

Undifferentiated Cardiac Sarcoma Metastatic to the Maxilla: Report of a Case

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Primary cardiac sarcomas represent a group of rare and aggressive malignant mesenchymal neoplasms with a notoriously poor prognosis. They comprise a relatively small percentage of all primary neoplasms of the heart. Presenting clinical signs and symptoms associated with any cardiac sarcoma vary in accordance with the individual tumor's particular site of origin in the heart (eg, left or right atrium, etc). These tumors typically invade contiguous vital anatomic structures and have a marked propensity for metastasis.¹ Although there are only a limited number of published case reports of primary cardiac sarcomas, none mentions metastasis to the jaws. The following is a report of a case in which a cardiac sarcoma metastasized to the maxilla.

Report of a Case

On November 11, 2004, a 49-year-old man was referred to the Clinical Oral Pathology Service by his cardiologist for diagnosis and management of a rapidly growing mass in the right maxilla of 2 weeks' duration. The lesion was tender and bled readily, making it difficult for the patient to maintain oral hygiene. Clinical examination showed a firm, 3.5 cm × 3.5 cm ulcerated mass involving the buccal and palatal gingiva in the upper right premolar-molar area.

Abundant friable necrotic debris was present on the buccal and interdental surfaces of the swelling (Fig 1). A periapical radiograph of the area showed an ill-defined radiolucency in the alveolar bone between the maxillary right second premolar and first molar. The bone destruction extended superiorly to involve the floor of the right maxillary antrum. Loss of lamina dura was evident on both the mesiobuccal root of the first molar and on the distal aspect of the second premolar root (Fig 2). On testing, all of the teeth in the area were vital. The clinical differential diagnosis included an aggressive infectious process (osteomyelitis) or a malignant neoplasm (primary or metastatic).

The recent medical history was significant for undifferentiated high-grade cardiac sarcoma of the left atrium with metastases to the brain, diagnosed in September 2004. The primary tumor had been treated in early October by surgical resection followed by bovine pericardial patch reconstruction. During the immediate postoperative period, the patient suffered a cerebrovascular accident and subsequently received radiation treatments plus Dilantin (diphenhydantoin; Mylan Laboratories, Canonsburg, PA), Decadron (dexamethasone; Merck, Whitehouse Station, NJ), and Temodar (temozolomide; Schering, Kenilworth, NJ) for the metastatic brain lesions. Radiation therapy had been completed on November 8, 2004. The medical history was positive for hypertension, insulin-dependent diabetes mellitus, hepatitis B, and depression, all of which were well controlled with appropriate medications.

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FIGURE 1. Metastatic cardiac sarcoma presenting as a large ulcerated gingival mass, right maxilla.

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FIGURE 2. Periapical radiograph shows ill-defined lytic destruction of interdental bone between maxillary right second premolar and first molar extending superiorly to involve floor of right maxillary antrum.

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A representative incisional biopsy specimen of the oral mass was obtained.

HISTOPATHOLOGIC FINDINGS

Microscopic examination showed an extensively ulcerated mass of mucosal tissue covered by abundant fibrinonecrotic and microbial debris. Within the submucosa there was a diffuse, densely cellular, angiocentric proliferation of sheets of plump, spindly to ovoid neoplastic cells with

vesicular, moderately pleomorphic nuclei. Occasional mitotic figures and foci of tumor necrosis were seen. The neoplastic proliferation involved both deep and lateral surgical margins (**Fig 3**).

IMMUNOHISTOCHEMISTRY

Tumor cells were negative for endothelial markers (factor VIII, CD31, CD34), cytokeratin (AE1/3), S100, melan-A, HMB-45, actin and desmin, and were positive for vimentin. Approximately 50% of the tumor cells were positive for MIB-1 (Ki-67), indicating a high proliferation index. None of the composite findings indicated a definitive line of cellular differentiation.

Both the histomorphological features and immunohistochemistry profile of the oral tumor mass were essentially identical to those observed in the recently resected left atrial tumor mass (**Fig 3**). Therefore, the composite findings were interpreted as diagnostically consistent with undifferentiated high grade cardiac sarcoma metastatic to the maxilla.

CLINICAL COURSE

During the same week in which the patient completed his radiation therapy and the maxillary mass was diagnosed, he also developed radiation dermatitis with secondary pyoderma of the facial and postauricular skin, fever, and gram-positive bacteremia. Consequently, he was admitted to the inpatient unit and started on intravenous Vancomycin (vancomycin hydrochloride; ViroPharma, Exton, PA) and Augmentin (amoxicillin/clavulanate potassium; GlaxoSmith-Kline, Pittsburgh, PA). On November 13 he developed a generalized acute cutaneous rash with target lesions on the extremities, including the palmar surfaces of the hands,

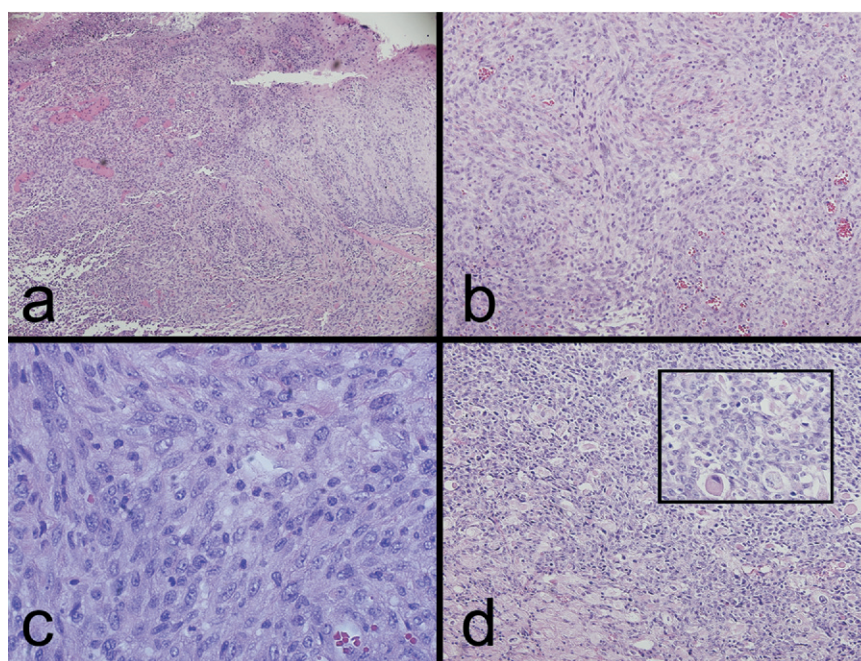


FIGURE 3. Undifferentiated cardiac sarcoma, metastatic to the maxilla. Incisional biopsy, gingival tumor mass. A, Surface ulceration overlying highly cellular, unencapsulated spindle cell neoplasm (hematoxylin & eosin; $\times 100$). B, Medium power photomicrograph, gingival tumor. Neoplastic cells are spindly to ovoid with vesicular, pleomorphic nuclei (hematoxylin & eosin; $\times 250$). C, High power photomicrograph, gingival tumor (hematoxylin & eosin; $\times 400$). D, Photomicrograph, surgical specimen of primary undifferentiated, cardiac sarcoma. Histomorphological features are identical to those seen in gingival mass. Tumor infiltrates cardiac muscle (hematoxylin & eosin $\times 250$; inset, $\times 400$).

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confluent erythematous macules and papules on the truncal skin, and a purulent, exudative ocular discharge accompanied by palpebral erythema. The composite findings were considered to be diagnostically consistent with Stevens-Johnson syndrome triggered by antibiotic therapy. Hence, the antibiotics were discontinued and aggressive supportive care for the mucocutaneous lesions was initiated. Over the next 10 days, the patient's systemic condition continued to decline and he expired on November 23, 2004. Permission for a limited postmortem examination was obtained. Samples of skin from the forehead were taken for immunofluorescence and a specimen for electron microscopy was obtained from the palatal aspect of the oral mass.

ELECTRON MICROSCOPY

The atrial and oral tumors showed essentially identical ultrastructural features. Tumor cells were plump and spindle-shaped with elongated, tapered cytoplasm at both poles and discernible intercellular junctions. External laminae were noted focally at tumor cell-stromal interfaces. Nuclei exhibited irregular, convoluted contours; multiple nucleoli were frequently observed. Cytoplasmic features included occasional lipid vacuoles and focally dilated rough endoplasmic reticulum. There was no evidence of vasoformative structures among the tumor cells (Fig 4). Cells with pinocytotic vesicles and Weibel-Palade bodies were interpreted as representing nonneoplastic endothelial cells. The composite ultrastructural findings were diagnostically indeterminate for any particular cell of origin and essentially confirmed the undifferentiated sarcomatous nature of the tumor.

MICROSCOPIC FINDINGS (SKIN)

The postmortem skin specimens were examined with conventional and immunofluorescence microscopy. Light microscopic findings showed focal epidermal necrosis and ulceration associated with a predominantly neutrophilic infiltrate within the epidermal-dermal interface region. The immunofluorescence analysis showed bright fluorescence for fibrinogen at the dermo-epidermal junction and superficial dermis, but was otherwise negative for IgA, IgG, IgM, C3, C4, Clq, and albumin. Composite findings were interpreted as diagnostically nonspecific, but supportive of the clinical impression of erythema multiforme, Stevens-Johnson type.

Discussion

Primary tumors of the heart are rare.¹ A retrospective study of 480,331 autopsies performed between 1932 and 1948 showed the incidence of primary cardiac tumors to be only 0.0017%.² Roughly 75% of all cardiac tumors are benign, and a majority of these are myxomas. Among the far more rare malignant cardiac neoplasms, 80% are various sarcomas.^{1,3} Worldwide, cardiac sarcomas are found in fewer than 0.2% of all decedents autopsied. These tumors frequently escape both preoperative and antemortem diagnosis. They account for only 0.00025% of all sudden unexpected deaths.⁴

The most common sarcomas of the heart and pericardium are angiosarcoma, undifferentiated sarcoma,

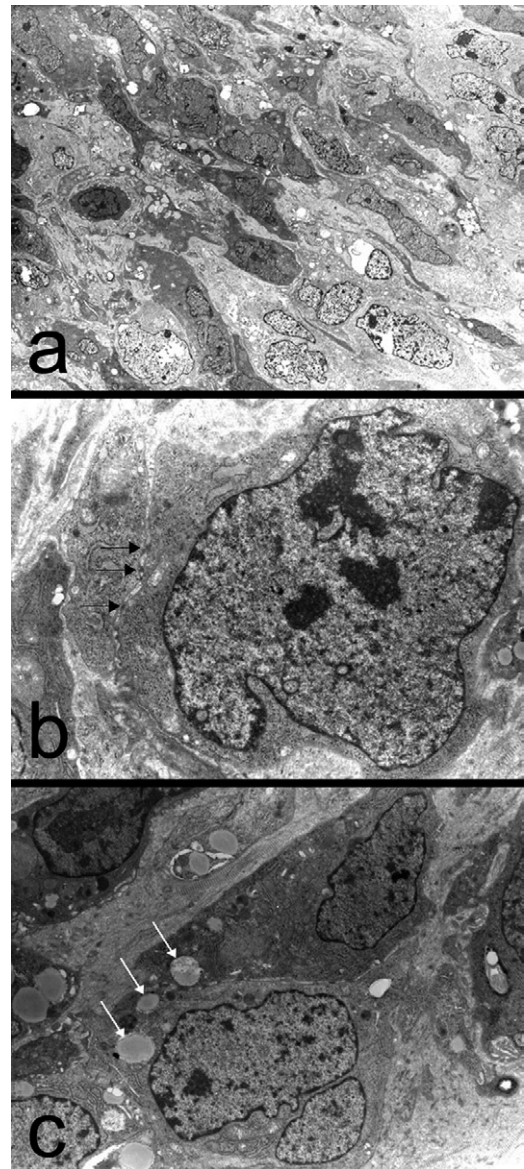


FIGURE 4. Electron micrograph, undifferentiated cardiac sarcoma (glutaraldehyde fixation). A, Tumor cells are spindle-shaped with tapered cytoplasm. B, Convoluted nuclear contour with multiple nucleoli; intercellular junctions adjoin tumor cells (black arrows). C, Lipid vacuoles (white arrows).

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fibrosarcoma, leiomyosarcoma, neurogenic sarcoma, and rhabdomyosarcoma.⁵ Burke et al reviewed 75 patients diagnosed with primary cardiac sarcomas and found that angiosarcomas were the most common type, while undifferentiated sarcomas constituted the second most common type.⁶ In another series of 24 primary cardiac sarcomas, the prevalence of angiosarcomas and undifferentiated sarcomas was comparable.⁷ Rhabdomyosarcoma is the predominant type of childhood cardiac sarcoma.⁸

Presenting clinical signs and symptoms in patients with cardiac sarcomas are wide-ranging and diagnos-

tically nonspecific. They include chest pain, dyspnea, hemoptysis, rales, friction rubs, heart murmurs, intractable arrhythmias, diminished cardiac sounds, abnormal electrocardiogram findings, and constitutional signs such as weight loss, fever, and malaise. Less commonly, patients may present with congestive heart failure, cyanosis, pericardial disease, syncope, and abdominal pain. Cerebrovascular accident and organ infarction also can result from left-sided embolic phenomena.⁹ In our patient's case, the initial event was a cerebrovascular accident, which ultimately led to the diagnosis of primary cardiac sarcoma.

The frequency of undifferentiated sarcoma varies from 1% to 24% in all reported series of cardiac sarcomas.¹⁰ A majority of undifferentiated sarcomas (>90%) are left-sided, as compared with angiosarcomas, which tend to occur more frequently in the right atrium. Undifferentiated sarcomas proliferate rapidly; distant metastases are frequently encountered at diagnosis. Progressive heart failure is typically the cause of death.^{1,4,5,9}

The prognosis for cardiac sarcomas is very poor. In aggregate, the mean survival ranges from 9 to 16.5 months from time of initial diagnosis.^{11,12} Median survival for undifferentiated types is 6 months from diagnosis. In spite of technological advances in diagnosis, the bleak outlook for these tumors is largely due to the rarity and lack of awareness of cardiac sarcomas in general. Therefore, their poor prognosis is attributable to several related factors, the most significant of which are delays in diagnosis and advanced tumor stage at initial diagnosis. There is no apparent correlation between the histological type of sarcoma and prognosis.¹³ In some studies it was found that the histological grade of a primary cardiac sarcoma correlated with survival. Both extent of tumor necrosis (>50%) and high mitotic index (10 mitotic figures per 10 high power fields) appeared to be independently associated with poor survival.^{6,7} Death is typically attributable to locally destructive effects of the primary tumor that result in arrhythmia or intractable cardiac failure.^{1,9} In our patient's case,

systemic complications secondary to an adverse drug reaction resulted in both a rapid decline of systemic health and imminent death.

Cardiac sarcomas are highly aggressive malignancies whose initial presentation may include a spectrum of nonspecific signs and symptoms plus disseminated foci of metastasis,⁹ as we observed in the case of our patient. Along with the unusual site of metastatic involvement in the maxilla, this report illustrates the aggressive behavior and complications that can result from this rare tumor. Despite the rarity of cardiac sarcomas, this case shows that the possibility of metastasis of a primary malignant neoplasm of the heart should be entertained in a patient diagnosed with an undifferentiated sarcomatous lesion in the oral-maxillofacial region.

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