

Extravascular papillary endothelial hyperplasia of the larynx: A case report and review of the literature

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Abstract

Papillary endothelial hyperplasia (PEH), a tumor that falls along the spectrum of reactive to neoplastic vascular lesions, must be diagnosed carefully because it can resemble an angiosarcoma. PEH is generally considered to be the result of an unusual form of thrombus organization, exhibiting excessive papillary endothelial proliferation that is usually confined to the lumen of preexisting vessels or vascular malformations. Most cases of PEH are of the intravascular type; extravascular PEH is rare. We describe what we believe is the first reported case of an extravascular PEH in the larynx.

Introduction

Proliferative vascular lesions are classified along a spectrum that ranges from reactive to neoplastic. One of these lesions is papillary endothelial hyperplasia (PEH). PEH is generally considered to be the result of an unusual form of thrombus organization, exhibiting excessive papillary endothelial proliferation that is usually confined to the lumen of preexisting vessels or vascular malformations. PEH resembles an organizing thrombus, hemangioma, or angiosarcoma, and therefore the diagnosis must be made carefully.¹⁻¹¹

There are three types of PEH: (1) a pure (primary) form that arises de novo in dilated vessels; (2) a mixed (secondary or reactive) form that occurs focally in preexisting varices, hemangiomas, or arteriovenous malformations; and (3) a rare extravascular form that arises in hematomas.¹¹

In this article, we describe a unique case of extravascular PEH in an uncommon location.

Case report

A 37-year-old man complained of a 3- to 4-month history of hoarseness. He reported no dysphagia, weight

loss, cough, or ear pain. On laryngeal examination, we detected an ulcerovegetative lesion that had arisen on the mucosal surface of the epiglottis and extended to the anterior commissure.

Three biopsy specimens were obtained during direct laryngoscopy. The first sample was taken from the bulk of the lesion; it measured 2.0 × 1.5 × 0.5 cm and contained small, brown-gray particles. The second and third specimens were taken from the left and right ventricular bands, respectively.

On microscopy, the first sample exhibited many papillary projections that were made up of hyalinized collagen cores lined by a single layer of endothelial cells (figure, A). The lining cells were positive on staining with factor VIII-related antigen (streptavidin-biotin complex method; BioGenex; San Ramon, Calif.). The endothelial cells were swollen, but they lacked significant pleomorphism and mitotic figures (figure, B). The surrounding tissue resembled an unorganized thrombus. However, no evidence of a vessel wall was observed. The other two specimens contained epithelial hyperplasia, which we believed had arisen secondary to underlying chronic inflammation.

All of these histomorphologic findings were consistent with the presence of a PEH arising in a hematoma—that is, an extravascular PEH. The patient was placed on an antibiotic and an inflammatory drug for 1 week. He was examined twice within 6 months of resection; he reported no complaints, and findings on his laryngeal examination were normal. At 2 years of follow-up, no recurrence was evident.

Discussion

PEH occurs in sites throughout the body.¹⁻¹¹ In most cases, it arises in the veins of the dermis and subcutis in the head and neck and the extremities.^{1,2,5,7-11} Most lesions are intravascular and associated with hemangiomas, varices, and arteriovenous malformations.^{1,3,4,6,9,11} Extravascular lesions are rare; when they do occur, they usually arise in the context of a hematoma.^{1,2,5,10}

The differential diagnosis of the intra- and extravascular types depends on whether there is a vessel wall in the near

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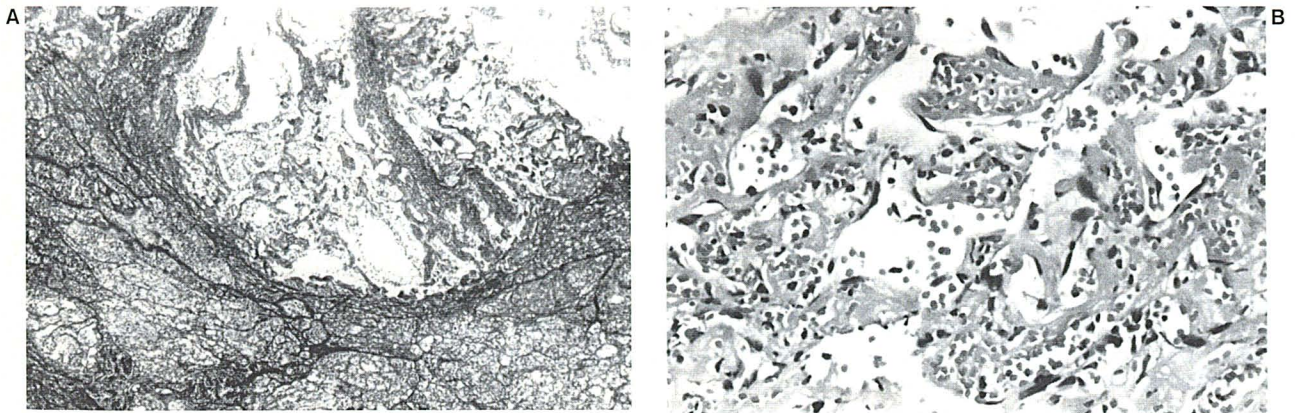


Figure. **A:** Microscopic examination reveals the papillary projections in the center of a thrombus (H&E, original magnification $\times 40$). **B:** Endothelial cells line the hyalinized cores of papillae (H&E, original magnification $\times 200$).

vicinity or at the periphery of the lesion. In our patient, we detected no nearby vessel wall despite serial sections, and we believed that the lesion arose extravascularly in a hematoma. In fact, there is a hypothesis that PEH occurs as a result of a peculiar organization of a thrombus, and its pathogenesis involves the secretion of endothelial basic fibroblast growth factor, which stimulates endothelial cell proliferation.^{2,5}

All vascular lesions should be considered in the differential diagnosis. The spectrum of these lesions varies from benign to malignant, including hemangiomas, hemangioendotheliomas, and angiosarcomas.^{1,3,6} It can be difficult to differentiate an intravascular papillary hemangioma from an intravascular capillary hemangioma or an intravascular pyogenic granuloma, both of which may contain innumerable vascular channels (although the latter displays lobulation that is not apparent in the other two entities).^{3,7} Further complicating this distinction is the fact that PEH may develop within a hemangioma.¹

The most significant aspect of PEH is the regularity with which it is confused with angiosarcoma.⁸ Some cases have followed an aggressive clinical course and exhibited positive radiologic findings.¹¹ From a morphologic point of view, the primary concern about malignancy is the presence of more cellular, solid areas or foci that appear to have broken through vessel walls.⁴ In contrast to an extravascular PEH, the overall configuration of an angiosarcoma is characterized by infiltrating, freely anastomosing vascular channels with frequent mitoses, necrosis, and multiple layers of endothelial cells.^{3,6}

Intravascular angiosarcomas are extremely rare. They represent an intimal or mural form made up of proliferating pleomorphic cells that can occur in large arteries such as the aorta.³ Extreme nuclear atypia may be observed in intravascular PEH, which leads to the diagnostic confusion.¹ The nuclei may be hyperchromatic and pleomorphic,

but they lack the prominent nucleoli and atypical mitoses seen in angiosarcomas.

In our patient, the distinction between PEH and angiosarcoma was arrived at easily because the lesion was not cellular and there was no pleomorphism, mitotic activity, or necrosis in the sections.

When PEH is resected, the prognosis is excellent. Recurrence has been reported in partially resected cases.¹

To the best of our knowledge, this is the first reported case of extravascular PEH localized in the larynx.

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