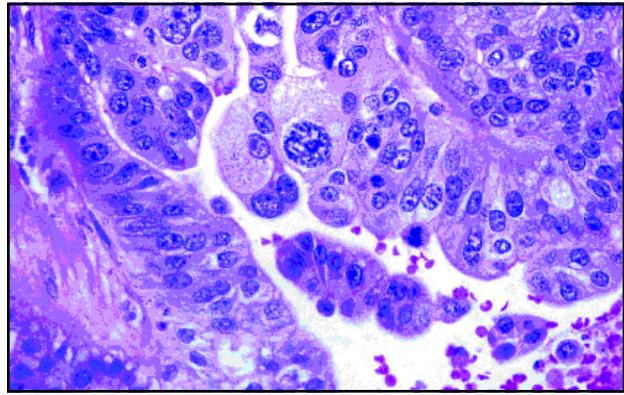


Figure 2 - Brain tumor. Microscopic section shows a highly cellular malignant neoplasm, mostly arranged in complex papillary pattern. Tumor cells are columnar, show marked variation in size and shape, have large irregular hyperchromatic nuclei. (Hematoxylin & Eosin x 400).

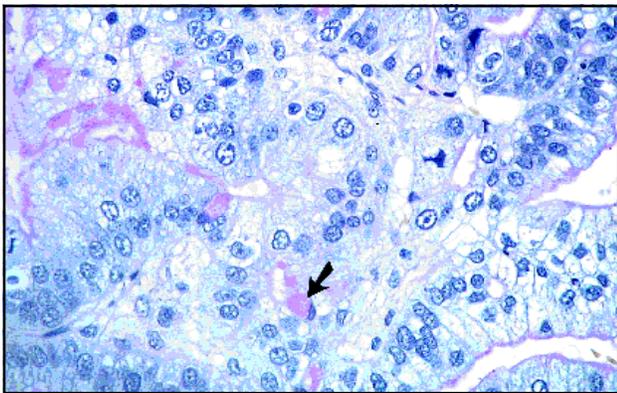


Figure 3 - Photomicrograph of brain tumor specimen showing papillary adenocarcinoma, with increased mitotic activity and some of tumor cells containing mucin [arrow]. (Hematoxylin & Eosin x 400).



Figure 4 - Post-contrast axial CT scan of the abdomen showing mildly distended gallbladder with thick edematous irregular wall, with multiple enhancing soft tissue nodules (long arrow) inside as well as porcelain gallbladder calcification indicating chronic cholecystitis. It contains multiple stones and biliary sludge and calcific rim inside. It is associated with suspected intrahepatic extension of the lesion. Right liver lobe shows multiple ill-defined small irregular hypodense soft tissue masses in segments 8, 7, & 5, suggestive of metastatic deposits (short arrow). Multiple (3) variable-sized enlarged porta hepatis lymph nodes with subsequent moderate dilatation of intra-hepatic biliary radicles.

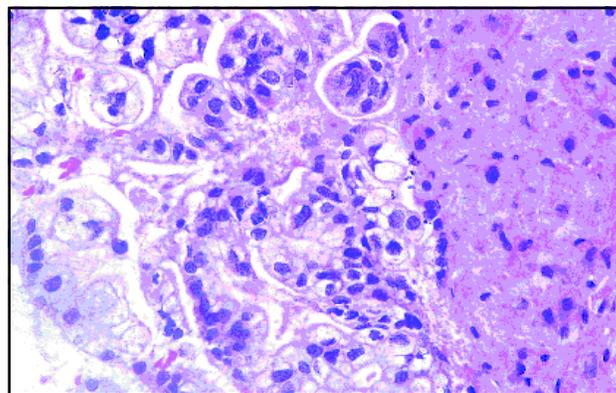


Figure 5 - Liver biopsy. Hepatic tissue with adjacent metastatic papillary tumor, which shows cytoplasmic mucin. (Hematoxylin & Eosin x 400).

DISCUSSION. Distant metastasis to the CNS from gallbladder cancer rarely occurs. In the literature, only 12 cases of CNS metastases from gallbladder carcinoma have been reported.^{1,2,3} Interestingly, in these cases there is so far only one case reported by Takano et al in 1991³ who had solitary brain metastasis from gallbladder carcinoma completely removed 4 months after operation for the primary tumor. Other anatomical sites of CNS metastases were the meninges and venous sinuses, without intracerebral or intracerebellar metastases.

The median survival of patients with CNS metastasis is 3-12 months and is not necessarily compromised by the CNS lesions, if the diagnosis is established, and therapy promptly instituted.⁴ Patients with solitary brain metastasis from gallbladder carcinoma can achieve a better outcome and longer survival after removal of the brain metastasis if there is no other metastasis. In the case of Takano et al,³ the 68 year-old female patient led a normal life 4 years later. In the presence of multiple metastases elsewhere, the prognosis becomes poor. The 5-year survival rate is a dismal 1-12%.^{5,6} In our case, the patient was diagnosed at a late stage when she presented with solitary left frontal lobe tumor and multiple liver metastasis.

In conclusion, although rare, brain metastasis should be considered as an important differential

diagnosis in solitary intracranial tumor and a high index of suspicion should always be exercised for better approach and treatment planning.

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