Received: 2019.09.20
Accepted: 2019.10.16
Published: 2019.11.12

e-ISSN 1941-5923
© Am J Case Rep, 2019; 20: 1664-1668
DOI: 10.12659/AJCR.920181

Intravascular Papillary Endothelial Hyperplasia of the Vocal Cord: A Case Report and Review of the Literature

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Conflict of interest: None declared

Patient: Male, 51
Final Diagnosis: Intravascular papillary endothelial hyperplasia
Symptoms: Changes in his voice
Medication: —
Clinical Procedure: Laryngomicrosurgery
Specialty: Otorhinolaryngology

Objective: Rare disease
Background: Intravascular papillary endothelial hyperplasia (IPEH), is a vascular tumor characterized by the proliferation of endothelial cells with papillary formations. It is a rare benign disease; therefore, it is important to exclude malignant vascular neoplasm in order to prevent misdiagnosis and inappropriate overtreatment.
Case Report: Herein, we describe the case of a 51-year-old male who reported changes in his voice, and who was preoperatively diagnosed with vocal cord polyp and hemorrhagic change based on laryngoscopy. He underwent laryngomicrosurgery and the lesion was completely excised via the microflap surgical method. Histopathology analysis was consistent with IPEH.
Conclusions: Herein, we report an extremely rare case of IPEH arising from the true vocal cord, and we provide a brief review of the relevant literature and a detailed discussion of this rare clinical entity.

MeSH Keywords: Endothelial Cells • Laryngeal Diseases • Vocal Cords

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/920181>

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Background

Intravascular papillary endothelial hyperplasia (IPEH) is a rare benign vascular lesion characterized by reactive proliferation of endothelial cells with papillary formations related to a thrombus [1,2]. It was first described by Pierre Masson in 1923, who referred to it as “vegetant intravascular hemangioendothelioma”; therefore, it is also known as Masson’s tumor [3]. In addition, IPEH has been referred to as Masson’s pseudo-angiosarcoma, endovascularite proliferante thrombopoietique, intravenous atypical vascular proliferation, intravascular angiomatosis, vascular angiomatosis, intravascular endothelial proliferation, reactive papillary endothelial hyperplasia, and intravascular papillary endothelial hyperplasia [4–6]. The condition typically exists within the lumen of dilated vascular spaces or preexisting vascular lesions [2,6–8]. It is more common in women, and can occur at any age [6,8]. The associated clinical manifestations and radiology findings are nonspecific, and diagnosis is based on histopathology analysis [5,9].

IPEH constitutes approximately 2% of vascular tumors, and the most frequently involved sites are the skin and subcutaneous vessels. It has a particular predilection for the hand, extremities, and the head and neck region [2,5,6]. In the head and neck regions, it often affects the skin and subcutaneous tissue, lip, oral mucosa, tongue, gingiva, or buccal mucosa. In very rare cases it can affect the orbit, parotid gland, masseter muscle, nose, sinus, mandible, pharynx, or thyroid [2,10]. To the best of our knowledge, only 1 case of IPEH of the glottis region had been reported in the English literature [11]. Distinguishing IPEH from angiosarcoma and other benign or malignant vascular neoplasms can be challenging [2,5]. Complete surgical excision is the optimal treatment for IPEH. Herein, we report a second case of IPEH presented as a mass of the true vocal cord with associated voice changes, and who was diagnosed after complete surgical excision.

Case Report

A 51-year-old male presented at the clinic reported that he had experienced changes in his voice over the past 6 weeks. He had no history of cough, dysphagia, bleeding, hemoptysis, blood tinged sputum, or dyspnea. He was not a professional voice user. The patient was healthy, and his medical history was unremarkable. The patient reported that he currently consumed alcohol in social situations and used to be a light smoker (0.5 pack/day for 10 years) but had quit 20 years ago and is currently a non-smoker. Laryngoscopic examination revealed a vocal polyp with hemorrhagic change in the mid portion of the left true vocal cord. There were no other abnormal lesions from the oral cavity to the larynx. Symptomatic or enlarged lymph node in the neck was not identified in a physical examination. Laboratory blood test results were unremarkable.

Figure 1. Intraoperative view of laryngomicrosurgery. Under suspension laryngoscopy a vocal polyp or submucosal lesion with hemorrhagic change was noted on the left vocal fold.

Figure 2. Intraoperative view of laryngomicrosurgery. After removal of the lesion the remaining mucosa was carefully repositioned to cover the defect.

The patient underwent laryngomicrosurgery under general anesthesia. Based on suspension laryngoscopy, the lesion on the left true vocal cord was suspected to be a vocal polyp with hemorrhagic change, or a submucosal lesion such as an intracordal cyst with hemorrhagic change (Figure 1). It was excised using the subepithelial microflap resection technique. Upon subepithelial infusion of saline, a change in the overlying epithelium was noted. A mucosal incision was made at the superolateral border of the lesion in order to facilitate medial retraction. The lesion was separated from the normal superficial lamina propria, but it was not easily separated from the overlying mucosa. It was carefully peeled away while maintaining the normal mucosa to the greatest extent possible, notwithstanding hydrodissection using saline. The lesion was completely resected and the overlying mucosal microflap and superficial lamina propria were preserved. The overlying mucosa was then carefully repositioned to cover the defect, and the surgery was completed (Figure 2). The patient received reflux

Figure 3. Histopathology results. (A) Vascular spaces in the stroma (100× magnification). (B) Intravascular papillae with hyalinized stroma depicted via high-power microscopy (400× magnification). (C) Endothelial cells lining the papillae were positive for CD34 (400× magnification).

management and was discharged the day after surgery with strict instructions to rest his voice for approximately 2 weeks.

In the microscopic examination, the surface squamous epithelium was intact and the subepithelial stroma exhibited slit-like vascular spaces (Figure 3A). Under high-power magnification, intravascular papillary projections with hyalinized stroma were evident, and the papillae were lined with a flattened single layer of cells (Figure 3B). In immunohistochemistry analysis the cells were positive for the vascular endothelial cell marker CD34 (Figure 3C). The definitive diagnosis was IPEH. Postoperative laryngoscopic imaging indicated that the mass was completely excised, and the operation site recovered well. After the surgical excision the patient was satisfied with his voice, and he remains completely disease free to date.

Discussion

IPEH can be divided into 3 types, based on the involvement of proliferating endothelial cells around a thrombus in the context of venous stasis [12,13]. One type is a pure (or “primary”) form that arises within the *de novo* lumen of dilated vascular spaces; often a vein, or more rarely an artery. Approximately 56% of IPEHs have been classified as this type [12,13]. The second most common type is a mixed (or “secondary”) form that

develops subsequent to focal changes in preexisting vascular lesions such as hemangioma, pyogenic granuloma or vascular malformation, aneurysm arteriovenous malformation, lymphangioma, or vascular hamartomas. Approximately 40% of IPEHs have been classified as this type [12,13]. The third and rarest type (approximately 4%) is the extravascular form that develops in association with the organization of hematomas, and this type is difficult to differentiate from angiosarcoma [12,13]. The patient in the present case was not a professional voice user and had no history of voice abuse. Therefore, the IPEH was considered to be of the primary form, originating from the true vocal cords.

The pathogenesis of IPEH is unknown, but several mechanisms have been proposed [2,6,13]. One is an intravascular endothelial cell proliferation with papillary formation, which could advance to necrosis and degeneration [5]. Alternative mechanisms include exuberant endothelial proliferation with papillary formation originating from a thrombus; blood stasis and perivascular inflammation; a pseudotumor lesion derived by a cumulative process of thrombotic materials [5,14]. With regard to associations between IPEH and thrombus, it has been proposed that the thrombotic process may have a causative role. Macrophages attracted by the thrombus may promote endothelial cell proliferation via the release of basic fibroblast growth factor, resulting in further secretion of basic fibroblast growth factor, in a vicious cycle resulting in increasing proliferation [6]. There are some indications that trauma might be one of the causes of abnormal organization and proliferation of endothelial cells around a thrombus, although in putative cases such as this, a relevant clinical history has not always been determined [6].

Histopathologic examination is an important component of a definite diagnosis of IPEH. Clinical and radiological characteristics of IPEH are nonspecific and resemble various vascular neoplasms such as angiosarcoma, malignant endovascular papillary angioendothelioma, Kaposi's sarcoma, and hemangioma, and lymphangioma [2,6,9,15]. The very similar histopathological features of IPEH and angiosarcoma make differential diagnosis difficult [6]. Important histopathological findings that could potentially differentiate IPEH from angiosarcoma include 1) endothelial cell proliferation being confined within the vascular lumen, contrary to angiosarcoma which rarely remains within the vascular lumen and tends to invade surrounding tissue and exhibit an infiltrative growth pattern; 2) a lack of necrosis and an absence of cellular pleomorphism, or atypical mitoses; and 3) most of the papillary structures being associated with thrombi [2,6]. While histopathological examination is sufficient for diagnosing IPEH, additional immunohistochemical staining may help to facilitate or confirm differential diagnosis. IPEH typically presents as positive for CD31 and CD34, which are the most sensitive markers indicating the vascular origin of the lesion [2,6,9]. In the present case endothelial cells were positive for CD34.

It is important to exclude malignant vascular neoplasm during differential diagnosis of IPEH in order to prevent misdiagnosis and inappropriate overtreatment, because IPEH is a benign condition [2,6]. The best treatment for IPEH in the head and neck region is complete surgical excision [2,5,8,11,15], but sometimes this is not feasible. Adjuvant radiotherapy or chemotherapy for remaining parts of a lesion after incomplete resection or in cases of multiple intracranial lesions, could contribute to lesion stabilization and short-term regression [11]. Although recurrence of IPEH is rare, it has been reported after incomplete resection [2]. There have been no reports of metastatic cases, suggesting that the condition is strictly benign [2,6,8,15]. The prognosis of IPEH is usually good, but fatal clinical courses have been reported in some patients with intracranial hemorrhages [11].

The present patient was initially diagnosed with a vocal cord polyp with hemorrhagic change based on preoperative laryngoscopy. Postoperatively, it was determined that histopathologic features were consistent with IPEH. Suspension laryngoscopy suggested the possibility of a submucosal lesion with hemorrhagic change, but the lesion was not well separated from the epithelial layer via hydrodissection using saline. The microflap surgical technique was used to completely resect the lesion while preserving the overlying mucosa to the greatest extent possible. While it has been reported that proliferation of endothelial cells around a thrombus caused by trauma may be related to the development of IPEH, a clinical history of trauma has not always been determined in such cases [6]. In the current patient, complete surgical excision of a primary IPEH arising from the true vocal cords was achieved via the above-described methods, and because the excision was evidently complete, a good prognosis is expected.

Conclusions

IPEH is a rare benign vascular lesion, and histopathologic investigations including immunohistochemical staining are required to confirm its diagnosis because radiological characteristics of IPEH are nonspecific and resemble those associated with various vascular neoplasms. The optimal treatment for IPEH in the head and neck region is complete surgical excision, which can result in an excellent prognosis.

Acknowledgements

The authors would like to thank Dr. Joo Yeon Kim (Department of Pathology, Haeundae Paik Hospital, Inje University, College of Medicine, Busan, Republic of Korea) for valuable histopathological discussion.

Conflict of interest

None.

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