Solitary Papillomas of the Lower Airways

Epidemiological, Clinical, and Therapeutic Data during a 22-Year Period and Review of the Literature

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Introduction: Solitary respiratory papillomas (SRPs) are considered uncommon yet benign neoplasms of the lower respiratory tract. Most of our understanding stems from single case reports or limited case series.

Objective: To determine the incidence of solitary SRPs and more accurately describe the localization, distribution of subtypes of solitary SRPs, clinical features, and the risk of malignant transformation. This retrospective report is based on data collected in a busy single-center bronchoscopy practice during a 22-year period.

Methods: Among 36,780 patients who underwent bronchoscopic procedures between 1986 and 2008, we identified 32 patients with SRPs. This patient group was compared with 69 patients with SRPs described in the English literature as case reports, case series, or diagnostic dilemmas.

Results: Twenty-three patients were men (male/female ratio of 3:1), and 21 patients were former smokers (65.6%). The mean age of initial presentation in men and women was 56.9 ± 14.3 versus 53.3 ± 14.4 years, respectively. The presenting symptoms included cough in 18 patients (40.6%), hemoptysis in 11 (25%), dyspnea in seven (21.8%), and fever in five patients (15.7%). Two patients with papillomas in the subglottic region had wheezing and were on aerosolized bronchodilator therapy. In one patient, the papilloma was incidentally discovered on a chest computed tomography scan. The histologic analysis of lesions revealed squamous papillomas in 65.6%, a glandular subtype in 18.75%, and a mixed subtype in 15.6%. Malignant transformation was observed in five patients (15.7%). The malignancies consisted of squamous cell carcinoma in two patients, and single cases of small cell lung carcinoma, glandular carcinoma, and low-grade carcinoma.

Conclusion: In our experience, the estimated incidence of SRPs is 3.95 cases/100,000 patients/yr. SRPs occur more commonly in men (ratio 3:1). Squamous papillomas occur commonly during the fifth decade of life, glandular papillomas predominate in the sixth decade, and the distribution of mixed type papillomas is from the third to the sixth decade of life. Malignant transformation was observed in a minority of patients.

Key Words: Solitary respiratory papillomas, Benign pulmonary neoplasms, Bronchoscopy, Squamous, Glandular, Mixed.

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The Solitary respiratory papillomas (SRPs) is an uncommon pathologic condition of the lower respiratory tract.[1,2] Although the precise etiology of respiratory papillomas remains unknown, the general consensus is that the majority are due to infection caused by the human papilloma virus (HPV). Multiple papillomas of the upper airways, often referred to as juvenile laryngotracheal papillomatosis, are more common in the pediatric population. In adults, however, solitary SRPs are more common. Papillomas are normally classified into three separate categories: multiple papillomas, inflammatory polyps, and solitary papillomas,[3,4] The SRPs have been classified according to histologic features, namely (1) squamous, (2) glandular, and (3) mixed type. This publication's intent is to report the incidence of solitary SRPs and more precisely describe the localization, distribution of subtypes of SRPs, clinical features, and the risk of malignant transformation.

PATIENTS AND METHODS

During the 22-year period (1986–2008), 32 patients were found to have SRPs after bronchoscopic procedures performed in our institution (Department of General Hospital "G. Papanikolaou" in Thessaloniki, Greece). It is the sole public tertiary care bronchoscopy unit serving a population of 2.5 million people in Northern Greece.

All patients underwent computed tomography (CT) of the chest with evidence of a solitary lesion in the airway or lung. All SPRs were histologically confirmed. Patients with two or more nodules or patients with laryngeal papillomas were excluded from our study.

The clinical information was obtained from an electronic database, routinely collected and updated in our bronchoscopy department.

The literature review was conducted using PubMed with the search terms "benign tumors of the lung," "solitary papillomas," "squamous," and "glandular papillomas." From

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the 219 references, we excluded all cases with multiple papillomas of the lung parenchyma, cases that were described only in abstract form, and cases with papillomas and lung cancer.

To specify more accurately the clinical features, anatomic localization, the distribution of the three subtypes of SRPs, and the danger of malignant transformation into malignancy, we correlated the published cases with our institutional experience. In this study, we describe the pooled analysis of the 101 patients. The differences observed between previously published cases and our own experience are also presented.

RESULTS

Our Results

During the 22-year period (1986-2008), 36,780 patients underwent bronchoscopic procedures at our institution. In only 32 patients (0.00087%) of these we found SRPs. This represents an incidence of 3.95 cases/10^5 patients/yr. Twenty-three of these were men (median age: 61 ± 16 years) and nine women (median age: 44 ± 12.32 years). Among the 32 patients, 21 patients (65.6%) were former smokers. Table 1 presents the demographic and histologic types of the patients in our study and in the published literature. None of the patients were receiving medications for chronic obstructive pulmonary disease or interstitial pulmonary fibrosis.

The symptoms that were observed in our patients included cough in 18 patients (40.6%), hemoptysis in 11 (25%), dyspnea in seven (21.8%), and fever in five patients (15.7%). Two patients with papillomas in the subglottic region, who had wheezing, were initially thought to have asthma and were on aerosolized bronchodilator therapy. In one patient, the papilloma was discovered on a chest CT scan obtained preoperatively.

The estimated reduction of the airway luminal diameter by SRPs was approximately 50% (range: 30–90%). The majority of the papillomas were evident in the trachea and mainstem airways. SRPs were seen in the trachea in nine patients (28.15%)—four of which were localized in the subglottic trachea, two in the midtrachea, and three in the lower trachea. Other sites of SRPs were the bronchus intermedius (eight patients, 25%) and the lingular bronchus (12 patients, 37.5%). In single cases, SRPs were visualized in third order bronchi, where they were barely visible in the bronchial lumen (Figure 1).

A histologic analysis of airway lesions revealed that 21 patients (65.6%) had squamous papillomas, six (18.75%) had glandular type, and five (15.6%) had a mixed type of papillomas. Synchronous malignant transformation was observed in five patients (15.7%)—three of whom had squamous papillomas and two had the mixed type. The malignancies observed consisted of squamous cell carcinoma in two patients and small cell lung carcinoma, glandular carcinoma, and low-grade carcinoma each on one patient (Table 2). Limited data were available about the HPV status in our patients. We had this information only in two patients with squamous cell papillomas.

Lobectomy was performed in 13 of our patients and surgical excision (bronchoplasty or wedge ectomy) in another 17. The decision about the type of surgical therapy was based predominantly on surgeons' ability and knowledge. Only one patient underwent photodynamic therapy. One patient received no treatment. Follow-up data showed no recurrence of papillomas on CT of the chest 12 months after surgery procedure. The patient receiving photodynamic therapy had no recurrence of papilloma after 18 months of follow-up.

Results from Published Data

Comparison of the clinical features of our patients with those of the 69 comparable patients identified from the PubMed data demonstrated no differences in gender distribution, smoking history, or incidence of the different types of papillomas (Table 1). The distribution of papillomas in the airways is shown in Figure 1. Similar to our patient group in the cases from the literature, solitary papillomas usually appeared in the lingular (37.5%), the right bronchus intermedius (28%), at the lower 2/3 parts of the trachea (15.65%), and beneath the vocal cords (12.5%). Subsegmental bronchial involvement occurred in less than 8% of the cases reported in the literature.

TABLE 1. Demographic Results, Smoking Habit, and Histologic Results of Patients in This Study and in the Published Data

	Our Data			Literature			Total		
	Men	Women	All Patients	Men	Women	All Patients	Men	Women	All
Demographics									
N (cases)	23	9	32	52	17	69	75	36	101
Age (yr)	55.65 ± 16	48.3 ± 12.3	53.6 ± 15.3	57.6 ± 12.3	55 ± 15.2	57.3 ± 13.7	57 ± 13.5	52.7 ± 14.7	55.9 ± 13.8
Smoking habit									
Yes	16	5	21 (65.6%)	14	2	16[a]			
No	7	4	11 (34.4%)	6	9	15[a]			
Histologic types of papillomas									
Squamous	14	7	21 (65.6%)	35	9	44 (63.75%)	49	16	65 (64.35%)
Glandular	4	2	6 (18.75%)	9	5	14 (20.3%)	13	7	20 (19.8%)
Mixed	5		5 (15.6%)	8	3	11 (15.95%)	13	3	16 (15.85%)

[a]There are no any estimated percentages because of missing values.