Angiectatic Nasal Polyps That Clinically Simulate a Malignant Process
Report of 2 Cases and Review of the Literature

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Background.—Approximately 5% of inflammatory or allergic sinonasal polyps develop extensive vascular proliferation and ectasia with deposition of pseudoamyloid. These so-called angiectatic nasal polyps (ANPs) can grow rapidly and exhibit an aggressive clinical behavior that could simulate malignancy preoperatively.

Objective.—To systematically address the differential histologic diagnosis of ANPs.

Methods.—We evaluated by light microscopy, immunohistochemistry, and electron microscopy biopsy and resection specimens from 2 large ANPs (8 and 10 cm in diameter) that presented in 2 adult men with life-threatening epistaxis and facial deformity, respectively.

Results.—The tumors were firm, lobulated, and covered by smooth, partially ulcerated mucosa. Histologically, clusters of dilated, thin-walled blood vessels embedded in pools of Congo red-negative eosinophilic material, associated with patchy necrosis and atypical stromal spindle cells, were seen. Electron microscopy and immunohistochemistry (CD34, factor VIII) confirmed the endothelial nature of the cells lining the spaces, whereas the atypical stromal cells were classified as myofibroblasts.

Conclusions.—These 2 cases represent extreme examples of ANPs that clinically simulate a malignant process. Awareness of the histological features of ANPs should prevent confusion of such lesions with other vascular or spindle cell lesions of the nasopharynx that would require different treatment and carry a different prognosis.


Inflammatory or allergic sinonasal polyps (SNPs) are the most common sinonasal lesions examined pathologically, and their diagnosis usually presents no difficulties to surgical pathologists. Most of these lesions appear grossly as gelatinous, semitranslucent masses that microscopically show expanded and markedly edematous lamina propria with variable infiltrates of inflammatory cells, often including numerous eosinophils.

Based on the predominant elements seen on histological evaluation, inflammatory SNPs have been classified into 5 types: edematous, glandular, fibrous, cystic, and angiectatic or angiomatous. The angiectatic nasal polyps (ANPs) are rare, representing only 4% to 5% of all SNPs.

Clinically, SNPs present as painless, movable swellings of the nasal, sinus, or nasopharyngeal mucous membranes; they have a smooth, bluish gray, shiny surface. The most common symptoms associated with SNPs are nasal obstruction and an alteration in olfaction. Occasional SNPs present with other manifestations, such as exophthalmos, proptosis, and visual disturbances, when they extend into the orbit. In a relatively uncommon presentation, SNPs may cause extensive bone erosion and remodeling or epistaxis. The presence of any of the latter features can raise clinically the suspicion for a malignant process.

On the other hand, histological evaluation of specimens clinically expected to be inflammatory nasal polyps can rarely reveal other tumors, such as papilloma, carcinoma, lymphoma, or a soft tissue neoplasm; all these entities have been reported to occur in the nasopharynx.

In the few reports that deal with SNPs with rich vascularity, it has been concluded that the principal diagnostic problem with these lesions is their potential confusion with nasopharyngeal angiofibromas or other vascular tumors. The histological differential diagnosis has been only partially addressed.

This report describes the findings in 2 large ANPs that caused significant clinical and pathological diagnostic difficulties at the time of their presentation. The differential diagnosis is discussed.

REPORT OF CASES

Case 1

A mute, deaf, 60-year-old white man presented to the emergency department with a 2-day history of epistaxis. After multiple attempts, the bleeding was controlled with nasal packing. Further evaluation revealed a mass in the nasopharynx. A biopsy was performed, which revealed an ulcer with underlying dilated blood vessels with thrombosis. The patient continued to be evaluated as an outpatient but was readmitted 10 days later for recurrent epistaxis. The tumor was suspected to be malignant because of its hemorrhagic nature and its large size. A second biopsy specimen showed squamous epithelium with pseudopitheliomatous hyperplasia, areas of ulceration, and underlying dilated blood vessels.
Surgical excision of the mass was planned, and while the patient was being medically cleared for surgery, he developed profuse hemorrhage from the tumor that could not be controlled with nasal packing. An emergency procedure was performed to control the bleeding and to excise the mass. At surgery, the tumor was localized in the nasopharynx and measured 8 cm in maximum diameter. The tumor had a thin pedicle that protruded through the middle meatus and was excised without complications. Small inflammatory nasal polyps were concurrently excised. The patient recovered uneventfully and is well after 39 months.

Case 2
A 52-year-old black male presented with swelling over the right side of his face that had lasted for several months. On physical examination, the patient had considerable right-sided proptosis and a nasopharyngeal mass. A biopsy was performed, which revealed squamous metaplastic mucosa with extensive necrosis and granulation tissue formation. The mass continued to increase in size, and the patient was referred to the University of Maryland Hospital. A computed tomographic scan showed a destructive lesion that measured up to 10 cm in diameter, involving the anterior and posterior maxillary walls and causing bowing of the medial maxillary wall. The tumor was suspected to be malignant, and surgical excision with a possible concurrent radical neck dissection was planned. At surgery, the tumor was found to extend through the right anterior maxillary wall from the maxillary sinus; a separate tumor that filled the nasal cavity was identified as protruding from the ethmoid sinus. These masses and other small polyps were excised. Intraoperative pathological evaluation of the tumors showed benign fibrovascular tissue. Bone invasion and destruction were not identified at surgery. The patient was well after 12 months.

MATERIALS AND METHODS
Material from the resection specimens from both patients was routinely processed and embedded in paraffin. Five-micron sections were stained with hematoxylin-eosin and Congo red stains. Paraffin sections were also stained with the peroxidase and antiperoxidase method for CD34 (prediluted, BioGenex, San Ramon, Calif), desmin (1:50, Dako, Glostrup, Denmark), Ulex europaeus (1:500, Dako), factor VIII (1:500, Dako), smooth muscle actin (1:200, Dako), and cytokeratin (1:10, Dako).

Small (<1 mm³) tissue samples were processed routinely for electron microscopy as previously described.²³

RESULTS

Gross Findings
In case 1, the excised nasopharyngeal mass consisted of a lobulated mass that measured 7.8 × 4.8 × 3 cm, with an overall smooth surface, partially covered by a shiny mucosa. The cut surface was firm, with glistening tan areas, alternating with yellow-brown and hemorrhagic zones that showed cystic degeneration (Figure 1).

In case 2, the specimen was received as multiple, lobulated fragments of firm tissue that measured in aggregate 12 × 8 × 8 cm. The average fragment size was 2 cm. The cut surface of the individual fragments showed features similar or identical to the ones described for case 1.

In both cases, approximately 10% of the sample consisted of soft, gelatinous fragments highly suggestive of typical inflammatory nasal polyps.

Light Microscopy
The microscopic morphology was similar in both cases. The surface of the lesions was mostly ulcerated with patchy areas lined by metaplastic squamous epithelium that showed pseudoepitheliomatous hyperplasia. Approximately 80% of the sections showed clusters of irregularly shaped, thin-walled blood vessels (Figure 2), often surrounded by pools of Congo red-negative eosinophilic extracellular material (Figure 3). Scattered blood vessels contained fibrin thrombi in their lumina (Figure 4). The stroma displayed scattered, markedly atypical spindle cells (Figure 4); the vascular spaces were also focally lined by markedly atypical cells (Figure 5). The atypical cells displayed oversized, red nuclei and basophilic cytoplasm (ganglion cell-like appearance). The areas with aggregates of cavernous-type blood vessels alternated with avascular zones. Other areas displayed cystic degeneration that contained complex formations of pseudopapillary projections lined by endothelium.

In some areas, particularly those close to the surface of the tumors, the eosinophilic extracellular material resembled fibrinoid necrosis and showed associated areas of or-
organization consistent with typical granulation tissue. Numerous hemosiderin-laden macrophages were seen scattered throughout the lesions and associated with patchy, recent hemorrhages. A small proportion of the sections showed features typical of classic inflammatory polyps.

Immunohistochemical Studies

Immunoperoxidase stains for endothelial markers (Ulex, factor VIII, and CD34) highlighted the endothelial cells in most of the vascular-looking channels, including the complex papillary-like projections. Stains for desmin and smooth muscle actin were positive in the walls only of a few blood vessels with normal-appearing structure, whereas they were negative in most dilated, cavernous vascular spaces. The cytoplasm of rare atypical and non-atypical stromal cells stained positive for smooth muscle actin, indicating their myofibroblastic nature; most stromal cells were negative, however. Cytokeratin stains were positive only in the epithelial component of the lesions.

Electron Microscopy

Ultrastructural examination in both cases revealed large numbers of capillary-type blood vessels lined by flat or plump endothelial cells surrounded by interrupted basal laminae (Figure 6). Fibrin and platelet thrombi were prominent in the lumina of the vessels and in the space beneath the endothelium (Figure 5). The pools of eosinophilic material consisted ultrastructurally of fibrin, cellular debris, and granular, fibrillar, and amorphous material (Figure 5). The stromal cells had features of fibroblasts or myofibroblasts (prominent rough endoplasmic reticulum, thin cytoplasmic filaments with focal dense bodies, micropinocytotic vesicles, and partial surrounding basal lamina-
na). No giant perichromatin granules or prominent nuclear fibrous lamina were seen.

**COMMENT**

The ANPs are relatively uncommon pseudoneoplastic lesions that can pose interesting pathophysiological questions and present a difficult diagnostic problem. Although the clinical and radiological features of ANPs have been well studied, the description of their pathological features has been limited.

The pathogenesis of inflammatory SNPs has been extensively analyzed. Chronic inflammatory infiltrates (particularly plasma cells) produce a vascular permeability factor that contributes to the interstitial edema, and it has been speculated that vascular congestion along with obstruction of the outflow of tissue fluids are also important in their formation. The SNPs show a decreased blood flow and a decrease in the number of blood vessels compared with normal nasal mucosa. The ANPs in contrast are characterized by large numbers of dilated capillary-like blood vessels. The accumulation of these elements in the extracellular space appears in light microscopy as large perivascular pools of cosinophilic amorphous material.

Bizarre, large pleomorphic spindle cells in the stroma are part of the reactive secondary changes seen only occasionally in SNPs overall but which are particularly prominent in ANPs. Similar to the vascular proliferation, pseudosarcomatous changes appear to be also more common in choanal polyps and have been diagnosed as angiectatic polyps and conversely have omitted angiectatic polyps misdiagnosed as angiofibromas. Although these extremely atypical mesenchymal cells can raise the suspicion for a soft tissue sarcoma (eg, malignant fibrous histiocytoma), they should be considered in the context of the reactive changes they are associated with.

Vascular tumors are the most common nonepithelial tumors of the nasal cavity and nasopharynx, and the prominent vascular component in ANPs can pose differential diagnostic problems. The ANPs should be mainly differentiated from capillary or cavernous hemangiomas. Angiomas are composed of irregular vascular channels lined by benign-appearing, usually flattened endothelial cells embedded in edematous stroma. Sinonasal angiomas present with nasal obstruction and epistaxis and do not show sex or age predilection. They occur more often in the anterior nasal septum, the turbinates, and the vestibule.

The ANPs have been confused with juvenile nasopharyngeal angiofibromas. The true incidence of ANPs cannot be accurately ascertained, because earlier reports undoubtedly have included angiofibromas misdiagnosed as angiectatic polyps and conversely have omitted angiectatic polyps misdiagnosed as angiofibromas.

There are several clinical and pathological features, summarized in the Table, that distinguish ANPs from juvenile nasopharyngeal angiofibromas. The hypovascular or avascular appearance of ANPs in angiography, although paradoxical, is explained by the fact that ANPs do not have a normal arborizing pattern of vascularity but rather irregular racemose arrangements of dilated capillary-type vessels and newly endothelialized spaces that often show superimposed thrombosis.

**Table: Angiectatic Nasal Polyp Versus Juvenile Nasopharyngeal Angiofibroma**

<table>
<thead>
<tr>
<th>Evaluation Method</th>
<th>Angiectatic Nasal Polyps</th>
<th>Juvenile Nasopharyngeal Angiofibromas</th>
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<tbody>
<tr>
<td>Light microscopy</td>
<td>Racemose aggregates of irregularly shaped blood vessels resembling dilated capillaries, no elastic or muscular layers</td>
<td>Stellate and staghorn blood vessels compressed by fibrous stroma; no elastic layer, incomplete or absent muscle layer</td>
</tr>
<tr>
<td></td>
<td>Acute and chronic inflammation common; hemosiderin-laden macrophages</td>
<td>No inflammation (except for areas of surface ulceration) mast cells</td>
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<tr>
<td></td>
<td>Heterogeneity from field to field; patchy areas with features of typical inflammatory polyps</td>
<td>Relative homogeneity from field to field</td>
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<tr>
<td></td>
<td>Paucicellular stroma with scattered fibroblasts and myofibroblasts; marked nuclear enlargement; large nucleoli; no mitoses</td>
<td>Cellular stroma with stellate fibroblastic cells with plump nuclei; nuclear pleomorphism and mitoses may be seen; stroma may have focal myxomatous changes</td>
</tr>
<tr>
<td>Electron microscopy</td>
<td>Typical fibroblasts and myofibroblasts with indistinct nuclear fibrous lamina; endothelial cells</td>
<td>Fibroblastic cells with distinctly prominent nuclear fibrous lamina and large perichromatin granules; endothelial cells</td>
</tr>
<tr>
<td></td>
<td>Amorphous extracellular matrix (fibrin, plasma, cellular debris)</td>
<td>Collagenous extracellular matrix better organized</td>
</tr>
<tr>
<td>Clinical symptoms</td>
<td>Nasal obstruction, alteration in olfaction; epistaxis; all ages and both genders affected</td>
<td>Nasal obstruction, spontaneous epistaxis; mostly young males affected</td>
</tr>
<tr>
<td>CT scan features</td>
<td>Do not invade pterygopalatine fossa or sphenoid sinus usually</td>
<td>Invade pterygopalatine fossa and/or sphenoid sinus usually</td>
</tr>
<tr>
<td></td>
<td>Non-enhancing lesions</td>
<td>Enhancing lesions</td>
</tr>
<tr>
<td>Surgical features</td>
<td>Easily &quot;shell out&quot; during surgery</td>
<td>Resected with difficulty</td>
</tr>
<tr>
<td>Angiography</td>
<td>Hypovascular or avascular</td>
<td>Extremely vascular; irritation from branches of the external carotid artery usually</td>
</tr>
</tbody>
</table>

**Angiectatic Nasal Polyps**


**Juvenile Nasopharyngeal Angiofibromas**

It is important that a correct diagnosis of these lesions is made, because they require different treatment and also carry a different prognosis. The ANPs share the benign clinical characteristics of all inflammatory SNPs, ie, excision is curative and recurrences are rare. This is in contrast to angiofibromas, which are frank neoplasms that require either surgical excision and/or radiotherapy to prevent recurrence.38

In both patients discussed in this report, the clinical presentation suggested aggressive tumors and the results of several preoperative biopsies were inconclusive, raising the possibility of vascular neoplasms, including juvenile nasopharyngeal angiofibroma. The striking vascular proliferation and ectasia associated with amorphous eosinophilic material present in all biopsy specimens were in retrospective evaluation consistent with ANPs. Because of reactive changes in the surface epithelium that included pseudoplasmonic hyperplasia, the suspicion of squamous cell carcinoma was also raised. Despite the preoperative concerns for malignancy, it became evident at surgery that the tumors were benign and easily excisable (in contrast to typical nasopharyngeal angiofibromas and epithelial and mesenchymal malignant tumors). Also, bleeding was minimal both during and after surgery.

In summary, this report highlights the potential difficulties in the pathological diagnosis of ANPs. Extensive vascular proliferation, accumulation of extracellular amorphous eosinophilic material, and atypical stromal cells are characteristic of ANPs. This pseudoneoplastic entity being the result of extensive reactive and reparative changes in inflammatory SNPs may present histologically with significant heterogeneity. The latter feature is also helpful in the diagnosis of ANPs similar to other pseudoneoplastic proliferations.

References