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Sinonasal-Type Hemangiopericytoma

A Clinicopathologic and Immunophenotypic Analysis of 104 Cases Showing Perivascular Myoid Differentiation

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Sinonasal-type hemangiopericytoma is an uncommon upper aerodigestive tract tumor of uncertain cellular differentiation. We report 104 cases of sinonasal-type hemangiopericytoma diagnosed between 1970 and 1995 from the files of the Armed Forces Institute of Pathology. There were 57 females and 47 males ranging in age from 5 to 86 years (mean 62.6 years). The most common clinical presentation was airway obstruction (n = 57) and/or epistaxis (n = 54), with symptoms averaging 10 months in duration. The tumors involved the nasal cavity alone (n = 47) or also a paranasal sinus (n = 26), were polypoid, and measured an average of 3.1 cm. Histologically, the tumors were submucosal and unencapsulated and showed a diffuse growth with fascicular (n = 37) to solid (n = 50) to focally whorled (n = 7) patterns. The tumor cells were uniform in appearance with minimal pleomorphism and had spindle-shaped (n = 82) to round/oval (n = 18) nuclei with vesicular to hyperchromatic chromatin and eosinophilic to amphophilic to clear-appearing cytoplasm with indistinct cell borders. Multinucleated (tumor) giant cells were identified in a minority of cases (n = 5). Mitotic figures were inconspicuous and necrosis was absent. The tumors were richly vascularized, including staghorn-appearing vessels that characteristically had prominent perivascular hyalinization (n = 92). An associated inflammatory cell infiltrate that included mast cells and eosinophils was noted in the majority of cases (n = 87). The immunohistochemical profile included reactivity with vimentin (98%), smooth muscle actin (92%), muscle specific actin (77%), factor XIIIa (78%), and laminin (52%). Surgery was the treatment of choice for all of the patients; adjunctive radiotherapy was given to four patients. Recurrences developed in 18 patients within 1–12 years from diagnosis. Ninety-seven patients were either alive (n = 51, mean 16.5 years) or dead (n = 46, mean 9.6 years) but free of disease. Four patients had disease at the last follow-up: three died with disease (mean 3.6 years) and one patient is alive with disease (28.3 years). Recurrent tumor (17.8%) can be managed by additional surgery. The majority of sinonasal-type hemangiopericytomas behave in a benign manner with excellent long-term prognosis (88% raw 5-year survival) following surgery alone. Sinonasal-type hemangiopericytomas have a characteristic light microscopic appearance with an immunophenotypic profile resembling that of glomus tumors.

Key Words: Sinonasal tract—Hemangiopericytoma—Glomus—Histology—Immunohistochemistry—Prognosis.

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Almost from its initial description by Stout and Murray as a tumor primarily composed of pericytic cells,[42] the diagnosis of hemangiopericytoma (HPC) as a specific tumor type has been questioned. This skepticism has been predicated on the absence of any differentiating features by light microscopy coupled with the fact that the diagnosis of HPC often rests on its architectural features, specifically the presence of ramifying or branching pattern of its vascular component. However, this "specific" vascular pattern is found in a wide array of neoplasms of divergent differentiation such that a diagnosis of HPC is made only after excluding other tumors with similar histologic features. To the argument that HPC does not exist as an independent entity[15] comes the identification of the solitary fibrous tumor (SFT), a tumor originally described as a pleural-based tumor but now known to occur throughout the body.[19,23,43] Solitary fibrous tumor shares a perivascular pattern and CD34-positive tumor cells with HPC, suggesting common cellular differentiation between these tumor types.

The questionable existence of soft tissue HPC as a specific entity is similarly posed relative to sinonasal

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tract HPC. The reasons for this skepticism are multifactorial, not the least of which include differences in the light microscopic features and overall biologic behavior between these sinonasal tract lesions and soft tissue HPC. As a result, the specific direction of differentiation for the sinonasal tract HPCs is still uncertain as attested to by the "hemangiopericytoma-like" designation with the implication that these tumors are related yet distinct from soft tissue HPC.[8] We undertook this study in an attempt to clarify some of the controversial issues surrounding the sinonasal-type HPC, specifically trying to suggest its possible link to other perivascular lesions. As we will discuss, our preferred terminology for this tumor is sinonasal-type hemangiopericytoma (SNTHPC).

MATERIALS AND METHODS

A total of 140 cases of SNTHPC involving the nasal cavity, paranasal sinuses (sphenoid, maxillary, ethmoid, and frontal sinuses), or nasopharynx were retrieved from the files of the Otorhinolaryngic-Head & Neck Tumor Registry of the Armed Forces Institute of Pathology, Washington, DC, between 1970 and 1995. However, 36 patients were excluded from further consideration because of at least one of the following reasons: 1) paraffin blocks were unavailable for additional sections or immunophenotypic analysis; 2) the original submitted case did not have sufficient demographic information supplied from which to obtain adequate follow-up information; and 3) the biopsies were too small or suffered from crush artifact. Therefore, the remaining 104 patients compose the subject of this study, chosen from a review of 20,156 (0.52%) benign or malignant primary sinonasal tract tumors seen in consultation during this time. Ninety-seven cases were obtained from civilian sources, including university medical centers and foreign contributors, three cases from military hospitals, and four cases from Veterans Administration Medical Centers. None of these cases was included in the previous report by Compagno and Hyams.[8]

Materials within the files of the Armed Forces Institute of Pathology were supplemented by a review of the patient demographics (gender, age, race) and symptoms at presentation (epistaxis, nasal obstruction, nasal mass, polyps, difficulty breathing, changes in breathing, sinusitis, headaches, congestion, discharge, pain, osmic changes) including duration. In addition, we reviewed the past medical history, surgical pathology, and radiology and operative reports and obtained follow-up information from oncology data services and tumor registries by written questionnaires or direct oral communication with the treating physician(s) or the patient (patient's family member[s]). Follow-up data, available for 101 patients, included information concerning the exact tumor site, the specific treatment methods used, the presence or absence of recurrent or metastatic disease, and the current status of the disease and patient. Seventy-six cases were submitted with a diagnosis other than HPC and included the following: angiofibroma, fibroma, fibromatosis, sinonasal polyps, fibrosarcoma, leiomyoma, leiomyosarcoma, neurilemoma (schwannoma), meningioma, glomus tumor, hemangioendothelioma, and metastatic carcinoma. This clinical investigation was conducted in accordance and compliance with all statutes, directives, and guidelines of the Code of Federal Regulations, Title 45, Part 46, and the Department of Defense Directive 3216.2 relating to human subjects in research.

Hematoxylin and eosin-stained slides from all cases were reviewed to confirm that established histopathologic criteria for the diagnosis of SNTHPC (or HPC-like) tumors were met.[8] A number of macroscopic and histologic observations were recorded for each tumor as follows: exact tumor location; tumor size (greatest dimension in centimeters); polypoid mass; surface epithelium (present or absent) and whether intact or ulcerated; separation from the surface (Grentz zone); bone invasion or extension by the tumor cells; architectural pattern of growth (fascicular, storiform, solid, whorled to meningothelial, reticulated, palisaded, peritheliomatous); cell type (epithelioid, spindled, round); cytoplasmic quality (clear, eosinophilic, amphophilic); pleomorphism (absent, mild, moderate); cell interactions (syncytial); vessel character (thin-walled, hyalinized, thick-walled); extravasated erythrocytes; presence or absence of necrosis; inflammatory response (lymphoid, eosinophils, mast cells); mitotic figures (number of mitotic figures per 10 high power fields [magnification at ×40 with a ×10 objective lens using an Olympus BX40 microscope]); atypical mitotic figures (present or absent, and defined by abnormal chromosome spread, tripolar or quadripolar forms, circular forms, or indescribably bizarre); and the presence of other microscopic pathologic findings (giant cells, lipomatous change, hematopoiesis, other tumors).

Immunophenotypic analysis was performed in 60 cases with suitable material by a standardized Envision method using 4-μm-thick, formalin-fixed, paraffin-embedded sections. Table 1 documents the pertinent, commercially available immunohistochemical antibody panel used. The analysis was performed on a single representative block for each primary tumor. When required, proteolytic antigen retrieval was performed by predigestion for 3 minutes with 0.05% Protease VIII (Sigma Chemical Co., St. Louis, MO, USA) in a 0.1 M phosphate buffer, pH 7.8, at 37°C. Heat-induced epitope retrieval was performed, as required, by using formalin-fixed, paraffin-embedded tissue treated with a buffered citric acid solution pH 6.0 (Citra, Dako Corporation, Carpinteria, CA, USA) and heated for 20 minutes in a steamer. Following this, the

TABLE 1. *Immunohistochemical panel*

Antigen/antibody	Type	Company	Dilution	Cellular conditioning
Vimentin	mm	BioGenex Labs, San Ramon, CA	1:400	N/A
Smooth muscle actin	mm	Sigma Chemical, St. Louis, MO	1:400	N/A
Muscle specific actin	mm	Ventana, Tucson, AZ	Neat	Protease digestion
Factor XIIIa	rp	Calbiochem, La Jolla, CA	1:800	Protease digestion
Laminin	mm	Sigma Chemical, St. Louis, MO	1:8000	Protease digestion
CD34	mm	BioGenex Labs	1:40	Steam
CD31	mm	Dako, Carpinteria, CA	1:100	Steam
Factor VIIIRAg	rp	Dako	1:50	N/A
CD68 (KP-1)	mm	Dako	1:500	Protease digestion
Desmin	mm	Dako	1:100	Protease digestion
Cytokeratin (AE1/AE3 and LP34)	mm	Boehringer Mannheim Biochemicals, Indianapolis, IN, and Dako	1:50 1:200	Protease digestion
Epithelial membrane antigen	mm	Dako	1:100	Protease digestion
K7	mm	Dako	1:200	Protease digestion
Glial fibrillary acidic protein	rp	Dako	1:2000	Protease digestion
S-100 protein	rp	Dako	1:800	N/A
Neuron-specific enolase	rp	Dako	Neat	N/A
Bcl-2	mm	Dako	1:20	Steam
CD117	mm	Biotechnology, Santa Cruz, CA	1:1600	Steam
Ki-67	mm	Immunotech, Westbrook, ME	1:20	Steam

mm, mouse monoclonal; rp, rabbit polyclonal; N/A, not applicable.

sections were allowed to cool at room temperature in a citric acid buffer solution for 45 minutes before continuing the procedure. Standard positive controls were used throughout, with serum used as the negative control. The antibody reactions were graded as absent to weak (0–1+), moderate (2+), and strong (3+) staining, and the fraction of positive cells was determined by separating them into four groups: <10%, 11–50%, 51–90%, and >90%.

A review of the English literature was performed, and all cases involving the nasal cavity, paranasal sinuses, and/or nasopharynx were included in the review. Single case reports were not avoided, but for the sake of brevity, only reports that included short series were critically reviewed. No foreign language articles were included.

Categorical variables were analyzed using χ^2 tests to compare observed and expected frequency distributions. Comparison of means between groups were made with unpaired t tests or one-way analysis of variance, depending on whether there were two groups or more than two groups, respectively. Multiple comparisons were analyzed using the Tukey method. Linear regression was used to investigate two measured variables, and Pearson correlation coefficients were generated to measure the strength of the association. Confidence intervals of 95% were generated for all positive findings. The alpha level was set at $p < 0.05$. All analyses were conducted using Statistical Package for the Social Sciences software (version 8.0 for PC; Chicago, IL, USA).

RESULTS

Clinical

The patients included 57 females and 47 males (Table 2), a difference that was statistically significant ($p = 0.001$). Even though the disease is statistically more common in women than men, there was no difference in their chance of developing a recurrence ($p = 0.064$) or of dying with disease ($p = 0.633$). Their ages ranged from 5 to 86 years, with an overall mean age at presentation of 62.6 years (median 66 years; mode 68 years). The average age at presentation for men was younger than women (59.5 vs 65.1 years, respectively), but this difference was not statistically significant ($p = 0.061$). In addition, older age at initial presentation, using cutoffs of 50, 55, 60, and 65 years did not increase the chance of developing recurrence ($p = 0.129$) or the chance of dying with disease ($p = 0.987$).

TABLE 2. *Clinical characteristics of 104 sinonasal-type hemangiopericytomas*

Clinical characteristics	No.
Gender	
Female	57
Male	47
Age	
Range	5–86
Mean	62.6
Women (mean)	65.1
Men (mean)	59.5
Symptom duration (mo)	
Range	1–60
Mean	10.0
Symptoms	
Epistaxis	54
Obstruction	57
Mass	13
Polyps	12
Difficulty breathing	10
Sinusitis	7
Headaches	3
Congestion	3
Pain, discharge, smell changes	1 each

The majority of patients presented clinically with symptoms of nasal obstruction, although many also presented with epistaxis (Table 2). A wide range of other nonspecific findings were identified, including a mass, polyps, difficulty breathing, sinusitis, headaches, congestion, pain, discharge, and changes in smell. The duration of symptoms ranged from 1 to 60 months, with an average of 10.0 months. The overall long duration of symptoms is most likely related to the generally nonspecific nature of the initial symptoms, which were frequently managed symptomatically without a specific diagnostic evaluation. There was no difference in the mean duration of symptoms between the genders (females, 9.5 months; males, 10.4 months; $p = 0.706$). There was a statistically significantly shorter duration of symptoms for patients whose tumors involved the maxillary sinus alone (mean 4.2 months; $p = 0.024$), but not for the remaining tumor locations ($p = 0.753$). However, of interest, if the patients had symptoms for a long duration (>10 months), they were more statistically likely to develop recurrent disease and have disease at last follow-up ($p = 0.001$).

TABLE 3. *Macroscopic findings of 104 sinonasal-type hemangiopericytomas*

	No.
Anatomic site	
Nasal cavity alone	47
Turbinate	10
Septum	8
Ethmoid sinus alone	7
Maxillary	5
Nasopharynx alone	1
Nasal cavity and sinuses (NOS)	26
Location	
Left	45
Right	46
Bilateral	7
Midline	2
Unknown	4
Size (cm)	
Range	0.8–8.0
Mean	3.1
Females (mean)	3.3
Males (mean)	2.8

NOS, not otherwise specified.

Radiographic Studies

Review of the records, which included detailed radiographic reports from the contributing institutes, showed that radiologic procedures were performed in 52 patients and included conventional skull radiographs, computer tomography, angiograms, ultrasound, and magnetic resonance imaging, with plain radiographs and computer tomography used most frequently. Nasal cavity or paranasal sinus opacification by a polypoid mass lesion, frequently accompanied by bone erosion and sclerosis, was noted in many cases. Sinusitis was also a prominent finding, obscuring the "mass" lesion in the background. In 22 patients the documentation indicated that the radiographic findings were "within normal limits" without the presence of a mass lesion. Cross-sectional images identified a destructive mass lesion of the nasal cavity or paranasal sinuses. Cribriform plate involvement was not identified in any of the tumors.

Pathologic Features

Macroscopic

The tumors most frequently arose in the nasal cavity alone ($n = 47$) although also associated with the paranasal sinuses in a fair number of cases ($n = 26$) (Table 3). Specific anatomic locations were described, but because this occurred in a limited number of cases (turbinate, $n = 10$; septum, $n = 8$), it is difficult to appreciate specific differences based on the anatomic location. Occasionally, the tumors arose in the ethmoid sinus ($n = 7$) or maxillary sinus ($n = 5$). These anatomic sites of origin did not influence the chance of developing recurrent disease ($p = 0.216$). The tumors were usually unilateral, affecting the right and left with equal frequency, and only a few cases were described as bilateral ($n = 7$) or large enough to appear to involve both sides. The tumors ranged in size from 0.8 to 8.0 cm, with a mean size of 3.1 cm. The tumors appeared to have a larger mean size in females (3.3 cm) than in males (2.8 cm), but this difference was not statistically significant ($p = 0.581$). Furthermore, the overall size did not increase the chance of recurrence or disease at the last follow-up ($p = 0.357$). The tumors were frequently polypoid and appeared to be without surface ulceration. The tumors were beefy red to grayish pink, soft, edematous, fleshy to friable masses, often demonstrating hemorrhage. Calcifications were not noted macroscopically.

Microscopic

At low magnification the tumors were submucosal in localization with a diffuse growth pattern. The surface epithelium was invariably intact ($n = 102$) and composed of respiratory epithelium, although metaplastic squamous epithelium could be found (Table 4). The neoplastic proliferation was seen to efface the normal components of the submucosa or to encircle residual minor salivary glands without effacement of these structures (Fig. 1). Bone invasion and destruction were noted in three tumors and when present did seem to predict an increased chance of developing recurrent disease and dying with disease ($p = 0.001$). A variety of growth patterns could be seen from tumor to tumor and within the same tumor that included fascicular, storiform, whorled,

TABLE 4. *Microscopic features of 104 sinonasal-type hemangiopericytomas*

Microscopic characteristic	No.
Surface intact	102
Growth pattern	
Fascicular	37
Solid	50
Whorled	7
Mixed	17
Cell shape	
Spindle	82
Round	18
Cigar	4
Cytoplasmic quality	
Clear	88
Eosinophilic	16
Pleomorphism	
None	93
Mild	10
Moderate	1
Syncytial arrangement	104
Vessel character	
Thin-walled, staghorn	104
Hyalinized	92
Inflammatory infiltrate	
Mast cells alone	13
Eosinophils alone	1
Acute inflammatory cells only	3
Mixed mast cells and eosinophils	87
Extravasated erythrocytes	100
Mitotic figures (per 10 HPF)	
Range	0–9
Mean	1.0
Bone invasion/destruction	3
Other histologic features	
Giant cells	5
Reticulated pattern	5
Necrosis	1
Lipomatous, hematopoiesis, combination solitary fibrous tumor	1 each

HPF, high-power field.

"meningothelial-like," palisaded, reticular, and mixed patterns of growth (Fig. 2). Long sweeping fascicles were not present in any of the cases. Whereas one pattern may be dominant, most tumors revealed a remarkable admixture of patterns. The particular pattern present (dominant pattern) did not increase the chance of developing a recurrence ($p = 0.994$) or increase the likelihood of dying with disease ($p = 0.525$).

The majority of the tumors were cellular, composed of spindle-shaped to ovoid cells with blunt-ended nuclei to occasional round cells (Fig. 3). The distinction of one cell type from another was not important because it did not change the overall outcome ($p = 0.372$). The neoplastic cells generally displayed a syncytium with indistinct cell borders containing cells with clear to slightly eosinophilic cytoplasm surrounding oval to spindled nuclei with coarse nuclear chromatin. Nuclear pleomorphism was absent to mild (Table 4). Moderate to severe pleomorphism was seen in two patients, which portended a higher chance of developing recurrent disease (Fig. 4) ($p = 0.037$) and a higher chance of dying with disease ($p = 0.001$).

A unique histomorphologic feature useful in the diagnosis of SNTHPC is the presence of characteristic hyalinized vascular spaces (Fig. 5). Whereas thin-walled, variable-sized vascular channels, including so-called "staghorn"-shaped vasculature have been well described in SNTHPCs and were present in our cases, the thick, acellular fibrosis arranged in a peritheliomatous fashion was quite helpful on "low power" in suggesting this diagnosis. To some degree, nearly every case had this feature ($n = 92$); therefore, it may be a valuable histologic feature to seek in the diagnosis of SNTHPC. Extravasated erythrocytes were also identified in nearly every case, a helpful feature in supporting the rich vascularized stromal component of this tumor. The presence of an inflammatory infiltrate composed of mast cells and eosinophils was nearly ubiquitously present in the tumors (Fig. 6). Whereas mast cells alone can be seen in a few cases ($n = 13$), a mixture of mast cells and eosinophils was seen in the majority of cases ($n = 87$). The type of inflammation present did not influence the patient outcome ($p = 0.468$).

Mitotic figures were identified at a very low rate (mean 1/10 high power fields [HPF]) (Fig. 7); atypical mitoses were not present. Therefore, although mitotic figures could be seen, they were not a dominant finding nor were they readily identified. An increased number of mitotic figures (>4/10 HPF) was noted in a single case, but increased mitotic figures did not statistically influence the chance of developing recurrence ($p = 0.185$) or in dying with disease ($p = 0.582$). Explained differently, six patients had no mitotic figures and yet developed recurrent disease. Moreover, three of these patients had disease at the last follow-up: one is alive with disease and two patients died with disease. Ten other patients had 1–2 mitotic figures /10 HPF and developed recurrent disease, but 35 patients had the same number of mitotic figures and did not develop recurrent disease.

A number of interesting features were identified. Tumor giant cells were seen in five cases (Fig. 8). One tumor was juxtaposed to areas showing features seen in SFT (Fig. 9), including the presence of spindle-shaped cells with associated keloid-like collagen deposition; this focus had a distinct immunohistochemical profile compared with the HPC-like areas. In addition, one case each demonstrated lipomatous change consistent with a lipomatous HPC, extramedullary hematopoiesis, and necrosis. The necrosis was only focally seen and appeared as apoptosis rather than confluent necrotic foci.

Histochemical Findings

When performed, reticulin stains were not particularly useful in demonstrating individual cell membrane

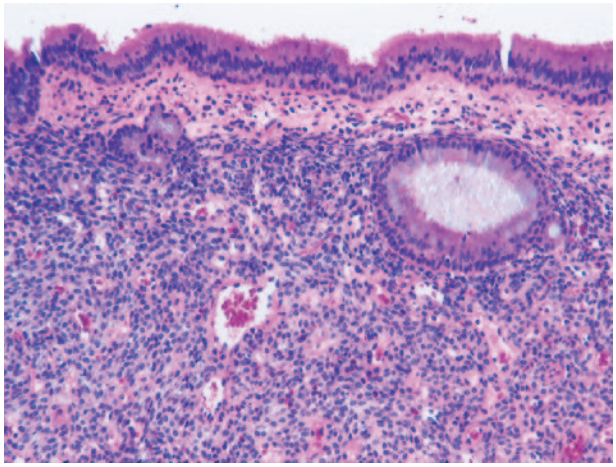

FIG. 1. Sinonasal-type hemangiopericytoma showing characteristic diffuse growth within the submucosa with effacement of the normal components of the submucosa and preservation of minor salivary glands. The overlying respiratory epithelium remains intact.

outlines. Giemsa stains highlighted the mast cell component.

Immunohistochemical Findings

The vast majority of tumors were immunoreactive with vimentin (98%), smooth muscle actin (92%), and muscle specific actin (77%) (Table 5; Fig. 10). The intensity of immunoreactivity varied from diffuse and strong to focal and weak. Many cases (78%) had factor XIIIa immunoreactivity, and there was an accentuation of the individual cells with laminin (52%). CD34 reactivity was focally present in five cases (8%), bcl-2 in one case (2%), S-100 protein in two cases (3%), glial fibrillary acidic protein in one case (2%), and CD68 in one case (2%). The tumor cells were not reactive for CD31, factor VIII-related antigen, desmin, keratins (AE1/AE3 and LP34 cocktail), cytokeratin 7, epithelial membrane antigen, neuron specific enolase, and CD117. Numerous mast cells were highlighted with the latter marker. Of particular interest, the tumor giant cells demonstrated the identical immunohistochemical antigenic profile as the tumor cells. As expected, the tumor giant cells were nonreactive with CD68. The proliferation marker Ki-67 was positive in 29 of 60 cases (48%); <1% of the nuclei showed variable intensity ranging from 1+ to 4+.

Treatment and Follow-up

All patients were treated by surgical excision, including wide surgical excision or polypectomy (Table 6). In addition, three patients received adjuvant radiation therapy; one of these patients is alive with disease (28.3 years) and the other two patients were free of disease at the last follow-up (mean 9.6 years). Chemotherapy was not used. The type of treatment (separated into specific surgery performed) did not adversely affect the patient outcome ($p = 0.783$) or the chance of developing recurrent disease ($p = 0.303$).

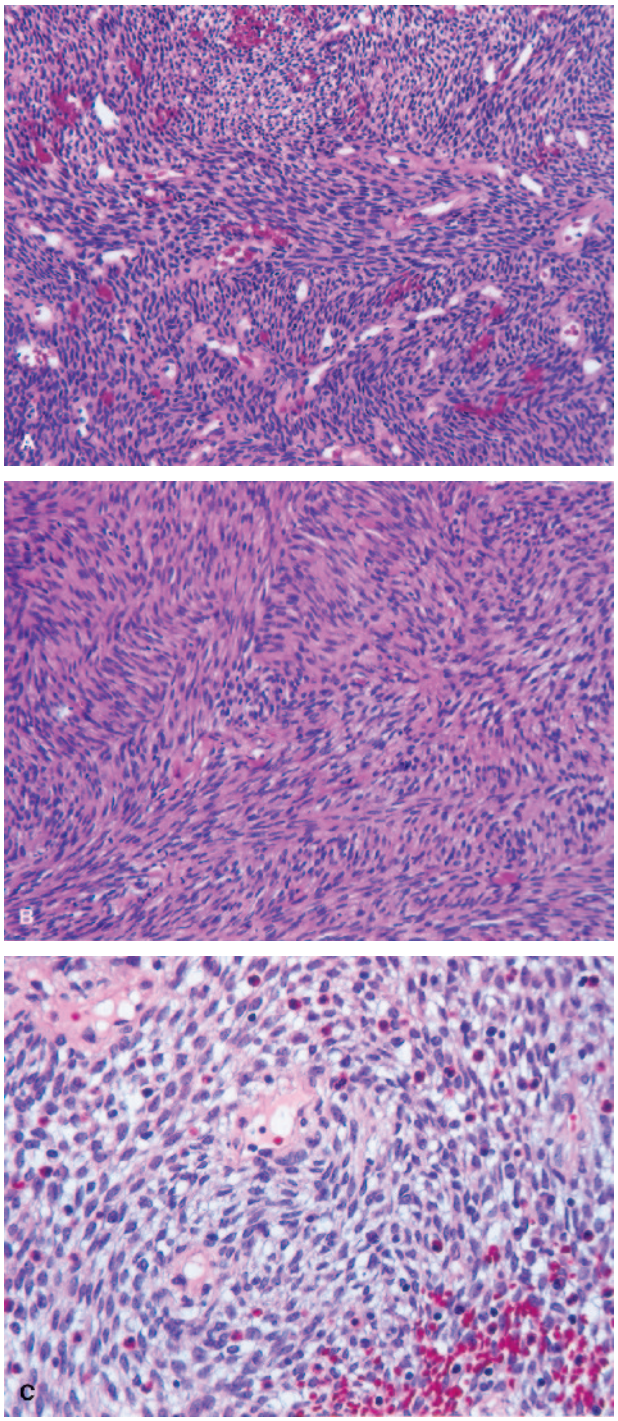

FIG. 2. Sinonasal-type hemangiopericytoma may show a variety of growth patterns, including fascicular (**A**), storiform (**B**), and whorled (**C**) patterns. Extravasated erythrocytes can be seen in the illustration of the whorled pattern.

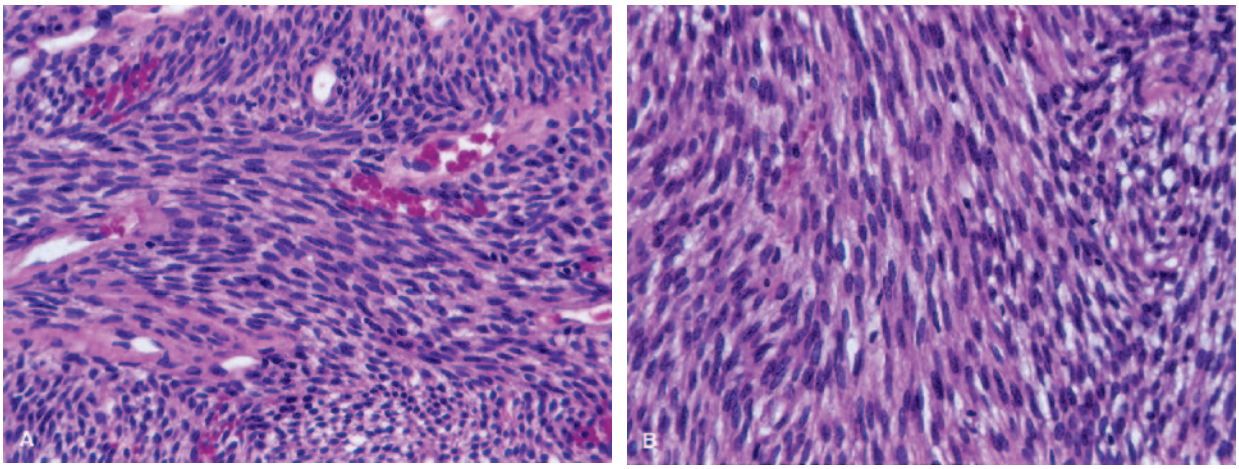

FIG. 3. (**A**) Sinonasal-type hemangiopericytoma showing a hypercellular proliferation composed of spindle-shaped cells with blunt-ended–appearing nuclei with coarse chromatin, eosinophilic-appearing cytoplasm, and indistinct cell borders. (**B**) Minimal to mild pleomorphism is present and mitotic figures are not identified.

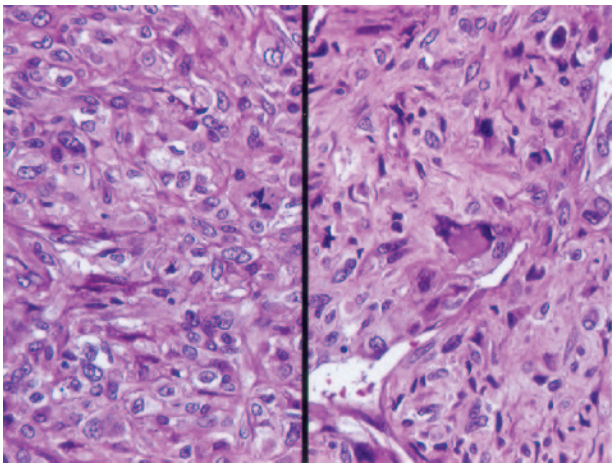

FIG. 4. In this example, there is moderate to severe pleomorphism, a decidedly uncommon feature in sinonasal-type hemangiopericytomas.

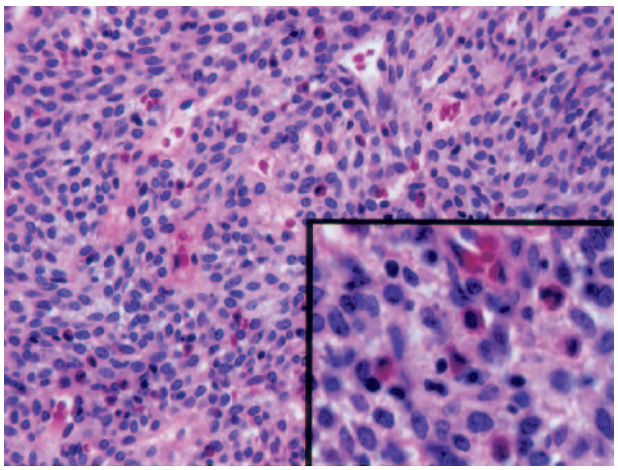

FIG. 6. An associated mixed inflammatory infiltrate composed of mast cells and eosinophils was a consistent finding in our cases. The neoplastic cells in this illustration show a more oval to round appearance with focal spindle-shaped cells.

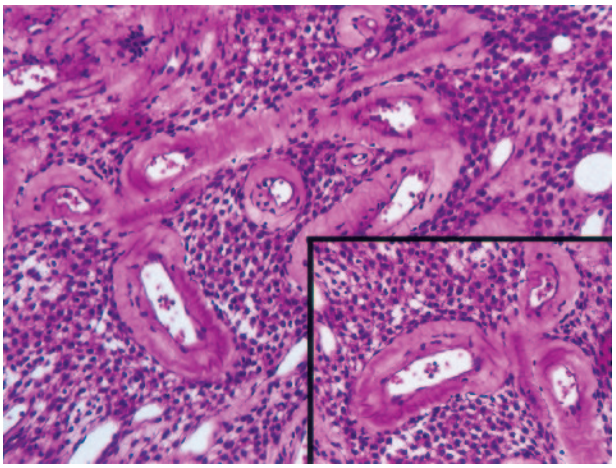

FIG. 5. A characteristic histomorphologic feature in sinonasal-type hemangiopericytomas is the presence of prominent perivascular hyalinization.

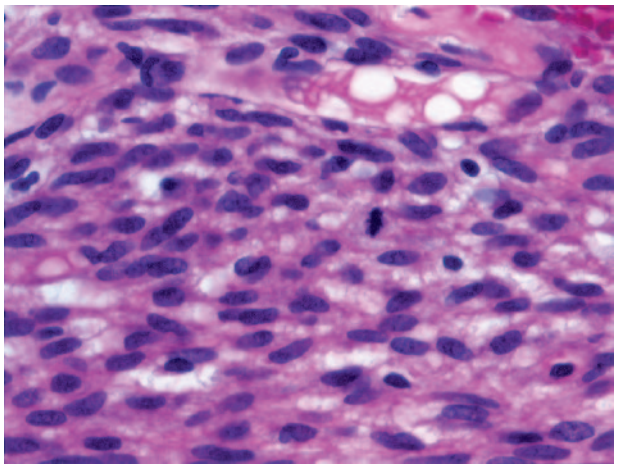

FIG. 7. Mitotic figures were an uncommon feature in sinonasal-type hemangiopericytomas.

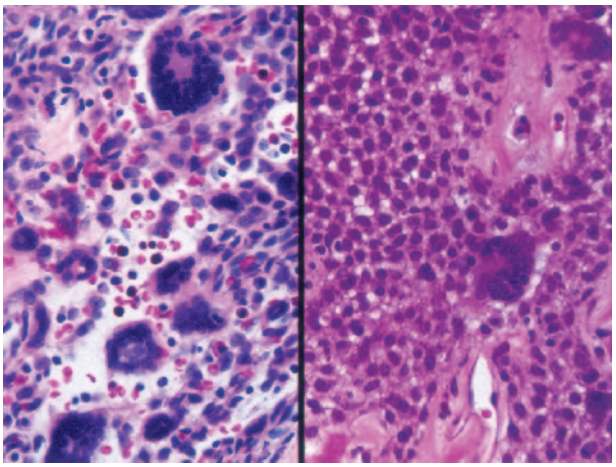

FIG. 8. Tumor giant cells were seen in five of our cases.

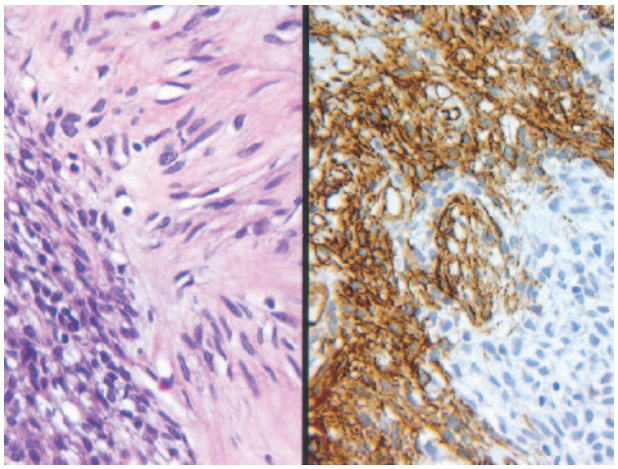

FIG. 9. In one of our cases the typical cellular infiltrate of the sinonasal-type hemangiopericytoma was adjacent to an area showing features of solitary fibrous tumor (left), including spindle-shaped cells with associated keloid-like collagen deposition and CD34 immunoreactivity (right).

The overall survival for SNTHPC was excellent. Follow-up data were available in 101 patients; three patients were contributed from foreign countries and were lost to additional follow-up. Of the 101 patients, three had died with local disease (mean 3.6 years) and one patient was alive with residual disease (28.3 years). All three of these patients were women, similar to the mean age of the rest of the group (61.0 years), with no specific anatomic localization of their tumors. The only unique histologic features were the presence of bone invasion ($n = 2$) and the presence of lipomatous change ($n = 1$), the latter in the patient who was alive with residual disease. These patients experienced from one to eight "recurrences" over a 5-month to 28-year time frame. Surgical excision was used each time, although radiation therapy was used for one patient who is still alive with disease. Although the patients died "with" disease, we cannot extrapolate that they died "from" disease; i.e., it was not their cause of death. No patients developed metastatic disease.

The remaining 97 patients were alive ($n = 51$, mean 13.1 years) or had died of unrelated causes ($n = 46$, mean 9.6 years) without evidence of disease (range, 0.3–33.9 years). This yielded a 5-year raw survival rate of 88.1%, a 5-year disease-free survival rate of 74.2%, a 10-year raw survival rate of 65.3%, and a 10-year disease-free survival rate of 64.4%.

Complete surgical removal of the tumor was the goal, but this was not always possible because of the complex anatomy of the nasal cavity and paranasal sinuses. Therefore, recurrent disease likely is a function of incomplete initial excision and is better considered to represent residual disease. Seventeen patients developed local disease recurrence, ranging from a few weeks to 12 years after the initial presentation. Ten of these recurrences developed within 1 year from the date of initial presentation, suggesting "residual" disease rather than a true recurrence. However, the remaining seven patients had their tumors develop between 5 and 12 years (5, 5, 6, 6, 7, 9, and 12 years, respectively). The recurrences developed at the same site of the previous tumor, although usually more "infiltrative" in the recurrence specimen. The average follow-up for patients with recurrent/residual tumors was 15.1 years. Obviously, all of the patients who died with disease developed a recurrence or had residual disease.

Clinicopathologic Correlations

Statistically, a few clinical and pathologic features were significant in the development of recurrent disease: long duration of symptoms ($p = 0.001$), bone invasion

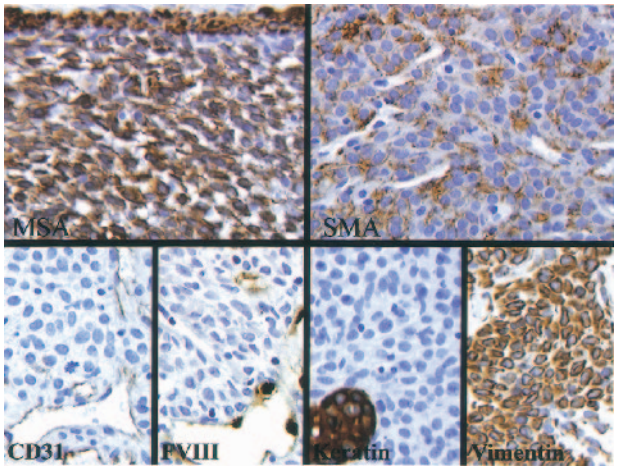

FIG. 10. Immunohistochemical staining in sinonasal-type hemangiopericytoma. Immunoreactivity is present with smooth muscle actin (SMA), muscle specific actin (MSA), and vimentin and negative with CD31, factor VIII-related antigen (FVIII), and keratin.

TABLE 5. *Immunohistochemical panel results for sinonasal-type hemangiopericytomas*

Antibody	No. of cases with positive reactions
Vimentin	59/60 (98%)
Smooth muscle actin (SMA)	55/60 (92%)
Factor XIIIa	47/60 (78%)
Muscle-specific actin (MSA)	46/60 (77%)
Laminin	31/60 (52%)
CD34	5/60 (8%)
S-100 protein	2/60 (3%)
CD68 (KP-1)	1/60 (2%)
Glial fibrillary acidic protein (GFAP)	1/60 (2%)
bcl-2	1/60 (2%)
CD31	0/60 (0%)
Factor VIIIRAg	0/60 (0%)
Desmin	0/60 (0%)
Cytokeratin (AE1/AE3 and LP34)	0/60 (0%)
Epithelial membrane antigen (EMA)	0/60 (0%)
CK7	0/60 (0%)
Neuron-specific enolase (NSE)	0/60 (0%)
CD117	0/60 (0%)
Ki-67	29/60 (48%)
Focal only	10/60 (17%)
1–5%	19/60 (32%)

($p = 0.001$), and severe nuclear pleomorphism ($p = 0.037$). A few features were also statistically significant for patients who died with disease: long duration of symptoms ($p = 0.001$), bone invasion ($p = 0.001$), and severe nuclear pleomorphism ($p = 0.001$).

None of the remaining clinical or pathologic features evaluated impacted either the development of recurrence or the presence of disease at the last follow-up. These features included age ($p = 0.129$), gender ($p = 0.064$), anatomic site ($p = 0.240$), macroscopic size ($p = 0.357$), pattern of growth ($p = 0.525$), cell shape ($p = 0.372$), type of inflammation ($p = 0.468$), increased mitotic figures (>4/10 HPF) ($p = 0.185$), any of the immunohistochemical antibodies studied, including proliferation markers ($p = 0.814$), or the type of therapy received ($p = 0.303$).

DISCUSSION

Clinical Features

In 1976, Compagno and Hyams[8] reported 23 cases of a sinonasal tract lesion that they designated "hemangiopericytoma-like," suggesting both similarities and differences from the soft tissue HPC.[13,42] Although not entirely convinced that their sinonasal tract tumors showed pericytic differentiation, these authors could not offer alternative cell differentiation and thus recommended the terminology of "hemangiopericytoma-like." The use of this terminology conveys a sense of uncertainty, prompting questions relative to the accuracy of this designation. Despite the controversy, there has yet to appear a comprehensive reevaluation of this topic specifically addressing the issue of cellular differentiation and nomenclature. At present, the preferred terminology is that of SNTHPC with defined clinical, pathologic, and biologic parameters.

Approximately 15% of all soft tissue HPCs occur in the head and neck region,[1] and in this region, HPCs predilect to the nasal cavity and paranasal sinuses. Table 2 details the clinical findings of the patients in our study. Our findings essentially match those reported in the literature, including its more frequent occurrence in patients in the 7th decade of life, presentation with nasal obstruction and epistaxis, and polypoid appearance. In contrast to the literature in which an equal gender incidence is noted, we found that SNTHPCs were more common in women than in men. Surgery is the treatment of choice for SNTHPC,[3–5,8,25,44] varying from simple polypectomy without extended resection[44] to wide excision with tumor-free margins.[3–5,25] There are no known etio-

TABLE 6. *Patient outcome for 101 sinonasal-type hemangiopericytomas (mean yr of follow-up)*

	All patients*	A, NED	A, WD	D, NED	D, D
All patients with follow-up	101 (13.1)	51 (16.5)	1 (28.3)	46 (9.6)	3 (3.6)
Follow-up range (yr)	0.3–33.9	4.1–33.9	28.3	0.3–21.0	0.5–9.2
Treatment type					
Excision	41 (14.0)	23 (16.6)	1 (28.3)	16 (10.3)	1 (0.5)
Wide excision	42 (12.3)	19 (16.0)	N/A	21 (9.6)	2 (5.2)
Polypectomy	18 (12.8)	9 (17.1)	N/A	9 (8.5)	N/A
Patients with recurrence	17 (15.1)	7 (19.7)	1 (28.3)	6 (13.4)	3 (3.6)
Anatomic site					
Nasal cavity alone	45 (14.6)	26 (16.6)	1 (28.3)	18 (10.8)	N/A
Septum	8 (10.9)	3 (15.4)	N/A	5 (8.1)	N/A
Turbinate	10 (12.5)	4 (15.1)	N/A	6 (10.8)	N/A
Ethmoid	7 (16.6)	3 (26.1)	N/A	3 (9.6)	1 (9.2)
Maxillary sinus	5 (12.8)	2 (13.4)	N/A	2 (18.0)	1 (1.1)
Nasal cavity and sinuses	26 (10.6)	13 (15.2)	N/A	1 (0.5)	12 (6.5)

* Follow-up available for 101 patients.

A, NED, alive, no evidence of disease; A, WD, alive, with disease; D, NED, dead, no evidence of disease; D, D, dead, with disease; N/A, not applicable.

logic factors associated with the development of sinonasal-type HPC. Soft tissue HPCs have been associated with hypoglycemia mediated through production of insulin-like growth factors by the tumor.[26,37,38] A similar association has not been found with HPC of the head and neck reported in the literature or in any of the cases herein reported. However, Catalano et al.[5] reported severe osteomalacia occurring in association with one of their cases of SNTHPC; the osteomalacia resolved following resection of the tumor. Soft tissue HPCs have been associated with oncogenic osteomalacia,[39] but many of these HPCs likely represent the so-called phosphaturic mesenchymal tumors.[36]

In general, SNTHPCs are indolent tumors. Local recurrence often results from inadequate surgical excision. Billings et al.[3] reported a 40% local recurrence rate, ranging from 4 months to 4 years following the diagnosis; two of these patients had multiple recurrences. Catalano et al.[5] reported local recurrence in three of their seven patients after 3, 5, and 10 years. Marianowski et al.[29] reported an 18% recurrence rate. Local recurrent tumor often occurs within 5 years, but recurrence may not appear for more than a decade.[1] Eichhorn et al.[11] and el-Naggar et al.[12] reported that recurrence of SNTHPC can be anticipated over extended follow-up periods (1–2 decades). Seventeen percent of our cases with follow-up (17 of 101) developed local recurrence, ranging from a few weeks to 12 years after the initial presentation. Ten of these recurrences likely resulted from inadequate excision because they developed within 1 year after excision. The remaining seven patients had their tumors develop between 5 and 12 years following the diagnosis with the recurrences developing at the same site of the previous tumor. In our cases there was a 5-year disease-free survival rate of 74.2% and a 10-year disease-free survival rate of 64.4%. Based on our findings and those cited from the literature, long-term follow-up is advocated because recurrence may be delayed by many years. Overall, the prognosis for SNTHPC is favorable. The raw 5-year survival rate of our patients was 88%, supporting the notion that the majority of SNTHPCs behave in a benign manner. Aggressive behaving SNTHPCs are uncommon but have been reported in the literature, including tumors that were locally destructive or metastatic.[3–5,8] Predicting the biologic behavior for HPC (soft tissue or sinonasal tract) is difficult. Catalano et al.[5] advocated a staging system akin to the Kadish staging system for olfactory neuroblastomas where they found that prognosis for SNTHPC strongly depended on tumor stage and the completeness of the primary resection. A distinction between benign and malignant soft tissue HPCs cannot be made in all cases on the basis of histologic findings.[13] Histologic features that may portend or are associated with aggressive behavior include increased mitoses with >4/10 HPF, atypical mitotic figures, increased cellularity with cellular pleomorphism, and necrosis.[3,5,8,13] Large tumor size ($\geq$6.5 cm) has also been associated with more aggressive behaving SNTHPCs.[2,13] DNA ploidy analysis of SNTHPC has not been found to be of predictive value.[12,14] SNTHPCs usually have low proliferative indices,[49] but a proliferative index of $\geq$10% has been suggested to be associated with more aggressive behaving neoplasms.[14,28] Metastatic disease typically is preceded by (multiple) recurrent tumor(s).[3–5] Adjunctive radiotherapy may be used in conjunction with surgery to control local disease and, in those cases with unresectable primary tumors or metastatic disease, radiotherapy and chemotherapy may be warranted.[4]

Pathologic Features

Histologically, our cases showed remarkable similarity from case to case, appearing as submucosal, delineated, but unencapsulated cellular tumors. At low magnification the tumors had a diffuse growth pattern, effacing or surrounding the normal structures of the submucosal compartment. The neoplastic cells were closely packed, appeared in short fascicles, and were richly vascularized. The vascular channels range from capillary size to large sinusoidal spaces that may have a "staghorn"-like or "antler"-like configuration. A feature that we found to be quite characteristic but not pathognomonic for SNTHPCs is the presence of prominent perivascular hyalinization. This finding in conjunction with the submucosal localization and diffuse growth should be diagnostic of SNTHPC and assist in differentiating it from similar-appearing sinonasal tract lesions. Although perivascular hyalinization is a characteristic feature, it may only be focally present or absent in any given lesion as the cellular component of HPC may compress and obscure the vascular component.

The neoplastic cells of SNTHPC are composed of closely packed oval to elongated, uniform-appearing cells with vesicular to hyperchromatic, round to oval to spindle-shaped nuclei, and amphophilic to eosinophilic to clear-appearing cytoplasm. Mild nuclear pleomorphism can be seen as can an occasional mitotic figure, but a marked nuclear pleomorphism, marked increase in the mitotic activity, and atypical mitoses were not present. Necrosis is not usually found. Fibrosis or myxoid stroma may be seen, especially in tumors undergoing degenerative change. Interestingly, tumor giant cells were present in five of our cases. To the best of our abilities, we could not identify a similar finding in any HPCs (of any site) reported in the literature. These tumor giant cells were an intimate part of the neoplastic proliferation in the cases where they were found and demonstrated similar immunohistochemical features as the nongiant cell neoplastic proliferation. We think that these

tumor giant cells likely represent an aggregation of cells as part of a degenerative phenomenon akin to similar-appearing cells seen in glomus tumors undergoing degenerative changes (so-called symplastic glomus tumor).[13] Rare examples of HPC containing mature adipose tissue, designated lipomatous HPC, have been reported[16,22,34]; one of our cases had associated lipomatous change and would be classified as a lipomatous SNTHPC.

Argyrophilic stains show envelopment of individual pericytes by a silver-impregnated matrix, a finding that was thought to be helpful in the diagnosis of HPC. While individual pericytic cells will be invested by argyrophilic positive material, as noted by Nappi et al.,[33] this feature reflects the presence of basal laminar material around each tumor cell and occurs in a variety of different tumor types.

There are no specific immunohistochemical markers for SNTHPC. Vimentin is consistently expressed by HPC of all sites. In contrast to soft tissue HPC and as documented in our study, SNTHPCs often express the myogenic markers smooth muscle actin (92%) and muscle specific actin (77%). In addition, we found factor XIIIa (78%) and laminin (52%) expression. CD34 was present in five of our cases (8%) but was focal in distribution and weak in intensity. Additional markers found to be present in isolated cases included S-100 protein (n = 2), CD68 (n = 1), glial fibrillary acidic protein (n = 1), and bcl-2 (n = 1). We did not find any immunoreactivity for epithelial antigens, endothelial antigens, desmin, neuron specific enolase, or CD117 (C-kit). In soft tissue sites, HPCs may occasionally express actins and desmin but almost always express CD34; typically, no immunoreactivity is present for cytokeratins, vascular antigens (e.g., CD31, factor VIIIRAg, *Ulex europaeus*), or S-100 protein.

The ultrastructural features are nonspecific for HPC in general and SNTHPC in specific and include the presence of pericellular basal lamina partly surrounding tumor cells and completely separating then from endothelium, tapered cytoplasmic extensions, intracytoplasmic (thin) filaments, intercellular junctions, and pinocytotic vesicles.[10,11,35] Ultrastructurally, the range of differentiation in HPC varies. Some tumors show a range of differentiation comparable to immature (fetal-type) pericytes, and others are differentiated to a degree comparable to mature (adult-type) pericytes.[10]

Differential Diagnosis

Given the absence of definitive light microscopic, immunohistochemical, or ultrastructural features, the diagnosis of SNTHPC rests on its architectural features. However, the neoplastic growth pattern and associated vascular proliferation are not unique to HPC and can be seen in a variety of other tumor types. The differential diagnosis primarily includes lobular capillary hemangioma, SFT, and glomus tumor.

Lobular capillary hemangioma has a lobular growth pattern, which contrasts to the diffuse growth of SNTHPC. On occasion, lobular capillary hemangioma may not be lobular in growth but still can be differentiated from HPC on the basis of its cellular components, which include a granulation tissue-like appearance composed of an admixture of cell types, including fibroblasts and inflammatory cells in and around endothelial-lined vascular spaces. The latter may simulate the vascular component of HPC except that the perivascular hyalinization seen in SNTHPC is not a feature of lobular capillary hemangioma. The absence of perivascular hyalinization, lobular (or lack of diffuse) growth pattern, and admixture of different cell types assists in differentiating lobular capillary hemangioma from SNTHPC. As indicated previously, the perivascular hyalinization of SNTHPC is not present in all cases, but differentiation from HPC is readily achieved given the differences in the cellular components of these two lesions.

Solitary fibrous tumor represents a relatively uncommon spindle cell neoplasm of intrathoracic (pleural-based) or extrathoracic origin.[19,23,43] Solitary fibrous tumors may occur in the upper aerodigestive tract primarily involving the nasal cavity and paranasal sinuses.[18,48,50] The clinical and macroscopic features of sinonasal SFT may be similar to those of SNTHPC.[27] Histologically, SFTs are composed of a variably cellular proliferation of bland spindle-shaped cells lacking any pattern of growth and associated with "ropey" keloidal collagen bundles and associated thin-walled vascular spaces. The latter may be prominent and have the appearance of the vascular component seen in HPCs. By immunohistochemical analysis, SFTs show diffuse reactivity with CD34; reactivity for bcl-2 and CD99 is also seen, but absent staining for actins, desmin, and S-100 protein.[50] In contrast to SFT, SNTHPCs only rarely show CD34 immunoreactivity and lack "ropey" keloidal-appearing collagen. As noted previously, one of our cases had intermixed foci of areas bearing histologic and immunohistochemical findings of SFT, perhaps suggesting overlap or a histogenetic continuum between these tumor types.

The broader differential diagnosis for SNTHPC includes other sinonasal tract mesenchymal tumors, including fibrohistiocytic tumors (benign or malignant fibrous histiocytoma), sinonasal smooth muscle tumors (leiomyoma and leiomyosarcoma), and peripheral nerve sheath tumors (benign and malignant peripheral nerve sheath tumors). The light microscopic and immunohistochemical antigenic profiles are sufficiently different as to allow differentiation of these mesenchymal tumors from SNTHPC.

Differentiation

In their original article defining HPCs, Stout and Murray identified a subset of cases showing that direct continuity could be traced between elongated cells without myofibrils to characteristic smooth muscle cells.[42] Based on this finding, these authors state that the pericyte is a modified smooth muscle cell. The myoid character of pericytes was substantiated by ultrastructural[10] and immunohistochemical studies.[10,30,41] Fletcher,[15] in his argument against the existence of soft tissue HPC as a specific tumor type, pointed out that ultrastructural[10] and immunohistochemical[9,30,40,41,47] studies do not frequently confirm pericytic differentiation (i.e., absence of myoid differentiation) in these tumors. Given the myoid appearance of SNTHPC, including the presence of more spindle-shaped cells with more evident eosinophilic cytoplasm, and evidence in our cases and those in the literature of myoid differentiation by immunohistochemical and ultrastructural analysis, it would appear that the SNTHPCs are nearer to pericytic differentiation than their soft tissue counterparts. Fletcher[15] suggested that, given their myoid differentiation, the SNTHPC perhaps were more closely related to glomus tumors; other authors have also noted that SNTHPC show conjoint features of HPC and glomus tumors.[6,8,21]

The proposition that HPCs were probably related to glomus tumors was initially suggested by Stout and Murray.[42] This proposed relationship between SNTHPC and glomus tumor is particularly appealing. Glomus tumors of the nasal cavity and paranasal sinuses are uncommon.[7,17] Glomus tumors are composed of well-circumscribed sheets, nests, and cords of organoid cells intimately associated with capillary-sized blood vessels. The glomus cell is distinctive, having a rounded to ovoid shape with a sharply punched-out round, centrally placed nucleus and amphophilic to eosinophilic cytoplasm. Cell outlines are distinct by hematoxylin and eosin staining and accentuated by periodic acid–Schiff or reticulin stains. Glomus tumors show immunoreactivity for smooth muscle actin, muscle specific actin, vimentin, and calponin with variable expression of heavy caldesmon and desmin.[7,31] Focal positivity for CD34 has been reported.[7,31] Laminin and type IV collagen outline the cell borders of glomus tumors.[7,24,31] Ultrastructural analysis supports myoid differentiation as seen by the presence of actin-like microfilaments.[32,45,46] Despite differences in their light microscopic features, glomus tumors and SNTHPCs share histologic, immunohistochemical, and ultrastructural similarities. Granter et al.[20] described a spectrum of tumors with perivascular myoid differentiation showing morphologic overlap, suggesting that they were closely related neoplasms forming a single spectrum. Among 24 cases described, these authors identified three categories that included adult myofibromatosis, glomangiopericytoma, and myopericytoma. The term glomangiopericytoma was introduced to describe tumors with composite features of HPC (i.e., presence of HPC pattern of branching vessels) and glomus tumor (i.e., presence of rounded cells with pale or basophilic cytoplasm).[20] Thus, although divided into three categories based on predominant histologic pattern, they suggested that this classification was artificial because adult myofibromatosis, glomangiopericytoma, and myopericytoma seem to comprise a histologic continuum of lesions showing perivascular myoid differentiation.

A similar argument could be made for SNTHPC and glomus tumor. The plausibility of kinship to glomus tumor would explain the differences in light microscopic features between SNTHPC and their soft tissue counterparts and resolve some of the controversy about SNTHPC. Shared perivascular myoid differentiation with glomus tumors would explain the histologic, immunohistochemical, and ultrastructural similarities of SNTHPC to glomus tumor. Further, like glomus tumor SNTHPC is a relatively indolent neoplasm with the overwhelming majority of cases behaving in a benign manner amenable to surgical resection. These findings would still make SNTHPC a perivascular neoplasm and, as detailed above, SNTHPCs are closer to showing pericytic differentiation than its soft tissue counterpart. For this reason and because it demonstrates consistent histologic and immunohistochemical findings, as well as being established in the literature, we advocate retaining the designation of sinonasal-type HPC.

In summary, we analyzed the clinicopathologic features of 104 sinonasal-type hemangiopericytomas. These tumors occur in adults, affect women slightly more than men, and show a relatively indolent behavior with a potential for local recurrence but not metastatic disease. The presence of ovoid to spindled cells with smooth muscle actin and frequent laminin positivity demonstrates kinship to glomus tumors, supporting the contention that the sinonasal-type hemangiopericytoma is a perivascular tumor with myoid or glomus-like differentiation distinctly contrasting with the hemangiopericytoma of soft tissues. □

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REFERENCES

1. Barnes L. Hemangiopericytoma. In: Barnes L, ed. *Surgical Pathology of the Head and Neck*. New York: Marcel Dekker, 2002:986–91.
2. Batsakis JG. The pathology of head and neck tumors: nasal cavity and paranasal sinuses, part 5. *Head Neck Surg* 1980;2:410–9.

3. Billings KR, Fu YS, Calcaterra TC, et al. Hemangiopericytoma of the head and neck. *Am J Otolaryngol* 2000;21:238–43.
4. Carew JF, Singh B, Kraus DH. Hemangiopericytoma of the head and neck. *Laryngoscope* 1999;109:1409–11.
5. Catalano PJ, Brandwein M, Shah DK, et al. Sinonasal hemangiopericytomas: a clinicopathologic and immunohistochemical study of seven cases. *Head Neck* 1996;18:42–53.
6. Chawla OP, Oswal VH. Haemangiopericytoma of the nose and paranasal sinuses. *J Laryngol Otol* 1987;101:729–37.
7. Chu PG, Chang KL, Wu AY, et al. Nasal glomus tumors: report of two cases with emphasis on immunohistochemical features and differential diagnosis. *Hum Pathol* 1999;30:1259–61.
8. Compagno J, Hyams VJ. Hemangiopericytoma-like intranasal tumors: a clinicopathologic study of 23 cases. *Am J Clin Pathol* 1976;66:672–83.
9. D'Amore ES, Manivel JC, Sung JH. Soft-tissue and meningeal hemangiopericytomas: an immunohistochemical and ultrastructural study. *Hum Pathol* 1990;21:414–23.
10. Dardick I, Hammar SP, Scheithauer BW. Ultrastructural spectrum of hemangiopericytoma: a comparative study of fetal, adult, and neoplastic pericytes. *Ultrastruct Pathol* 1989;13:111–54.
11. Eichhorn JH, Dickersin GR, Bhan AK, et al. Sinonasal hemangiopericytoma: a reassessment with electron microscopy, immunohistochemistry, and long-term follow-up. *Am J Surg Pathol* 1990;14: 856–66.
12. el Naggar AK, Batsakis JG, Garcia GM, et al. Sinonasal hemangiopericytomas: a clinicopathologic and DNA content study. *Arch Otolaryngol Head Neck Surg* 1992;118:134–7.
13. Enzinger FM, Smith BH. Hemangiopericytoma: an analysis of 106 cases. *Hum Pathol* 1976;7:61–82.
14. Finn WG, Goolsby CL, Rao MS. DNA flow cytometric analysis of hemangiopericytoma. *Am J Clin Pathol* 1994;101:181–5.
15. Fletcher CD. Hemangiopericytoma—a dying breed? Reappraisal of an 'entity' and its variant: a hypothesis. *Curr Diagn Pathol* 1994;1:19–23.
16. Folpe AL, Devaney K, Weiss SW. Lipomatous hemangiopericytoma: a rare variant of hemangiopericytoma that may be confused with liposarcoma. *Am J Surg Pathol* 1999;23:1201–7.
17. Fu YS, Perzin KH. Nonepithelial tumors of the nasal cavity, paranasal sinuses, and nasopharynx: a clinicopathologic study. I. General features and vascular tumors. *Cancer* 1974;33:1275–88.
18. Fukunaga M, Ushigome S, Nomura K, et al. Solitary fibrous tumor of the nasal cavity and orbit. *Pathol Int* 1995;45:952–7.
19. Gold JS, Antonescu CR, Hajdu C, et al. Clinicopathologic correlates of solitary fibrous tumors. *Cancer* 2002;94:1057–68.
20. Granter SR, Badizadegan K, Fletcher CD. Myofibromatosis in adults, glomangiopericytoma, and myopericytoma: a spectrum of tumors showing perivascular myoid differentiation. *Am J Surg Pathol* 1998;22:513–25.
21. Gudrun R. Haemangiopericytoma in otolaryngology. *J Laryngol Otol* 1979;93:477–94.
22. Guillou L, Gebhard S, Coindre JM. Lipomatous hemangiopericytoma: a fat-containing variant of solitary fibrous tumor? Clinicopathologic, immunohistochemical, and ultrastructural analysis of a series in favor of a unifying concept. *Hum Pathol* 2000;31: 1108–15.
23. Hanau CA, Miettinen M. Solitary fibrous tumor: histologic and immunohistochemical spectrum of benign and malignant variants presenting at different sites. *Hum Pathol* 1995;26:440–9.
24. Haque S, Modlin IM, West AB. Multiple glomus tumors of the stomach with intravascular spread. *Am J Surg Pathol* 1992;16: 291–9.
25. Herve S, Abd AI, Beautru R, et al. Management of sinonasal hemangiopericytomas. *Rhinology* 1999;37:153–8.
26. Hoog A, Sandberg Nordqvist AC, Hulting AL, et al. High-molecular weight IGF-2 expression in a haemangiopericytoma associated with hypoglycaemia. *APMIS* 1997;105:469–82.
27. Kempson RL, Fletcher CDM, Evans HL, et al. Fibrous and myofibroblastic tumors. In: Kempson RL, Fletcher CDM, Evans HL, et al., eds. *Atlas of Tumor Pathology: Tumors of the Soft Tissues*. Bethesda, MD: Armed Forces Institute of Pathology, 2001:23–112.
28. Kowalski PJ, Paulino AF. Proliferation index as a prognostic marker in hemangiopericytoma of the head and neck. *Head Neck* 2001;23:492–6.
29. Marianowski R, Wassef M, Herman P, et al. Nasal haemangiopericytoma: report of two cases with literature review. *J Laryngol Otol* 1999;113:199–206.
30. Miettinen M. Antibody specific to muscle actins in the diagnosis and classification of soft tissue tumors. *Am J Pathol* 1988;130: 205–15.
31. Miettinen M, Paal E, Lasota J, et al. Gastrointestinal glomus tumors: a clinicopathologic, immunohistochemical, and molecular genetic study of 32 cases. *Am J Surg Pathol* 2002;26:301–11.
32. Murad TM, von Haam E, Murthy MS. Ultrastructure of a hemangiopericytoma and a glomus tumor. *Cancer* 1968;22:1239–49.
33. Nappi O, Ritter JH, Pettinato G et al. Hemangiopericytoma: histopathologic pattern or clinicopathologic entity? *Semin Diagn Pathol* 1995;12:221–32.
34. Nielsen GP, Dickersin GR, Provenzal JM, et al. Lipomatous hemangiopericytoma: a histologic, ultrastructural and immunohistochemical study of a unique variant of hemangiopericytoma. *Am J Surg Pathol* 1995;19:748–56.
35. Nunnery EW, Kahn LB, Reddick RL, et al. Hemangiopericytoma: a light microscopic and ultrastructural study. *Cancer* 1981;47: 906–14.
36. Park YK, Unni KK, Beabout JW, et al. Oncogenic osteomalacia: a clinicopathologic study of 17 bone lesions. *J Korean Med Sci* 1994;9:289–98.
37. Pavelic K, Cabrijan T, Hrascan R, et al. Molecular pathology of hemangiopericytomas accompanied by severe hypoglycemia: oncogenes, tumor-suppressor genes and the insulin-like growth factor family. *J Cancer Res Clin Oncol* 1998;124:307–14.
38. Pavelic K, Pavelic ZP, Cabrijan T, et al. Insulin-like growth factor family in malignant haemangiopericytomas: the expression and role of insulin-like growth factor I receptor. *J Pathol* 1999;188: 69–75.
39. Plukker JT, Koops HS, Molenaar I, et al. Malignant hemangiopericytoma in three kindred members of one family. *Cancer* 1988; 61:841–4.
40. Schürch W, Skalli O, Lagace R, et al. Intermediate filament proteins and actin isoforms as markers for soft-tissue tumor differentiation and origin: III. Hemangiopericytomas and glomus tumors. *Am J Pathol* 1990;136:771–86.
41. Skalli O, Pelte M-F, Pecelt R. Alpha-smooth muscle actin, a differentiation marker of smooth muscle cells, is present in microfilamentous bundles of pericytes. *J Histochem Cytochem* 1989;37: 315–21.
42. Stout AP, Murray MR. Hemangiopericytoma: a vascular tumor featuring Zimmerman's pericytes. *Ann Surg* 1942;116:26–33.
43. Suster S, Nascimento AG, Miettinen M, et al. Solitary fibrous tumors of soft tissue: a clinicopathologic and immunohistochemical study of 12 cases. *Am J Surg Pathol* 1995;19:1257–66.
44. Thiringer JK, Constantino PD, Houston D. Sinonasal hemangiopericytoma: case report and literature review. *Skull Base Surg* 1995;15:185–90.
45. Toker C. Glomangioma: an ultrastructural study. *Cancer* 1969;23: 487–92.
46. Venkatachalam MA, Greally JG. Fine structure of glomus tumor: similarity of glomus cells to smooth muscle. *Cancer* 1969;23: 1176–84.
47. Winek RR, Scheithauer BW, Wick MR. Meningioma, meningeal hemangiopericytoma (angioblastic meningioma), peripheral hemangiopericytoma, and acoustic schwannoma: a comparative immunohistochemical study. *Am J Surg Pathol* 1989;13:251–61.
48. Witkin GB, Rosai J. Solitary fibrous tumor of the upper respiratory tract: a report of six cases. *Am J Surg Pathol* 1991;15:842–8.
49. Yasui R, Minatogawa T, Kanoh N, et al. Nasal septal hemangiopericytoma-like tumor: a case report with an immunohistochemical study. *Am J Rhinol* 2001;15:267–70.
50. Zukerberg LR, Rosenberg AE, Randolph G, et al. Solitary fibrous tumor of the nasal cavity and paranasal sinuses. *Am J Surg Pathol* 1991;15:126–30.