"Miliary" metastatic tumors in the brain

Case report

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An extremely unusual "miliary" metastatic tumor of the brain in a 69-year-old man is reported. Although there was no known primary tumor, the patient had innumerable brain lesions involving both cerebral and both cerebellar hemispheres, the basal ganglia, and the brainstem. There was no associated edema, mass effect, or brain parenchymal reaction. None of the lesions showed any calcification.

KEY WORDS • brain neoplasm • miliary • metastasis

Miliary metastatic tumors are extremely rare, even though the majority of brain tumors are multiple, with only 5% containing more than five lesions.1 A review of the literature yielded only three reported cases of miliary metastases in the brain: two from adenocarcinoma of the lung and one from acinar cell carcinoma of the pancreas.1,2,5 In these reported cases, all the metastatic lesions were calcified. The current case is that of a man with apparent "miliary" metastases in the brain involving both hemispheres of the cerebrum and cerebellum, the basal ganglia, and the brainstem, with no associated edema, mass effect, or calcification.

Case Report

This 69-year-old man presented with a 3-week history of impaired hearing in both ears along with some dizziness and impairment of gait. Dizziness and impairment of gait persisted and were accompanied by a diminished sense of balance, all of which became progressively worse over the next 2 weeks until the patient could not walk without support. Over the same time period, he also noticed certain parts of his field of vision were unclear or perhaps darkened. These visual symptoms also became progressively worse. In addition, his short- and long-term memory was deteriorating. The patient had quit smoking 5 years previously.

Examination. Neurological examination showed a moderate impairment of memory that related to both recent and remote events. The patient's motor system revealed a slight weakness in his left lower extremity that appeared during the finger-to-nose test. The patient's gait appeared to be very slow and ataxic, and almost fell down. The rest of the neurological examination was unremarkable.

Magnetic resonance (MR) imaging, including nonenhanced sagittal T1-, axial T1-, spin-density T2-, and coronal T2-weighted images obtained the day before the neurological evaluation showed "diffuse disease spread through both cerebral hemispheres, both cerebellar hemispheres, and the brainstem characterized by increased signal on the spin-density and T2-weighted sequences and slightly decreased signal on T1-weighted sequence" (unpublished radiology report). In the cerebellar hemispheres, the images showed effacement of the fourth ventricle. The lesions in the cerebral hemispheres appeared predominantly in the gray and white matter. Three days later, MR imaging of the brain obtained after gadolinium injection (T1-weighted axial, sagittal, and coronal images) showed multiple rounded lesions with ringlike enhancement in both cerebral hemispheres, both cerebellar hemispheres, the basal ganglia, and the brainstem. No associated edema was noted. There was no evidence of mass effect and no evidence of a midline shift. The ventricles appeared to be slightly dilated. There was a low signal within one of the lesions in the left cerebellum, possibly representing melanin or old blood product (Fig. 1). Spinal fluid, which was examined 3 days before surgery, was found to be negative for malignant cells.

Operation. On August 29, 1994, the patient underwent a left frontal craniotomy and a wedge resection of the anterior portion of his left frontal lobe.

Pathological Examination. Histological examination of permanent sections revealed a pattern that was most compatible with metastatic tumor. No parasites were seen. Given the patient's history of smoking and the histology of the neoplasm, the lung was considered to be a possible primary site of origin, although other locations could
not be excluded. The mucicarmine, carcinoembryonic and endomysial antigens, S-100 proteins, melanoma HMB45, and chromogranin preparations were all negative. Focal low-intensity positivity was identified with neuron-specific enolase in some tumor cells. The histology of the neoplasm was unusual in that the cells were not truly small. Both intermediate and large forms were seen, and organoid differentiation was not apparent. Focal tumor necrosis, typical of a small-cell lesion, was noted. Some palisading about vessels by the malignant cells was apparent. The chromatin appeared fine, but small nucleoli were present. Although multiple tumor deposits were found, no parenchymal brain reaction surrounding the tumor was seen. The final diagnosis was metastatic undifferentiated carcinoma, probably representing a variant of small-cell carcinoma (Fig. 2). Bronchoscopy and computerized tomography (CT) scanning of the lung, abdomen, and pelvis revealed no primary tumor.

Fig. 1. Gadolinium-enhanced MR images of the brain showing multiple rounded lesions. Left: Axial view showing lesions with ringlike enhancement in both cerebral hemispheres. Center: Coronal view showing lesions in both cerebellar hemispheres, in addition to both cerebral hemispheres. Right: Additional coronal view showing lesions in the brainstem, also with ring enlargement. There is no edema or mass effect apparent in any of the images.

Fig. 2. Photomicrograph showing that the histology of the neoplasm is unusual in that cells are not truly small. Both intermediate and large forms are seen and organoid differentiation is not apparent. Focal tumor necrosis, typical of a small-cell lesion, was noted. Some palisading about vessels by the malignant cells is apparent. The chromatin appears fine, but small nucleoli are present. No parenchymal brain reaction is seen. The tumor is probably best characterized as intermediate in size and contains a mixture of small and large forms. H & E, original magnification × 100.
Postoperative Treatment and Course. Postoperatively, the patient’s neurological status remained unchanged. Upon completion of 60-Gy whole-brain radiation therapy, MR imaging with gadolinium enhancement showed that most of the small lesions had disappeared although some remained. Four months after he had undergone the craniotomy, the patient died. No autopsy was performed.

Discussion

Our first impression was that we were dealing with a case of cysticercosis of the brain. However, other diagnoses, such as miliary metastases of the brain from primary tumor melanoma and bronchogenic carcinoma, were also considered. The fact that we were not able to find a primary lesion in spite of a very thorough diagnostic search did not rule out the possibility that this case represented miliary metastases from primary bronchogenic carcinoma or lung carcinoma. In cases in which a good quality chest radiograph is normal, CT scanning of the lung can demonstrate the systemic site of the clinical metastasis only very rarely. The lesions missed by routine chest films are the central, small, endobronchial lesions that are not well visualized on CT scanning.6

We have been unable to find cases in the literature of such diffuse and innumerable metastatic lesions in the brain, except three cases of calcified metastases,1,2,5 and in many ways those cases were different from this one. In spite of the fact that the entire brain, brainstem, and cerebellum were filled with miliary metastases, the patient presented with surprisingly minimal neurological deficit. Indeed, there was a complete lack of any brain tissue reaction surrounding these lesions and there was no mass effect.

The only explanation we have for such diffuse and numerous miliary metastatic lesions that involve the entire brain without any glial reaction is an unusually altered host’s brain immune response to the neoplasm. Survival in a patient with this type of metastases is poor. The survival time of approximately 3 months for untreated patients is lengthened to only 4 to 5 months,3 or at best to 9 months, with brain irradiation.4

References


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