Clinical Reasoning: A case of multiple intracerebral hemorrhages

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SECTION 1

Case presentation: A 47-year-old right-handed man presented with acute onset of right face, arm, and leg weakness; word-finding difficulties; and bifrontal headache. His medical history was remarkable for hyperlipidemia and spontaneous dissection of a distal coronary artery a year and a half previously. On examination, he had right lower face weakness, a plegic right arm, and distal greater than proximal right leg weakness. His speech was mildly dysarthric with word-finding difficulty. Comprehension was intact. Cardiac auscultation was normal.

Results of laboratory investigations, including complete blood count, electrolytes, renal function, liver function, prothrombin time, partial thromboplastin time, cardiac enzymes, antinuclear antibody test, erythrocyte sedimentation rate, and urine toxicology screen, were all normal or negative.

Initial noncontrast CT brain revealed a 3 × 3.5 × 3.5-cm left frontal subcortical intracerebral hemorrhage with surrounding edema, but no appreciable underlying mass (figure 1).

Figure 1 Noncontrast CT image of left frontal lobar hemorrhage at presentation

Questions for consideration:

1. What are the possible etiologies of this intracerebral hemorrhage?
2. What additional diagnostic testing would you consider at this point?

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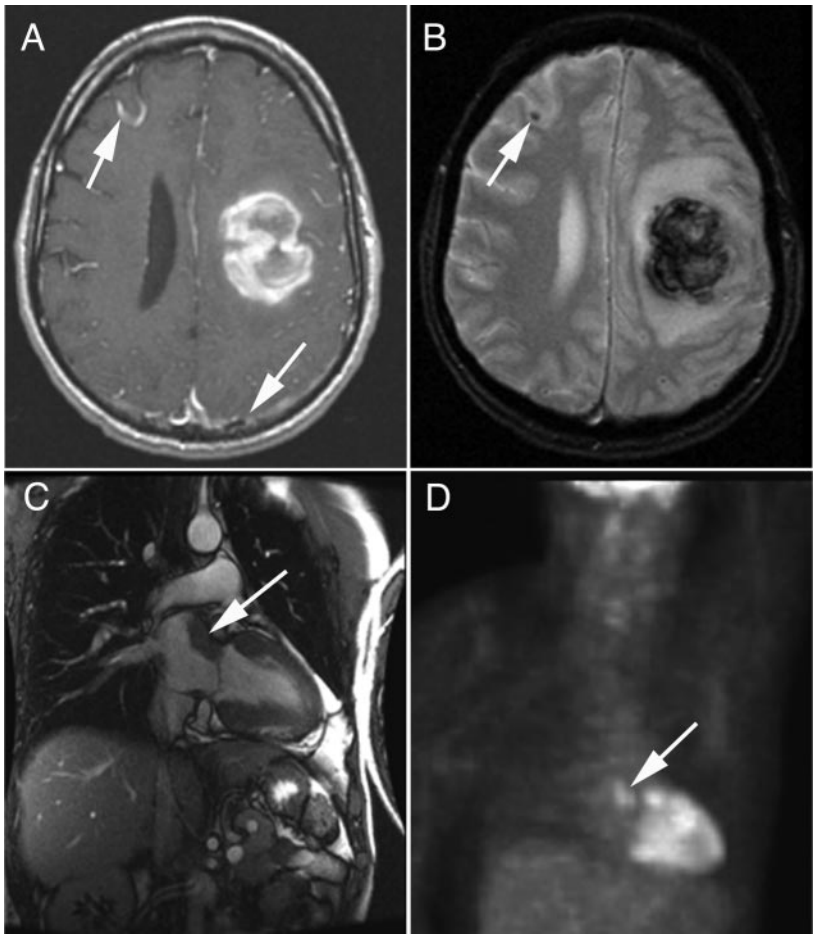
Figure 2 Brain MRI: gadolinium (A) and susceptibility (B); cardiac imaging: MRI (C) and PET (D)



SECTION 2

Brain MRI with gadolinium revealed two additional small enhancing lesions in the right frontal cerebral cortex at the gray–white junction (figure 2A) and within the white matter at the forceps minor (not seen in the selected slice of figure 2A). The larger anterior right frontal lesion was 1.5 cm and had a 1.0 × 1.2-cm focus of hemorrhage that was not present on the initial CT scan taken 4 days earlier (figure 2B). An evaluation for metastatic disease was initiated.

Whole body CT was negative for masses. A transthoracic echocardiogram visualized a 2.5 × 2.2-cm left atrial mass fixed to the lateral wall. Cardiac MRI confirmed the left atrial mass with a broad base of attachment along the posterolateral wall suggestive of a malignant lesion with possible left ventricular wall metastasis (figure 2C). Whole-body PET showed fluorodeoxyglucose uptake within the left atrium; no other metastases were seen on the PET (figure 2D).

Questions for consideration:

1. What is your differential diagnosis at this point?
2. What additional diagnostic tests would you consider at this point?

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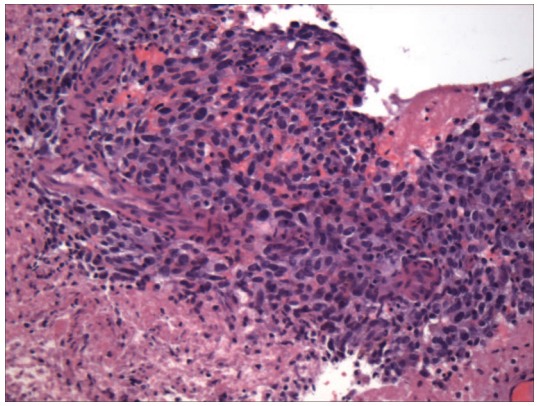
A brain biopsy of the left frontal lesion was performed. The initial sections from the block were nondiagnostic, demonstrating extensive reactive brain parenchyma with areas of inflammation and necrosis. Further sections from the pathology block were requested along with special stains. Before processing the pathologic specimen, an attempt to biopsy the cardiac mass via esophagogastroduodenoscopy (EGD)/endoscopic ultrasound was performed. However, the EGD revealed an ulcerated mass in the stomach cardia, which was biopsied instead. Further analysis of the brain specimen and stomach cardia specimen revealed similar atypical spindle cell proliferation (figure 3). Immunohistochemical evaluation of the brain biopsy was positive for vimentin but negative for epithelial, melanoma, smooth muscle, vascular, or glial cell markers. The tumor had five mitoses per high-power field, and electron microscopy demonstrated no specific line of differentiation. These findings confirmed an undifferentiated malignant epithelioid and spindle cell sarcoma.

Figure 3 Immunohistochemical evaluation of the brain biopsy



Questions for consideration:

1. How would you manage a patient with multiple intracerebral hemorrhages due to metastatic spindle cell cardiac sarcoma?
2. What is the prognosis?

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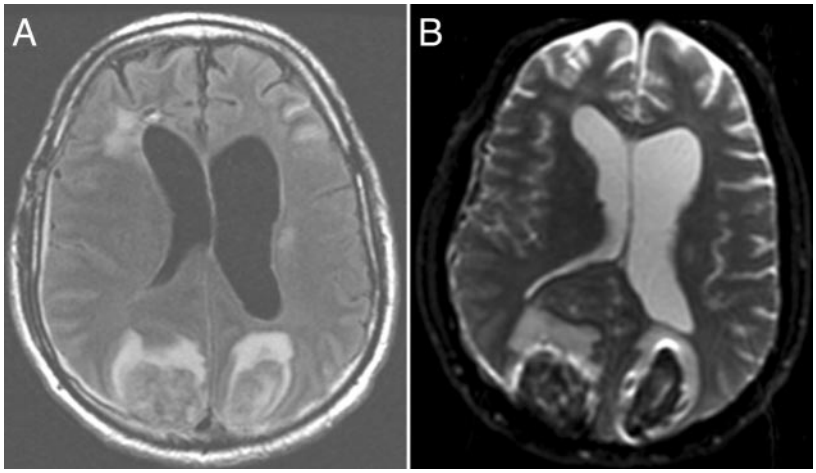
Figure 4 Brain MRI: FLAIR (A) and zero B (B)



SECTION 4

Approximately 1 month after presentation, the patient underwent bifrontal craniotomy for resection of right and left frontal lobe metastases. Interstitial radioactive iodine-125 pellets were placed intraoperatively to prevent local recurrence. He was also treated with six cycles of 2-mercaptoethanesulfonate (MESNA), doxorubicin, ifosfamide, and dacarbazine chemotherapy. His course was complicated by partial complex seizures with secondary generalization.

One month after completion of chemotherapy, a repeat brain MRI revealed two regions of enhancement in the bilateral occipital lobes with leptomeningeal enhancement along the occipital lobes bilaterally (not shown, but suggested by subtle enhancement of occipital leptomeninges noted by the arrow on his original MRI; figure 2). Lumbar puncture did not reveal malignant cytology. Two months after completion of chemotherapy, he was to undergo resection of the primary atrial sarcoma; however, his course was further complicated by bilateral occipital intracerebral hemorrhage into metastatic lesions (figure 4, A and B). He underwent a course of palliative whole-brain radiation to treat new frontal leptomeningeal enhancement. However, 2 days after completion of radiation treatment, the patient had new left frontal intracerebral hemorrhages. He died approximately 10 months after the initial intracranial hemorrhage.

DISCUSSION We present an unusual case of undifferentiated cardiac spindle cell sarcoma presenting with multiple recurrent intracerebral hemorrhages. Primary cardiac tumors are rare, with an incidence of 0.02%.[1] The majority of these tumors are benign, with myxoma comprising 50% of primary cardiac tumors. Malignant tumors account for 25% of primary cardiac tumors. Sarcoma is the main type of malignant cardiac tumor, accounting for 20% of primary cardiac tumors. They are often poorly differentiated, making an exact histologic diagnosis difficult.[2] The two most common types of sarcomas are angiosarcomas and undifferentiated sarcomas. Other groups include leiomyosarcomas, malignant fibrous histiocytomas, osteosarcomas, and fibrosarcomas. The most common presenting symptom is dyspnea.[3] Other common symptoms are chest pain, congestive heart failure, and pericardial effusion.[2]

Approximately 80% of patients with cardiac sarcomas have metastases at the time of diagnosis.[2] Malignant cardiac tumors primarily metastasize to the lungs or mediastinal lymph nodes by the time of diagnosis.[2] Our review of the literature suggests that only 21 (including our case) of 225 (9%) patients with a cardiac sarcoma have metastases to the brain. Our patient is unusual in that he had no cardiac signs or symptoms at presentation, nor a previously diagnosed primary cardiac sarcoma at the time of intracerebral hemorrhage.

Presentation of cardiac sarcomas with neurologic symptoms is rare, and documentation is limited to case reports. We found a total of 3 cases in the English literature in which a neurologic event was the presenting symptom of a metastatic cardiac sarcoma. One of these patients presented with neurologic symptoms from a mass lesion.[4] Another presented with intracranial hemorrhages from an angiosarcoma.[5] A third patient presented with an embolic stroke.[6] We found only 5 cases in which the intracerebral metastases were reported with hemorrhage.[5,7-10] Most cases did not specifically note whether hemorrhage was present. Given the low number of intracerebral metastases (21 total cases, with 6 documented hemorrhages), it seems that intracerebral hemorrhage is a common complication of metastasis.

Complete resection of the cardiac tumor and treatment with chemotherapy and radiation has been shown to prolong survival.[3] However, in our case, as well as two other cases with initial neurologic presentation,[4,6] rapid clinical deterioration prevented surgical resection of cardiac tumor.

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