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Carcinosarcoma of the Orbit: Report of Two Cases and Review of the Literature

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Abstract

Objective—To report the clinicopathologic features of 2 patients with carcinosarcoma of the orbit.

Design—Case reports.

Participants—Two patients with orbital carcinosarcoma were identified.

Methods—Retrospective chart review with clinicopathologic correlation and literature review.

Main Outcome Measures—Clinical examination, imaging studies, and histopathologic findings.

Results—Two patients, a 56-year-old woman and a 91-year-old woman, with orbital carcinosarcoma were identified. Both tumors contained sarcomatous and carcinomatous components and invaded periorbital structures.

Conclusions—Carcinosarcoma may arise in the orbit or extend into the orbit from the paranasal sinuses. This malignant neoplasm should be aggressively treated with a combination of surgical resection, chemotherapy, and radiation therapy.

Carcinosarcoma (true malignant mixed tumor) is a biphasic tumor consisting of intermixed malignant epithelial (carcinomatous) and mesenchymal (sarcomatous) components. Carcinosarcoma has been described to arise in many tissues, including the female genital tract,¹ lung,² kidney,³ bladder,⁴ esophagus,⁵ biliary tract,⁶ and skin.⁸ There are 3 reports of carcinosarcoma arising in the orbit^{9–11} and an additional case of parotid gland carcinosarcoma that metastasized to the orbit.¹² Although this is a rare orbital tumor, ophthalmologists and pathologists should be aware of the clinicopathologic features for aggressive management. We report 2 patients with carcinosarcoma of the orbit and briefly review the literature.

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Materials and Methods

After Emory University Institutional Review Board permission was obtained, the diagnoses of cases accessioned in the LF Montgomery Ophthalmic Pathology Laboratory between 1989 and 2007 were reviewed, and 2 cases of carcinosarcoma of the orbit were identified. The patients' clinical histories, including computed tomography (CT) images, were reviewed. The pathologic findings, including immunohistochemical stains, of the orbital tumors were studied. A literature review was performed using MEDLINE for the years 1950 to the present and EMBASE for 1980 to the present. The results of the clinical and pathologic findings of our patients were compared with previously reported cases.

Case Reports

Case 1—A 56-year-old African-American woman with hypothyroidism, but otherwise healthy, was evaluated for a 3 to 4-month history of right epiphora and a tender right orbital mass. The best-corrected vision was 20/40⁺ in her right eye and 20/30⁺ in her left eye. Examination showed a firm, tender 1×1×1-cm nodule between the nasal bone and the right medial canthus (Fig 1). There was mild edema and ecchymosis overlying the mass. Her intraocular pressures were 22 mmHg in both eyes. There was a slight limitation of the right upgaze and 2 mm of right proptosis. The remainder of the ophthalmic examination results was normal. An otolaryngologic examination performed 1 week earlier showed on direct visualization a submucosal bulge anterior to the attachment of the middle turbinate consistent with the lacrimal sac area. CT showed a 2.3×2.0×2.9-cm mass arising from the right nasofrontal recess and eroding into the ethmoid sinus, medial orbital wall, and inner table of the right frontal sinus (Fig 2). A right medial orbitotomy was performed, and the tumor was found to be posterior to the globe and adherent to the periorbita and skin. An incisional biopsy was performed, and a frozen section of the biopsy was diagnosed as spindle cell neoplasm. After examination of permanent sections, the tumor was diagnosed as carcinosarcoma. The treatment plan was extensive surgery, including orbital exenteration, resection of the right nasal bones, ethmoid sinus, and possibly the skull base followed by radiation therapy. The patient elected not to pursue further surgical intervention.

Five months later, the patient reported marked pain and difficulty opening her right eye. Examination showed worsening of the findings in her right orbit and contralateral swelling of the medial aspect of her left eyelids and frontal region. CT scan showed that the tumor now measured 5×5×5 cm. The patient was lost to follow-up, although she presented to the emergency department 2 months later with increased swelling and purulent drainage of her right orbit. A repeat CT scan showed that the mass had increased in size to 5.4×5.2×4.3 cm and exhibited extensive intracranial extension with midline shift (Fig 3). The patient died 3 months later (13 months after onset of symptoms).

Case 2—A 91-year-old woman with hypertension and heart disease was evaluated for a swollen area in the medial aspect of her left upper eyelid. The condition had progressively worsened during the past month. Her left upper eyelid had become ptotic during the past week. She also noted diplopia when she lifted her left upper eyelid. She reported an “ache” involving her left eye and forehead. She also reported decreased appetite and weight loss. Examination showed that she had a best-corrected vision of 20/25 in her right eye and 20/50 in her left eye. A firm, tender left upper anterior orbital mass was noted medial to the globe that appeared to be adherent to the globe (Fig 4). Extraocular movements of her left eye were limited, and she could only adduct the left eye. There was 3 mm of left proptosis. The remainder of the ocular examination results was normal. A left anterior orbitotomy revealed a 2.5×2.5-cm mass that molded to the globe and appeared to be confined to the orbit,

extending to the roof of the orbit superiorly and past the equator of the globe posteriorly. The specimen was completely resected, and the pathologic diagnosis was carcinosarcoma.

Pathologic Findings

Gross examination of the tumor from Case 1 showed that it was yellow to brown, irregular, and soft to fibrous with specks of adherent bone. Microscopic examination showed that the tumor was arranged in sheets, occasionally in fascicles, and that approximately half of the tumor was necrotic. The tumor was composed of pleomorphic cells with variable nuclear to cytoplasmic ratios and spindle, round, and bizarre-shaped nuclei (Fig 5). There were 5 mitotic figures in 40 high-power fields in the tumor. Immunohistochemical stains were positive for cytokeratins AE 1/3 and vimentin and negative for S100, HMB45, and smooth muscle actin in the tumor. Microscopic examination of the tumor from Case 2 showed a diffusely infiltrative neoplasm composed of cells with high nuclear to cytoplasmic ratios and pleomorphic, spindle to oval, vesiculated nuclei (Fig 6). Some of the nuclei contained prominent nucleoli. Occasional tumor cells were multinucleated. Immunohistochemical stains were positive for cytokeratins AE1/3 and vimentin and negative for smooth muscle actin in the tumor. The diagnosis for both tumors was carcinosarcoma.

Discussion

Carcinosarcoma is a true malignant mixed tumor and differs from other forms of malignant mixed tumor. The histogenesis of malignant mixed tumor remains unknown. Two antithetic hypotheses have been suggested to explain the histogenesis of biphasic malignant tumors. Although the multiclonal hypothesis proposes an origin from 2 or more undifferentiated progenitor cells (convergence hypothesis), the monoclonal hypothesis proposes an origin from a single totipotent stem cell that differentiates into separate epithelial and mesenchymal cells (divergence hypothesis). One study showed a monoclonal origin of systemic carcinosarcoma, thus supporting the monoclonal hypothesis.¹³

There are 3 forms of malignant mixed tumor.¹⁴ The most common form is carcinoma ex pleomorphic adenoma, which results from malignant change in a long-standing pleomorphic adenoma or a recurrent mixed tumor that has been incompletely removed. The second form is a metastasizing mixed tumor, which contains benign-appearing epithelial and stromal components. This is thought to arise from 2 progenitor cells, including epithelial (ductal) and mesenchymal (myoepithelial) precursor cells. The third form is a true malignant mixed tumor, also referred to as carcinosarcoma, which is composed of both a malignant epithelial and a malignant mesenchymal component. This form is thought to arise from a monoclonal stem cell that is totipotent (monoclonal hypothesis) and represented by both of our cases. The tumors in our patients may have arisen in accessory lacrimal glands and submucosal glands in the area of the lacrimal sac or paranasal sinus.

The first reported case of carcinosarcoma was in 1899 in a description of a uterine tumor.¹ The first reported case of carcinosarcoma of the orbit was in 1992 by Ni et al,⁹ who described a lacrimal gland tumor. There have only been 3 reported cases of primary carcinosarcoma of the orbit.^{9–11} Of those 3 cases, only 1 was described in sufficient detail to verify the presence of a bona fide carcinosarcoma.¹¹ One patient had no evidence of local recurrence or metastasis 10 months after surgical resection,¹¹ and another patient developed lung metastases.¹⁰ There was no follow-up information provided for the third patient.⁹ These 3 cases along with our current 2 cases are summarized in Table 1.

Because orbital carcinosarcoma may arise from or extend into the paranasal sinuses, we also reviewed previously reported cases of carcinosarcoma of the paranasal sinuses.^{15–26} We identified 5 cases of carcinosarcoma that originated in the maxillary sinus or ethmoid sinus

with extension into the orbit.^{15,16,19,23,26} These cases are summarized in Table 2. These patients were 45 to 86 years old, most were women (12/19), and most were Japanese (12/14). The most common symptoms were nasal obstruction and epistaxis. There were 2 patients with ophthalmic symptoms, and both had diplopia. Histologic examination of the tumors showed that the carcinomatous component was squamous cell carcinoma in all tumors and that the sarcomatous component included fibrosarcoma (6/14), osteosarcoma (4/14), sarcoma not otherwise specified (3/14), and leiomyosarcoma (1/14). The majority of the cases were treated with a combination of surgical resection, radiation, and chemotherapy, including vincristine, etoposide, ifosfamide, doxorubicin, 5-FU, and cisplatin. Because of the rarity of cases of carcinosarcoma, prospective trials evaluating chemotherapeutic regimens have not been performed. According to a review on ovarian carcinosarcomas, they seem to be sensitive to platinum-based chemotherapy and encouraging results have been shown with platinum-ifosfamide and platinum-taxane schedules, which are usually considered the treatment of choice.² Six patients had tumor recurrence, and 4 patients had evidence of metastasis. Four of the 6 patients with tumor recurrence had a recurrence of the sarcomatous portion of the tumor.^{15,20,22,23} Sites of metastasis included submandibular, submaxillary, and cervical lymph nodes; lung; pleurae; brain; diaphragm; bone; and liver. Although 1 patient was reported to be alive 28 months after diagnosis, most patients died within a few months to approximately 1.5 years after diagnosis.

The tumors in both of our patients arose in the medial canthal region. Both tumors were composed of poorly differentiated carcinoma and sarcoma, not otherwise specified. Although the tumor in our first patient appeared to originate in the lacrimal sac area, it is possible that the tumors in both patients arose in the nasal cavity or paranasal sinuses. Both patients were women and presented with nonspecific symptoms. Our first patient died 14 months after diagnosis, and our second patient was lost to follow-up.

The pathologic differential diagnosis of carcinosarcoma includes spindle cell carcinoma, pleomorphic carcinoma, desmoplastic melanoma, teratocarcinosarcoma, and malignant teratoma. Histologic features and immunohistochemical findings differentiate these entities from carcinosarcoma. Carcinosarcoma is an aggressive neoplasm that exhibits local tissue invasion and often metastasizes. Carcinosarcoma of the orbit may locally invade the intracranial cavity, as seen in our first patient, and thus be related to a high rate of mortality. For these reasons, we recommend aggressive surgical excision of orbital carcinosarcoma along with adjuvant chemotherapy and radiation therapy. It appears that the carcinomatous component of the tumor is more sensitive than the sarcomatous component to radiation and chemotherapy.^{20,22}

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Figure 1.
Case 1 clinical appearance. There is an erythematous lesion between the nasal bridge and the medial canthus of the right eye.

Figure 2.
Case 1 CT scan. At the time of diagnosis, there is a 2.3×2.0×2.9-cm mass in the right medial orbit extending into the ethmoid sinus.

Figure 3.

Case 1 CT scan. At 7 months after diagnosis (10 months after onset of symptoms), the mass now measures 5.4×5.2×4.3 cm and extends through the roof of the orbit into the cranial cavity (*arrows*). **A**, Axial view. **B**, Coronal view.

Figure 4. Case 2 clinical appearance. There is ptosis of the left upper eyelid and a superonasal orbital mass displacing the left eye inferolaterally.

Figure 5.

Case 1 pathologic findings. **A**, The tumor is composed of sheets and fascicles of cells with pleomorphic, round to spindle-shaped nuclei. **B**, Some of the nuclei are hyperchromatic and contain prominent nucleoli. **C**, Immunohistochemical stains for cytokeratins AE1/3 are positive (*arrows*, brown reaction product) in scattered tumor cells. **D**, Immunohistochemical stains for vimentin are strongly positive (brown reaction product) in numerous tumor cells. **A**, Hematoxylineosin, 25 $\times$. **B**, Hematoxylineosin, 100 $\times$. **C** and **D**, Peroxidase-antiperoxidase, 100 $\times$.

Figure 6.

Case 2 pathologic findings. **A**, The tumor is composed of interdigitating fascicles of cells with spindle-shaped and round nuclei. **B**, The nuclei are vesiculated and pleomorphic, and numerous nucleoli are visible. **C**, Immunohistochemical stains for cytokeratins AE1/3 are positive (brown reaction product) in scattered tumor cells. **D**, Immunohistochemical stains for vimentin are positive (brown reaction product) in numerous tumor cells. **A**, Hematoxylineosin, 25 $\times$. **B**, Hematoxylineosin 100 $\times$. **C** and **D**, Peroxidase-antiperoxidase, 100 $\times$.

Carcinosarcoma of the Orbit

Table 1

Authors, Year	Age (y)	Race	Sex	Laterality	Location	Symptoms	Pathology	Immunohistochemical Stains	Treatment	Mortality	Metastasis
Ni et al, ⁹ 1992	NR	NR	NR	NR	Lacrimal gland	NR	NR	NR	NR	NR	NR
Font et al, ¹⁰ 1998	NR	NR	F	NR	Lacrimal gland	NR	NR	NR	NR	Lost to follow-up	Lung
Takahira et al, ¹¹ 2005	80	Japanese	F	Right	Lacrimal gland	Eyelid swelling, exophthalmos, decreased vision	Arising from pleomorphic adenoma: carcinoma, osteosarcoma	Cytokeratin AE1,3 +, CAM5.2 +	Surgical resection	No recurrence at 15 mo after symptoms began (10 mo post-resection)	None
Current study	56	AA	F	Right	Medial canthus	Epiphora, pain, decreased vision, rhinorrhea, headache	Sarcomatoid carcinoma, likely SCC	Cytokeratin AE1,3 +; vimentin +	Tumor debulking	13 mo	Unknown
Current study	91	W	F	Left	Medial upper eyelid	Mass, ptosis, diplopia, pain	Sarcomatoid carcinoma	Cytokeratin AE1,3 +; vimentin +	Anterior orbitotomy	Unknown	Unknown

AA = African American; CAM = cell adhesion molecule; F=female; NR = not reported; SCC = squamous cell carcinoma; W = white; + = positive staining.

Carcinosarcoma of the Paranasal Sinuses

Table 2

Authors, Year	Age (y)	Race	Sex	Laterality	Location	Symptoms	Pathology	Immunohistochemical Stains	Treatment	Mortality	Metastasis
Meyer and Shklar, 15 1957	62	White	F	Right	Maxillary sinus extending into the oral cavity and orbit	Bilateral chronic maxillary sinusitis, painful antrum	Carcinoma, spindle cell neoplasm (NOS)	NR	Surgical resection and radiation	Recurrence and metastasis, died ~1 y after presentation	Submaxillary, submandibular, and cervical LN
Feinmesser et al, ¹⁹ 1982	71	NR	F	Right	Maxillary and ethmoidal sinuses extending into the orbit	Recurrent epistaxis, nasal obstruction	Carcinosarcoma	NR	Radiation, surgical resection	Few months	None
Okada et al, ¹⁶ 1990	69	Japanese	F	Left	Maxillary sinus	Nasal congestion, painful swollen cheek, diplopia	SCC, fibrosarcoma	SCC (keratin+), fibrosarcoma (vimentin+)	Radiation, chemotherapy, and surgical resection	9 mo	None
Shindo et al, ²³ 1990	53	Hispanic	M	Right	Ethmoid and maxillary sinuses with orbital extension	Nasal obstruction and epistaxis	SCC, rhabdomyosarcoma	NR	Surgical resection; repeat surgical resection, radiation, and chemotherapy for recurrence	Recurrence, no further recurrence 9 mo after repeat resection	None
Sadaba et al, ²⁶ 2006	45	NR	M	Left	Maxillary sinus	Eyelid swelling, conjunctivitis, pain, diplopia, exophthalmos	Not specified	Cytokeratin (CAM2, 5) +; vimentin +; S100 +	External radiotherapy, chemotherapy	28 mo after symptoms began	Bone and liver

CAM = cell adhesion molecule; F = female; LN = lymph node; M = male; NOS = not otherwise specified; NR = not reported; SCC = squamous cell carcinoma; + = positive staining.