Pathology of Pulmonary Disease, edited by Mario J. Saldana.
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Papillary Tumors of Surface Epithelium

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Papillary tumors of surface epithelium (PTSE) arise within the larynx, trachea, and bronchi. On close examination, they frequently display a distinctive, finely granular texture. Histopathologically, this feature is created by innumerable papillae, which are fingertip projections of neoplastic epithelium covering a fibrovascular core (Fig. 53-1). In benign variants of PTSE, a basement membrane underlying the epithelial proliferation is prominent; it becomes partially effaced or lost in malignant variants when the epithelial proliferation infiltrates the stromal core and tissues beyond.

PTSE usually appear as broad-based (*i.e.*, sessile) lesions, less frequently as lesions with narrow points of attachment to the mucosa, and only exceptionally as lesions with long and narrow pedicles. They can be single or multiple. Characteristically, they distend the airways and produce bronchiectasis with mucus plugging and obstructive pneumonia. They are white-yellow to tan-gray; rusty brown discoloration and hemorrhagic foci are seldom seen. PTSE are firm, frequently friable growths on palpation or while being sectioned with the scalpel. Because of their vascularity, they can bleed when biopsied.

The previous description of PTSE excludes a variety of solid, nonpapillary tumors arising in large airways that, by necessity, grow as intraluminal polypoid masses sometime during their development. In the series of Olmedo and colleagues, these tumors were usually squamous cell carcinomas, adenoid cystic carcinomas, carcinoid tumors, sarcomas, or plasmacytomas.[1] Excluded by the definition of PTSE are papillary growths arising distal to major cartilage-bearing airways as well-circumscribed masses embedded in lung tissue. These papillary growths are rarely benign (*i.e.*, papillary adenoma); most are malignant and represent bronchogenic adenocarcinoma of the papillary type. Variants of bronchioloalveolar carcinoma with a striking papillary structure and composed of Clara cells and type II pneumocytes have already been described (see Chap. 47).

PTSE represent a distinctive gross and microscopic pattern of growth rather than a specific histologic category. Because their epithelial component, whether benign or malignant, can be columnar-glandular, squamous, transitional, or undifferentiated, the legitimacy of placing these tumors in a separate category can be questioned. Nevertheless, PTSEs have been assigned a place of their own in the constellation of lung tumors because of their unique and distinctive gross and microscopic features, because their papillary structure probably reflects an inherently less aggressive behavior than the frankly infiltrative manner of growth of most common types of bronchogenic cancer, and because lesions are frequently recognized early in their course as a result of manifestations of bronchial obstruction, a fact that may contribute to their better prognosis.

A classification of PTSE is presented in Display 53-1. We have included in this classification metastatic papillary tumors (*e.g.*, thyroid, ovary, breast, endometrium) that can mimic their pulmonary counterparts.

BENIGN PAPILLARY TUMORS

Squamous Papillomas

In adults, squamous papillomas are usually single and benign.[2–12] The tumors affect more men than women. In Laubscher's series of six patients, there were five men and one woman.[7] The youngest patient was 54 years of age, and the oldest was 74 years of age. Squamous papillomas usually arise in lobar or segmental bronchi

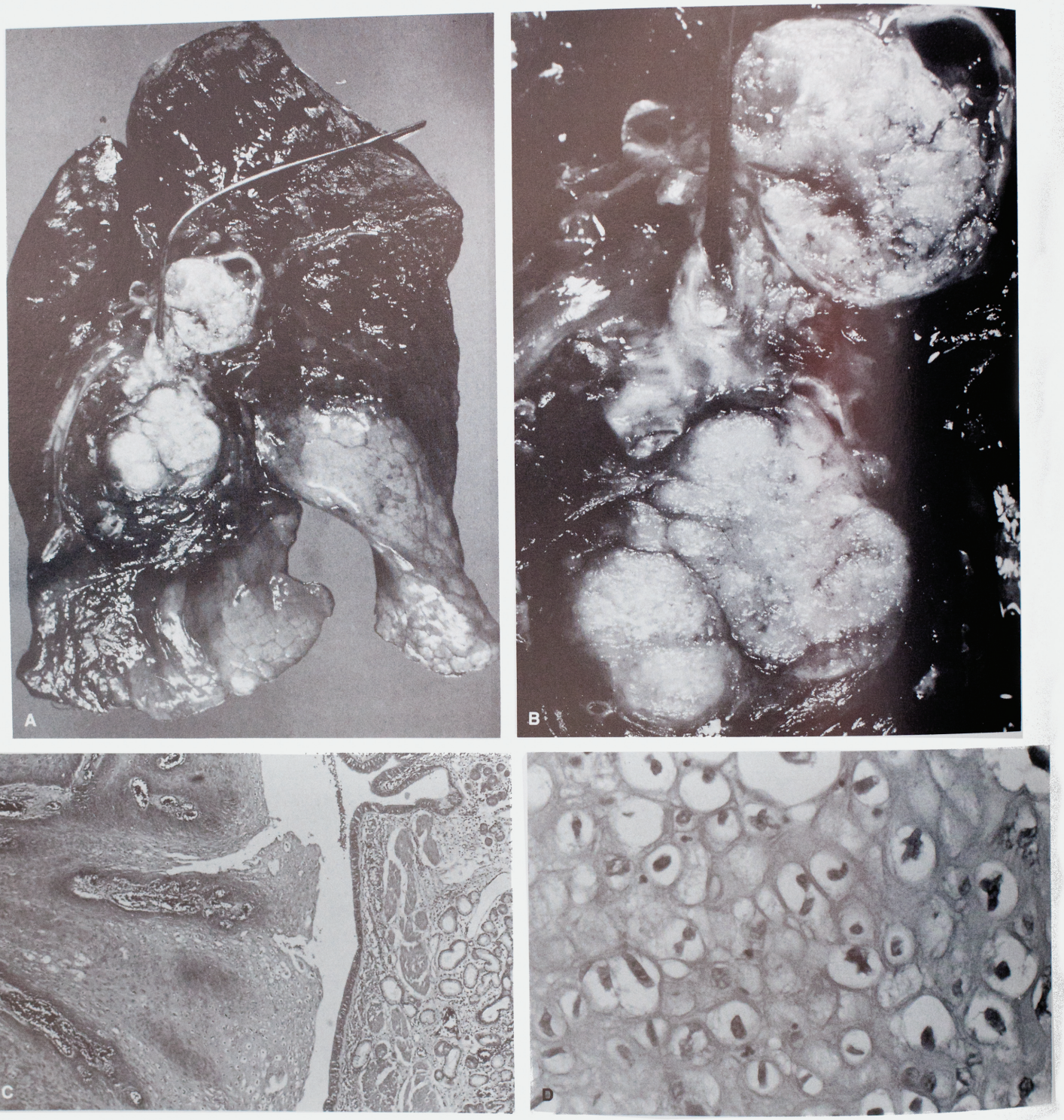

FIGURE 53-1. (**A**) In a left pneumonectomy specimen from a patient with papillary squamous cell carcinoma of the major bronchi, there is marked distention of the bronchi by a tumor that focally invaded through the wall of the left upper lobe bronchus. (**B**) Notice the finely granular, glistening appearance of the tumor surface. Although the bronchial wall is infiltrated by tumor, the hilar lymph nodes are uninvolved. (**C**) A microscopic view of the tumor shows the features of a squamous cell papillary carcinoma within a bronchus. (H & E stain; low magnification.) (**D**) Focally, the tumor exhibits changes of koilocytotic atypia consistent with human papillomavirus infection. (H & E stain; intermediate magnification.) (**E**) A portion of the bronchial wall contains infiltrating squamous cell carcinoma. (H & E stain; low magnification.) (**F**) Detail of the previous picture shows the well-differentiated squamous papillary carcinoma with no production of keratin arising in bronchial epithelium. (H & E stain; low magnification.)

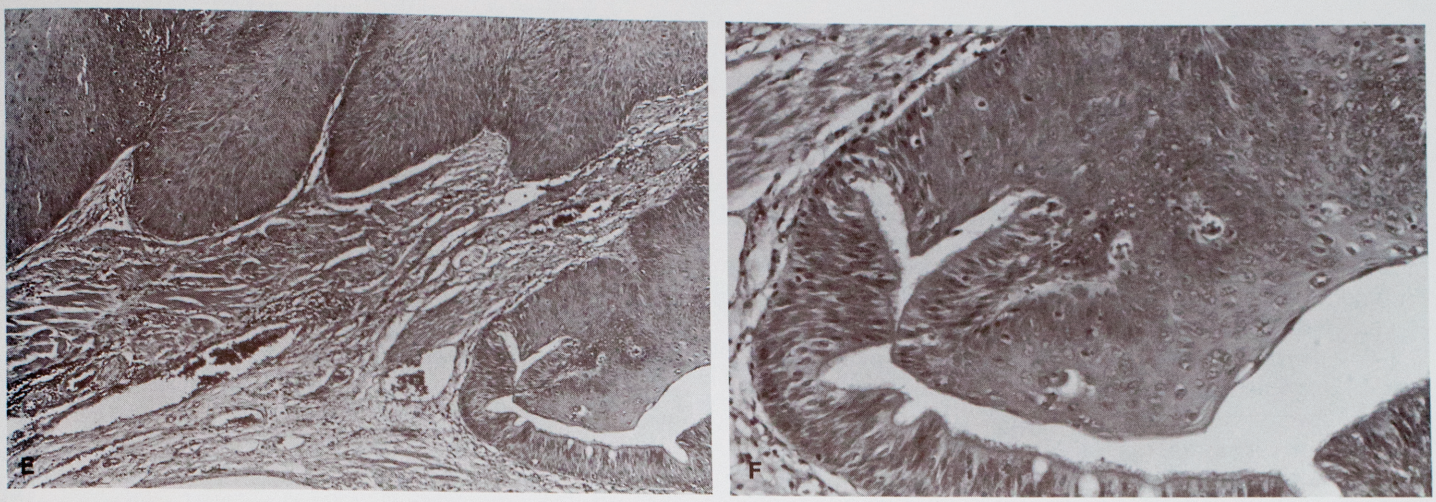

FIGURE 53-1. (*Continued*)

and are visible by bronchoscopy. Because they produce bronchial obstruction, bronchiectasis, endogenous lipid pneumonia, and suppuration are usual findings distal to the papilloma. Clinical manifestations of pneumonia and pleural effusions often call attention to their occurrence.

Histologically, squamous papillomas are characteristically well-differentiated squamous lesions resembling papillomas of the skin and other squamous mucosa (Fig. 53-2). Barzo and colleagues reported the association of solitary squamous papillomas with aspirated foreign bodies in three of eight tumors.[11] In none of these three cases was the foreign body incorporated into the papilloma; they were instead adjacent to the lesions. Two of the three tumors resolved spontaneously, and one was removed endoscopically with no recurrence.

Green and colleagues described the case of a 48-year-old man in whom a computed tomography scan of the chest revealed right middle and lower lobe atelectasis with loculated pleural effusion.[12] The right middle lobe bronchus was narrowed by a white, cauliflowerlike lesion. Histologically, the lesion had features of squamous papilloma. A brown-black foreign body was extracted from inside the papilloma. On gross examination, it consisted of a well-preserved sunflower seed husk. After removal of the papilloma and foreign body, the patient recovered fully.

In the case reported by Berman and associates, an aspirated foreign body was associated with an inflammatory polyp rather than a squamous papilloma.[10] The polyp consisted of chronically inflamed vascular and edematous granulation tissue covered partially by normal, ciliated, respiratory-type epithelium. According to Saini and Wahi, most inflammatory polyps of the bronchial tree associated with foreign bodies resemble nasal polyps.[5]

Atypical histologic changes and carcinoma *in situ* are occasionally observed in some of these lesions.[7,9] Like their counter-

DISPLAY 53-1. PAPILLARY TUMORS OF SURFACE EPITHELIUM

Benign Solitary

Squamous papillomas
Transitional papillomas
Mixed-type papillomas
Mixed-type papillomas associated with underlying bronchial mucous gland cystadenoma

Potentially Malignant

Juvenile laryngotracheal papillomatosis

Malignant

Squamous cell carcinoma arising in juvenile tracheobronchial papillomatosis
Papillary squamous cell carcinoma
Mucoepidermoid carcinoma
Adenocarcinoma
Transitional cell carcinoma
Metastatic papillary carcinoma (*e.g.*, thyroid, ovary, breast, endometrium)

From Saldana MJ. Localized diseases of the bronchi and lung. In: Silverberg SG, ed. Principles and practices of surgical pathology. 2nd ed. New York: Churchill-Livingstone, 1990:735.

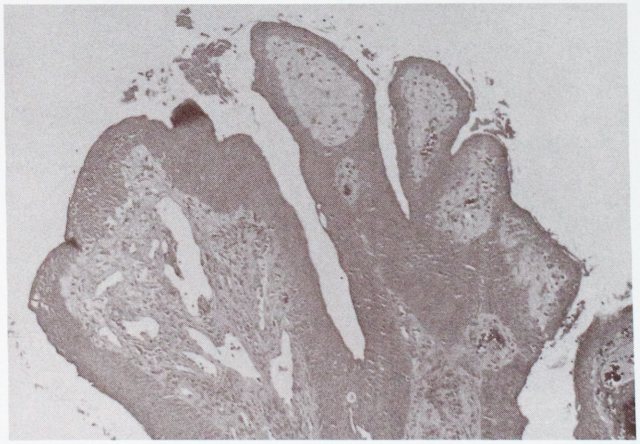

FIGURE 53-2. Fragments of benign squamous papilloma extirpated through a bronchoscope. (H & E stain; panoramic view.)

parts in the intestinal epithelium, some of these squamous papillomas probably undergo malignant transformation.

Transitional Papillomas

Papillomas with transitional cell features resemble their counterparts in the urothelium and nasopharynx.[9,13] Assor described a 69-year-old nonsmoking woman who presented with obstructive pneumonia and abscesses involving much of the left upper lobe parenchyma.[13] The cause was a large, exophytic, gray-white papillary growth arising in the main bronchus to the left upper lobe. Case 14 in Spencer's study was a 70-year-old male heavy smoker who underwent a right upper lobectomy for three small papillary tumors of the main lobar bronchus.[9] All three tumors were covered by transitional epithelium and bore a striking resemblance to grade 1 papillary lesions of urothelium. There was no invasion of the stroma or bronchial wall at their attachments, and the hilar lymph nodes were free of tumor. One year later, the patient developed a pathologic fracture and enlargement of the hilar lymph nodes. The observers speculated that these changes might have resulted from malignant transformation of another bronchial tumor, but no pathologic proof was available. It is probable that some transitional cell papillomas undergo malignant transformation.

Mixed Papillomas

Papillomas can exhibit a combination of histologic features, including columnar, cuboidal, undifferentiated, multilayered, ciliated, and well-differentiated squamous epithelium. The underlying stroma frequently contains granulation tissue with foci of hyalinization. Spencer and colleagues described two papillomas of this type that were associated with an underlying mucous cystadenoma of bronchus, and they referred to a third case in the literature (Color Fig. 53-1; Fig. 53-3).[9,14]

POTENTIALLY MALIGNANT PAPILLARY TUMORS

Juvenile Laryngotracheal Papillomatosis

Juvenile laryngotracheal papillomatosis (JLP) is a disease of younger persons in which papillomas of the larynx extend to involve the trachea or bronchi. The laryngeal papillomas result from viral contamination of the oropharynx of the newborn at the time of passage through the birth canal. The human papillomavirus seems to be the cause of these papillomas.[15,16]

Laryngeal papillomas can spread to the trachea and bronchi, as was described in 2.1% of the patients in four series described by Singer.[17] In a series of 310 patients, Lukens found three (1%) tracheal papillomas.[18] Among 101 cases of laryngeal papillomatoses studied by Majoros and associates, 8 (8%) extended to the trachea and 4 (4%) to the bronchi.[19] According to Al-Saleem and colleagues, the incidence of lower tract papillomas in patients with laryngeal papillomatosis is between 2% and 3%.[20]

The most florid examples of JLP are characterized by innumerable squamous papillomas of various sizes studding the mucosa of the trachea, bronchi, bronchioles, and alveoli.[17–23] The disease can be explosive in nature, and the prognosis is poor. Patients usually present before 5 years of age and sometimes as early as 1 to 2 years of age; in an exceptional case, disease was found in a patient 48 days of age.[22] Characteristically, the multiple recurrences require repeated surgical excisions and tracheostomy in the most severe cases. Majoros and associates found that 56% of the patients with tracheostomy had distal spread, compared with only 10% for those without tracheostomy.[19] This probably means that tracheostomy is required for the more severe cases, not that the tracheostomy is the cause of the distal spread of the papillomas.

Proliferation of the papillomas leads to destructive changes of the bronchial tree with formation of bronchiectatic sacs that can be observed on the chest radiograph. Obstructive pneumonia and suppuration frequently occur, and the patient experiences fever, cough, and weight loss. The papillomas are composed of mature,

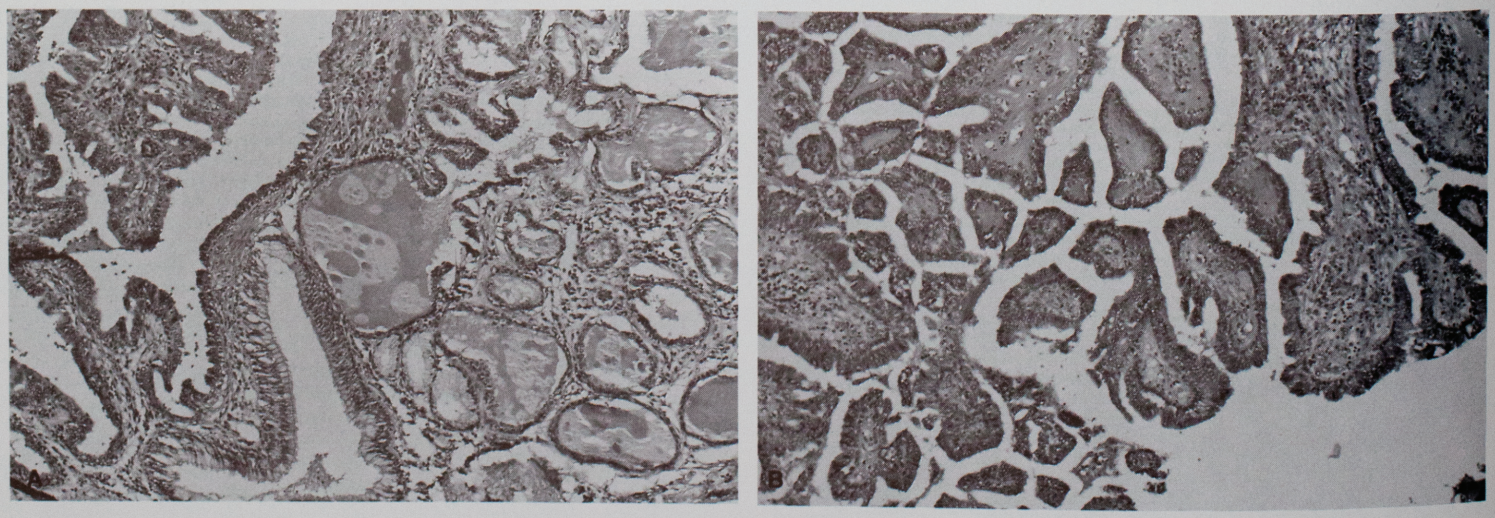

FIGURE 53-3. (**A**) A mixed-type papilloma associated with mucous gland cystadenoma is composed of a papillary component (*left*) and a mucous gland adenoma (*right*). (**B**) The papillary component, (see Color Fig. 53-1) of the same lesion. (H & E stain; low magnifications.)

nonkeratinizing or minimally keratinizing squamous epithelium with chronic inflammation of their fibrovascular stalks. Death may occur as the result of respiratory insufficiency or associated lung infections.[6]

MALIGNANT PAPILLARY TUMORS

Squamous Cell Carcinoma Arising in Juvenile Tracheobronchial Papillomatosis

Squamous cell carcinoma arising in JLP has been well documented (Fig. 53-4), particularly after irradiation.[24–28] Ogilvie was able to demonstrate lymphangitic spread to lymph nodes.[24] In the case of a 10-year-old boy described by Runckel and Kessler, a 10-cm left lower lobe squamous cell carcinoma invaded the diaphragm and spleen and displaced the left kidney downward.[26] At necropsy, multiple sessile papillomas extended from the tracheostomy stoma down to and included both main stem bronchi. Saccular bronchiectases occurred throughout the lung, and multiple small nodules of squamous cell carcinoma were found in all pulmonary lobes. In another remarkable case described by Moore and Lattes, it took 34 years for JLP to transform to squamous cell carcinoma.[25]

Papillary Squamous Cell Carcinoma

Series of squamous cell carcinomas with papillary features have been described in several studies.[29–31] In the study by Smith and Dexter, there were eight examples of papillary squamous cell carcinoma with a warty or mulberrylike appearance projecting into the lumens of major bronchi.[29] Seven tumors were localized lesions with no invasion of the bronchial wall; the eighth case grew endobronchially but did not invade the lung parenchyma. Sherwin and colleagues described eight cases of squamous cell carcinoma of bronchus with a warty polypoid appearance within major bronchi; a ninth case was interpreted histologically as undifferentiated carcinoma.[30] Six of the nine patients had adequate follow-up periods for assessment: two patients were alive and well 8 years

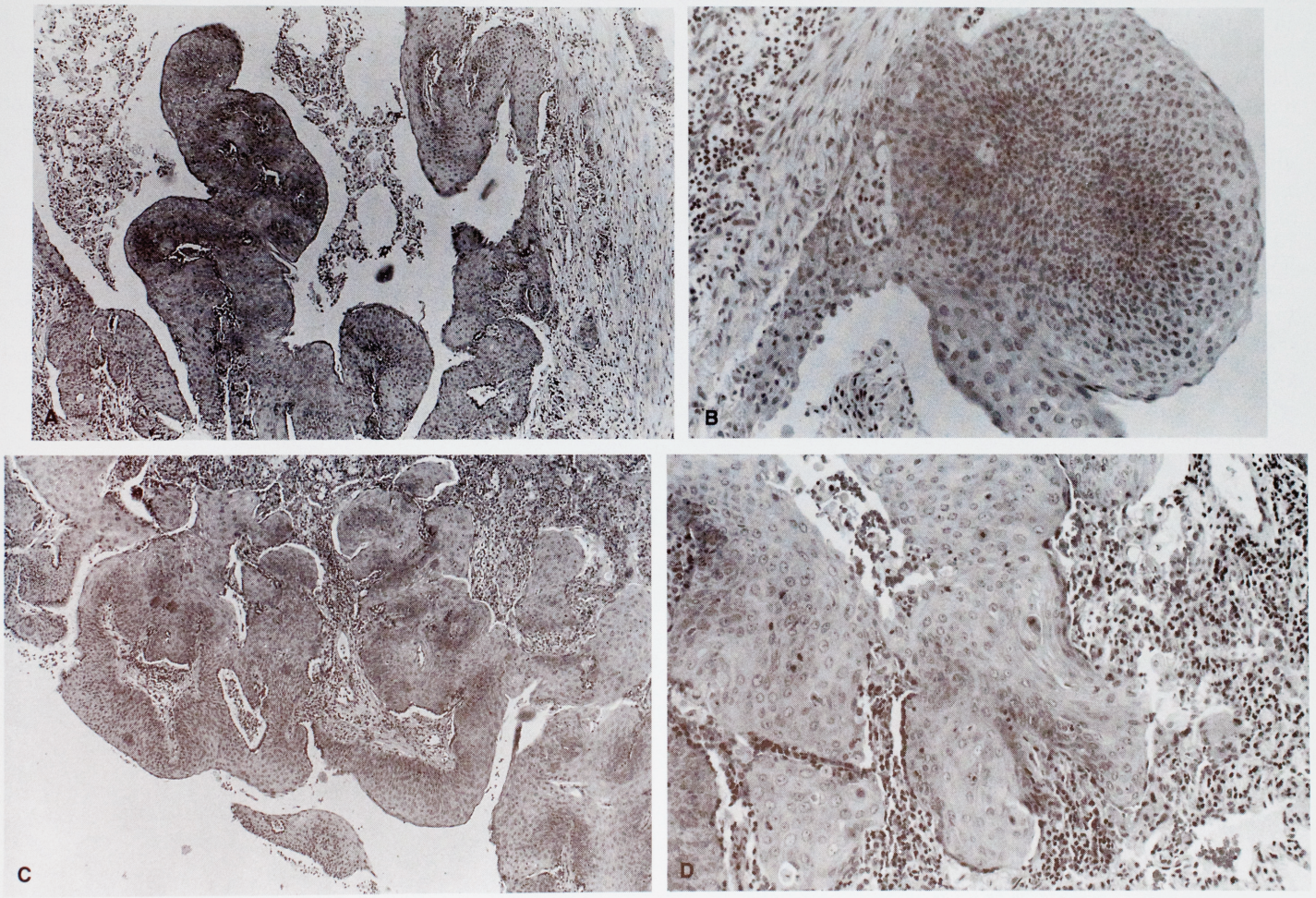

FIGURE 53-4. This juvenile tracheobronchial papillomatosis evolving into invasive squamous cell carcinoma was discovered in a 31-year-old man who had a history of laryngeal papillomatosis since childhood. (**A**) Atypical squamous papillomas were found within the large airways. (H & E stain; panoramic view.) (**B**) Squamous papilloma with atypia was also found in a peripheral airway. (H & E stain; low magnification.) (**C**) *In situ* and infiltrating squamous cell carcinoma were seen within the wall of an airway. (H & E stain; low magnification.) (**D**) Well-differentiated squamous cell carcinoma infiltrated the alveolar tissue. (H & E stain; intermediate magnification.)

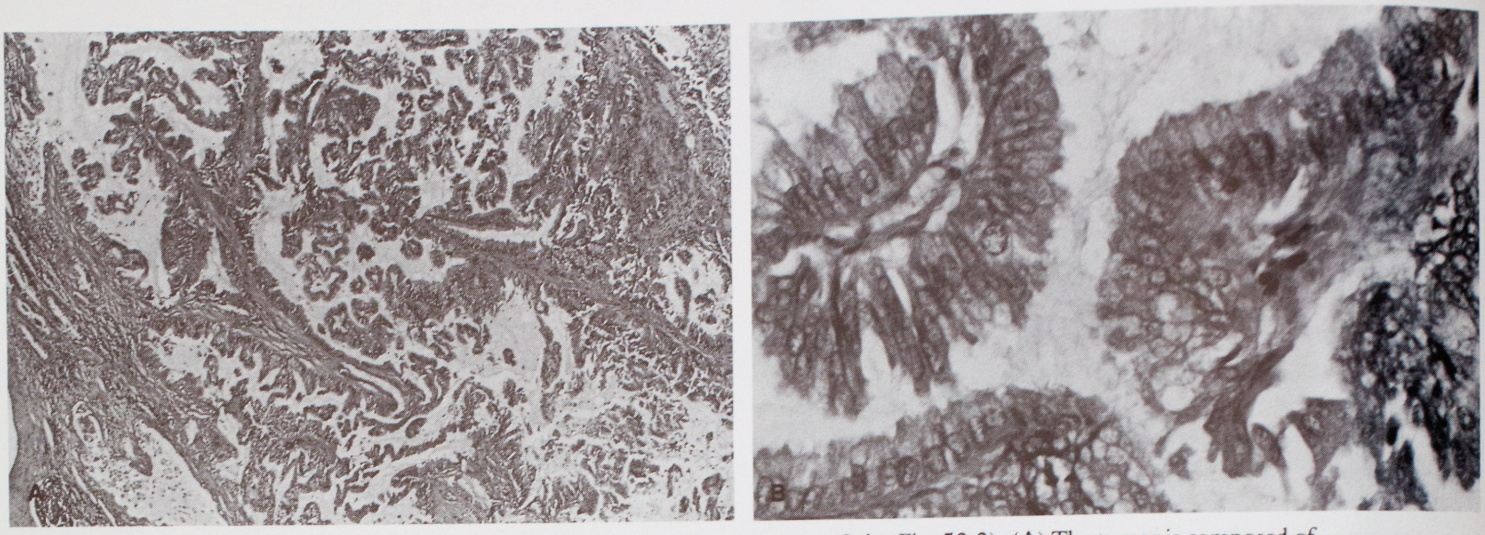

FIGURE 53-5. Papillary adenocarcinoma of the bronchus (see Color Fig. 53-2). (**A**) The tumor is composed of numerous papillary growths with characteristic fibrovascular stalks. (H & E stain; low magnification.) (**B**) The papillae are composed largely of columnar glandular epithelium with focal areas of transitional and squamous cells. (H & E stain; intermediate magnification.)

after resection; one other patient died 11 years after surgery from an unrelated disease; one died 8 years after resection from cancer arising in the opposite lung, which was probably unrelated; and the sixth patient died 20 months after resection from recurrent tumor at the bronchial stump.

A remarkable series of 34 cases of exophytic endobronchial squamous cell carcinoma was reported by Dulmet-Brender and associates.[31] There was a predominance of male patients, and the mean age at presentation was 58 years. Most tumors were stage T1N0, but these lesions represented a special variant of bronchogenic carcinoma rather than tumors detected at an early stage.

Mucoepidermoid Carcinoma

Mucoepidermoid carcinomas can arise in the surface epithelium of bronchi and grow in a papillary fashion. All five such cases described by Sniffen and colleagues were low-grade malignant tumors, comparable to their bronchial gland counterparts.[32] The tumors appeared as endobronchial, soft, friable masses attached to the bronchial wall at discrete points. Histologically, they had a characteristic combination of squamous and mucin-producing cells. In keeping with the bland gross and microscopic features of their lesions, the outcome for all five patients was favorable after surgery.

Other Malignant Tumors

Adenocarcinoma and transitional cell carcinomas with papillary features can grow in bronchi (Color Fig. 53-2; Fig. 53-5). Kodama and associates described five unusual adenocarcinomas of the lung with a predominantly endobronchial growth.[33] All five were papillary adenocarcinomas. Features of bronchial cell differentiation, including mucin production, and bronchiolar differentiation were observed. Metastatic papillary thyroid cancers rarely

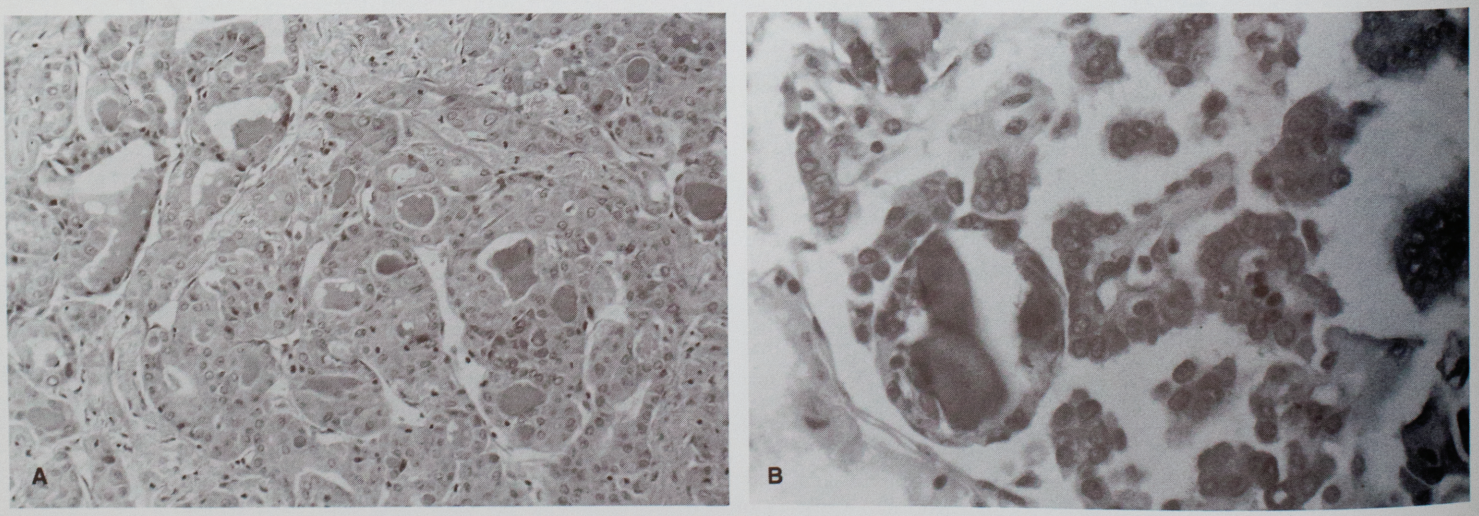

FIGURE 53-6. Innumerable papillary deposits studded the tracheobronchial mucosa and alveolar tissue in this 75-year-old man who had a papillary carcinoma of the thyroid resected 40 years earlier. The metastases were strongly positive for thyroglobulin by the immunoperoxidase technique. (**A**) Notice the presence of a follicular pattern with colloid material. (H & E stain; low magnification.) (**B**) Another field with distinct papillary features includes a psammoma body. (H & E stain; high magnification.)

infiltrate the trachea and bronchi or simulate a papillary tumor of the airways (Fig. 53-6).[9]

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