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Case Report Open Access

The Unusual Entity of Mixed Squamous and Glandular Papilloma

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Abstract

Mixed squamous and glandular papilloma of the lung is uncommon. Current literature demonstrates that there are less than 20 cases documented worldwide, though likely underreported. We present a case of a 58 y.o. female with history of COPD who was found to have mixed squamous and glandular papilloma, confirmed by histology. This case highlights an unusual etiology of endobronchial lesion that can mimic a malignancy. Clinicians should be aware of this entity because resection can be curative and prognosis is good.

Introduction

Mixed squamous and glandular papillomas (mixed papilloma) are the least identified sub-classification of pulmonary papillomas. Prior reports suggest among 12 to 20 documented cases in the English literature. Incidence is estimated at less than 5 per 100,000 bronchoscopies; however, as lung cancer screening programs are likely to expand, we estimate an increase in it [1]. Etiology is currently unknown. Current medical literature estimates 50% of squamous papillomas are associated with HPV, but not clear correlation exists for mixed papillomas. Additional studies are needed.

Treatment often includes resection, given the concern for malignancy, as these benign growths are found in middle aged, tobacco users.

We report a case of mixed papilloma with histological description and brief literature review.

Case Report

A 58 years old female with 50 pack year history of tobacco (who had quit smoking eight years prior) and known diagnosis of COPD, was referred for worsening shortness of breath. Chest CT demonstrated a small focus of consolidation within the lingula. Pulmonary function tests reflected FEV1/FVC ratio 70 with FEV1 41% predicted, with a normal FVC, with evidence of air trapping demonstrated by RV/TLC ratio of 155%. DLCO was severely decreased at 35% predicted.

A bronchoscopy discovered a flesh colored polypoid lesion in the left upper lobe (Figure 1). Endobronchial biopsies were obtained. Histologic examination revealed changes consistent with a mixed squamous and glandular papilloma (Figures 2a, b, and c). The columnar component was represented by ciliated epithelium. The lesion was devoid of cytologic atypia, viral cytopathic changes, and significant inflammation. Immunohistochemistry was negative for p16.

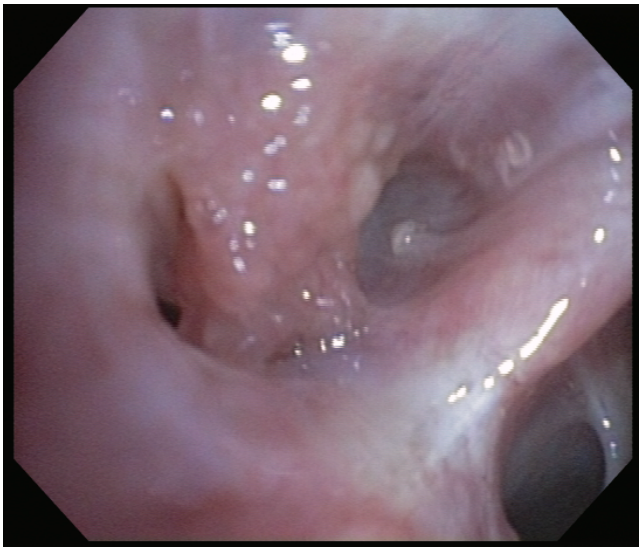

Figure 1: Endobronchial lesion: polypoid lesion at orifice of left upper lobe bronchus.

Due to the severity of COPD and no evidence of obstructive pneumonia, the patient was considered not a candidate for any procedure. After observation for six months the patient is doing well [2].

Discussion

Mixed squamous and glandular papillomas are a sub-classification of pulmonary papillomas, which as a group constitute an unusual benign growth. It is estimated that papillomas account for 0.38% of all lung tumors, although these go underreported, as many biopsies are non-conclusive [3]. We anticipate that as further development of lung cancer screening continues and the implementation of these programs in health systems are applied, more of these cases will be recognized.

Current literature organizes papillomas into squamous cell, glandular, and mixed squamous and glandular [4]. Of these three sub-groups, mixed papillomas are the least frequent, and there is limited knowledge within the medical literature to explain their etiology.

Review of prior case reports suggests that mixed papillomas occur primarily in middle-aged and elder patients. Additional risk factors include male gender and smoking, although large scale epidemiologic studies are lacking.

A review of 41 papilloma cases found 76% to occur in men [5]. Additional studies have investigated HPV as a potential association. In squamous papillomas, HPV DNA is estimated in 50% but in mixed papillomas the association is rare [5].

Mixed papilloma can present with a wide range of pulmonary symptoms. Depending on the size of the lesion, patients may present with cough, post-obstructive pneumonia, or hemoptysis [1-9]. Several case reports document asymptomatic presentation, with incidental discovery.

Anatomically, the majority are endobronchially located with the lower bronchial tree most frequently involved. Uniquely, the current case was found within the upper bronchial tree. Additionally, lung parenchymal involvement has been described. A prior study citing 18 cases contends 15 were endobronchial compared to 3 peripheral [5].

CT findings often show a nodule or mass centrally located though endobronchial involvement can be difficult to confirm without bronchoscopy. Additionally, there are descriptions of increased PET avidity of these lesions. A case report by Kozu et al. found a 1.8cm papilloma with 3.4 SUV on PET scan [6]. Other reviews suggest PET avidity can approach 10 SUV. These findings could increase concern for malignancy illustrating the need for tissue proven diagnosis. A PET scan was not obtained on our patient, therefore direct comparison could not be done.

Histologically, these lesions grow in an exophytic pattern leading to a polypoid growth. Microscopic examination demonstrates glandular and squamous surface epithelium (Figures 2a, b, and c). Ciliated or non-ciliated epithelial cells are often present [1-4]. Centrally, these lesions have a fibrovascular core.

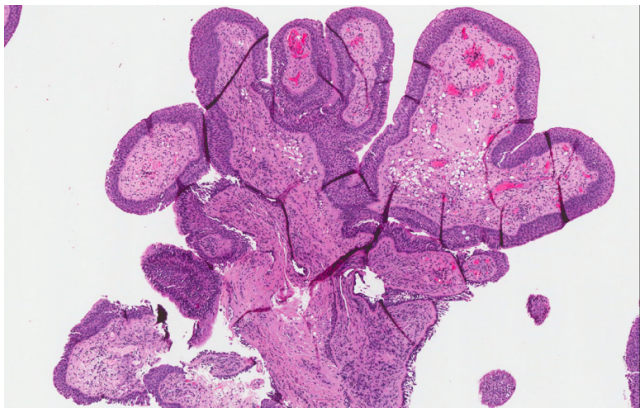

Figure 2a: Low magnification shows a papillary lesion with arborization of fibrovascular cores (hematoxylin and eosin stain, original magnification x 6.2.).

Due to the low number of reported cases there is not a characteristic immunophenotype of mixed papillomas. Separate reports have documented positive immunohistochemistry stainings for CK 5/6, CK19, and CAM 5.2. Two separate studies report positivity for CEA and CA 19-9 with mixed papillomas but the correlation to malignant potential has yet to be demonstrated [3]. We did not perform immunohistological analysis of our case, as it was not required in establishing the diagnosis.

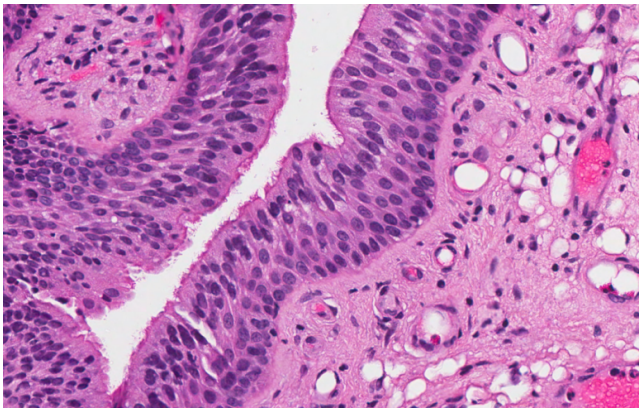

Figure 2b: High magnification of the glandular component reveals ciliated epithelium (hematoxylin and eosin stain, original magnification x 40).

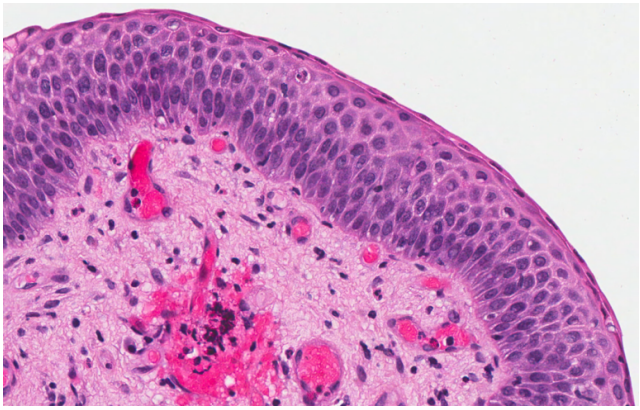

Figure 2c: High magnification of the squamous component shows flattened surface epithelial cells without atypia (hematoxylin and eosin stain, original magnification x 40).

Squamous papillomas can transform to malignancy. The current theory says that HPV positivity could play a role facilitating the transformation, as squamous papillomas are more likely to express HPV. It is unlikely for a mixed papilloma to transform to malignancy, however, we did find a case report by Lagana et al. [9], illustrating a mixed papilloma of the lung transforming to spindle and squamous cell carcinoma. The pathogenesis of transformation is not known, but squamous cell metaplasia may play a role. In this example, the patient was found to have stage 1B and had surgical resection. The case we describe did not have malignant transformation.

Treatment of mixed papillomas includes resection. After diagnosis, there is often concern for malignancy as these occur in high risk patients. However, given that incidence for transformation is not clear, observation is an option. Prognosis of patients undergoing surgery is favorable and at up to five years post-operatively we were unable to find literature of a recurrence [7].

Further studies are needed to advance our understanding of mixed papillomas. Our case report highlights the need for tissue diagnosis, as often, mixed papillomas can be mistaken for malignancy. Additionally we illustrate that in patients unable to undergo resection, close observation may provide more benefit than the risky complications of thoracic surgery.

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