Cardiac Malignant Fibrous Histiocytoma Metastasizing to the Brain: Development of Multiple Neoplastic Cerebral Aneurysms

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We report a case in which bilateral occipital brain metastases and neoplastic cerebral aneurysms developed from primary cardiac malignant fibrous histiocytoma. The origin of metastases was confirmed at autopsy. The clinical presentation, radiographic features, and autopsy findings are presented along with a histopathologic analysis of the tumor.

KEY WORDS: Brain metastasis; Neoplastic aneurysm; Cardiac malignant fibrous histiocytoma

It has been suggested that the prolonged survival of many patients with metastatic sarcoma has resulted in an increased incidence of intracranial metastasis in these patients [5,7]. Among soft tissue sarcomas, malignant fibrous histiocytoma (MFH) is a rather common sarcoma metastasizing to the brain [9]. However, its presentation as a primary cardiac tumor is rare [1], and its metastasis to the brain has not previously been reported. We report a case of pathologically confirmed primary cardiac MFH with brain metastasis and neoplastic cerebral aneurysm formation.

Case Report
A 44-year-old woman presented with a 9-month history of periodic scintillating scotoma. Neurologic findings were normal, but an ophthalmologic examination revealed right homonymous hemianopsia. Laboratory data including those for tumor markers were negative. Head computed tomography (CT) scan revealed round high-density masses, which were faintly enhanced by contrast medium, in both occipital lobes (Figure 1). Cerebral angiography demonstrated a fusiform aneurysm in the right anterior cerebral artery, a left peripheral saccular middle cerebral artery aneurysm, and a fusiform aneurysm in the left posterior cerebral artery as well as a tumor stain (Figure 2).

Metastasis of a malignant tumor or brain abscess was suspected, but no abnormality was detected even after examination for malignancy or bacterial focus. Bilateral occipital craniotomy was performed with the patient in the prone position. The cortical surface appeared normal, but intraoperative ultrasonography indicated that tumors were located 5 mm below the cortical surface. The brownish tumors were elastic and hard and easily separated from the brain tissue.

Light microscopy revealed that the tumors were hypercellular and that the tumor cells were arranged in a sheet-like fashion with a slight whorl formation. Vascularity was rich, and the vessels showed a staghorn configuration. Lymphocytic infiltration was slight. The tumors consisted of polygonally shaped cells containing pale cytoplasm with round to ovoid nuclei. Many nuclei in giant cells contained intranuclear cytoplasmic pseudo-inclusions (Figure 3 A and B). The cytoplasm contained PAS positive fine granules. Oil red O-positive lipid droplets were prominent in the cells around the perinecrotic foci. Ailcan blue stain and Mallory's stain were negative, while silver stain demonstrated fine argyrophilic fibers around the tumor cells. The findings regarding immunohistochemical reactivity are summarized in Table 1.

Metastatic poorly differentiated sarcoma was tentatively diagnosed and the patient underwent combined irradiation (50 Gy to the whole brain) and intravenous injection of ACNU (Nidran). At the end of the treatment period, she suddenly developed right hemiparesis and left oculomotor palsy. Head magnetic resonance imaging (MRI) showed multiple foci of small infarctions located bilaterally in the cerebellar hemispheres, the right side of the pons, bilateral cerebral peduncles, left midbrain, and the right parieto-occipital lobe, as well as bilateral frontal lobe recurrent tumors. She died due to sudden respiratory distress shortly after the MRI study.
An autopsy was performed. The brain surface was covered with slight subarachnoid bleeding and a massive cerebellar hemorrhage compressed the brainstem. Multiple infarcts were scattered throughout the brain, while only two metastatic foci were found bilaterally in the frontal lobes. Coronal sectioning of the fusiform aneurysm revealed tumor cells present in the vessel wall around the lumen, and the internal elastic lamina was disrupted (Figure 4).

The primary tumor was found in the left auricular appendage of the heart. It was a grayish-yellow, fragile tumor about $50 \times 40 \times 40$ mm. It filled the lumen of left auricular appendage and involved the papillary muscles of the left ventricle above the mitral valve (Figure 5). Microscopically the tumor consisted mainly of...
Figure 3. (A) Polygonally shaped cells containing pale cytoplasm. Intranuclear pseudoinclusions were also seen (arrows) (× 200, HE stain). (B) Higher power view demonstrating bizarre nuclei (arrows) (× 400, HE stain).

Table 1. Immunohistoreactivity of the Tumor

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<th>Lysosome</th>
<th>AAT</th>
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Abbreviations: AAT, alpha-1 antitrypsin; AACT, alpha-1 antichymotrypsin.
spindle cells in a fascicular arrangement and a few interwoven collagen and argyrophil fibers. Xanthoma cells and an area of cellular pleomorphism were also observed. Findings regarding the immunohistochemical reactivity of the cardiac tumor are shown in Table 1. Electron microscopy revealed lipid droplets and lamellar bodies in the cytoplasm and the presence of a few intercellular collagen fibers, but no myofilaments. There were also many tumor emboli in the kidneys and lungs.

Discussion

Sarcomas, which do not exhibit signs of differentiation beyond fibroblastic and histiocytic differentiation even after careful histopathologic and electronmicroscopic examination, are referred to as MFH [9]. Because our case showed mainly fibroblastic differentiation, fibrosarcoma was ruled out. The cardiac tumor lacked immunohistoreactivity for lysozymes, which are specific for histiocytes, but morphologic confirmation of histiocytic differentiation was established, and no other differentiation could be detected. Therefore, the tumor was diagnosed as MFH.

The presentation of MFH as a primary cardiac tumor is rare. In eight recently reported cases [6] including our case, it occurred in the left atrium; six of the eight patients were females. Furthermore, the differences in characteristics of MFH in the heart and in the soft tissue are noteworthy; the mean reported age at presentation of patients with MFH of the heart is 36 years, but MFH of the soft tissues occurs primarily in the sixth or seventh decade.

Cardiac MFH may be clinically confused with benign atrial myxoma [14]. Several cases of brain metastasis of benign atrial myxoma have been reported [4,8,12,13], and there are similarities in clinical signs and pathologic features of the metastatic site, as well as neoplastic aneurysmal formation [2,3,10,11].

The mechanism of neoplastic aneurysmal formation in our case resembled that in patients with benign atrial myxoma. One proposed mechanism is that tumor cells occasionally grow in the vessels, subsequently undergo aneurysmal dilation, with the surviving tumor in the embolic site focally disrupting the internal elastic lamina [10]. However, another proposed mechanism is disruption of the internal elastic lamina by tumor emboli and recanalization [3]. In cardiac MFH, the latter mechanism might be responsible for neoplastic cerebral aneurysm formation, because serial sections of the aneurysm site showed only one disrupted site of the internal elastic lamina and in this area, the tunica media was disrupted while the tunica adventitia was preserved. Tumor cells did not invade the surrounding vascular wall. These processes lead to pathologic and angiographic changes in the involved arteries, such as occlusion by the tumor, narrowing of the lumen, recanalization, and nodular areas of thickening of the vessel wall associated with stenosis or true aneurysmal dilation. These phenomena probably contributed to the intracranial hemorrhage observed in our patient.

Recognition of these angiographic features, MRI findings of metastatic tumor with multiple small infarctions, and clinical signs of embolism are extremely helpful in establishing a diagnosis of cardiac tumor, because
these changes are otherwise rarely observed except for cases of septic cerebral emboli. Differential diagnosis from benign atrial myxoma, the most common cardiac tumor, is important because it is a surgically curable lesion, whereas MFH has a poor prognosis even after radiotherapy or chemotherapy.

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References