A Note from History:
The Road to Discovery of an Uncommon Tracheobronchial Tumor

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Keywords: history of pathology, history of medicine, history of cancer, mucoepidermoid tumors

It took nearly 50 years to comprehend the histogenesis and the nature of mucoepidermoid tumors. This story began in 1945 with the publication of a 24-page article, containing 18 photomicrographs and 2 tables, on “mucoepidermoid” tumors of the salivary glands [1]. The principal writers were pathologists, Fred W. Stewart (1894-1991) and Frank W. Foote (1911-1989), of the Memorial Hospital for Cancer and Allied Diseases in New York City (Fig. 1). Among the 700 major and minor salivary gland tumors they had diagnosed during a period of 18 years, there were 45 tumors with a distinct combination of epidermoid (non-squamous pearl-forming) and glandular (mucinous) differentiation. Consequently, they coined the descriptive term “mucoepidermoid.”

Stewart and Foote traced the origin of the mucoepidermoid tumors to the salivary ducts. They separated the 45 tumors into 2 groups, benign (26 cases) and malignant (19 cases). The benign tumors were predominantly composed of well-differentiated mucous glands and minute foci of epidermoid and intermediate (basal or basaloid) cells. The malignant tumors were dominated by epidermoid and intermediate cells, with occasional nests of
mucinous glands, goblet cells, and hydropic clear cells. Although a few of the benign tumors were locally aggressive and recurred after surgical excision, no patient died with metastasis. On the other hand, the malignant tumors were highly lethal. Only one patient was alive and free of tumor for more than 5 years. The tumors showed no sex predilection; patients with benign tumors averaged 10 years younger than those with malignant tumors. Four of the patients were children and their tumors were all benign.

Seven years after Stewart and Foote’s 1945 report, a histologically similar tumor was described in the lung under the label of bronchogenic adenoma [2], and the same term was employed in the first AFIP Fascicle on lung tumors [3]. Having seen that mucoepidermoid tumors were being renamed by others as adenomas, Foote decided to set the records straight. In 1953 and 1954, Foote and Frazell [4, 5] advanced their belief that mucoepidermoid tumors are all carcinomas and they should be separated into 2 groups—low grade and high grade—based on their histopathologic appearance. They justified this view by reporting that nearly all patients with histologically high grade lesions died and nearly all patients with low grade tumors were alive. In 1955, at the Annual Tumor Seminar in Texas, Foote reconfirmed and established once and for all the existence of 2 distinctly separate categories of mucoepidermoid carcinomas—low grade and high grade—in salivary glands [6]. Foote added that mucoepidermoid carcinomas are the most common malignant tumors of the salivary gland.

In 1961, a former trainee of Stewart and Foote, William Christopherson, and his associates, adopted Foote’s classification and reported 1 low grade and 3 high grade mucoepidermoid carcinomas of the bronchus [7]. They emphasized that the tumors were centrally located in the main bronchi, and arose from the submucosal minor salivary glands. At this point, it was clear that mucoepidermoid carcinomas occurred in the salivary glands and the lung, but how about mucoepidermoid carcinomas in the trachea? In 1970, Foote and others reported 4 cases of mucoepidermoid carcinomas among 41 cases of primary tracheal carcinomas [8]. They emphasized that the 4 mucoepidermoid tumors were all high grade, could be traced to submucosal minor salivary glands, and as a whole represented 10% of tracheal carcinomas. In 1971, 12 cases of mucoepidermoid carcinoma of the lung were reported by Turnbull in collaboration with Foote and others [9]. This paper documented the extremely uncommon occurrence of these tumors in the lung. Less than 0.1% of lung tumors studied were mucoepidermoid carcinomas. In contrast, of 492 tumors of minor salivary gland origin, 15% were mucoepidermoid carcinomas [10]. In 1976, 2 mucoepidermoid carcinomas (1 low grade and 1 high grade) of the larynx were reported by us among 18 patients with minor salivary gland carcinomas of the larynx [11].

In 1979, Joseph Eggleston—another of Foote’s trainees—and his associates reported the first electron microscopic study of mucoepidermoid carcinomas [12]. They showed that bronchial mucoepidermoid carcinomas are ultrastructurally identical with those in salivary glands [12]. A large series of mucoepidermoid carcinomas of the lung, 58 cases, from the Armed Forces Institute of Pathology, was reported in 1987 [13]. The authors listed the various entities that one should consider in the differential diagnosis of mucoepidermoid carcinomas, eg, adenosquamous carcinoma. They pointed out that combined experience with mucoepidermoid carcinomas showed that most of the patients were non-smokers. This observation was supported by a report of 25 cases of tracheobronchial mucoepidermoid carcinomas in children [14]. The youngest of these patients was 3 months old. With the conclusion that smoking and other known toxic agents were unlikely to be risk factors for mucoepidermoid tumors [15], search for the causative agent extended to human papilloma virus (HPV). It is interesting that while 4 of 6 adenosquamous carcinomas of the lung tested positive for HPV, HPV DNA was not detected in a single case of mucoepidermoid carcinoma [16]. Confirmation of the distinct nature of mucoepidermoid carcinomas, regardless of their anatomic sites, came from cytogenetic studies reported during the past decade [17-19]. The karyotypic changes, translocations 11;19, that have been found in salivary gland and bronchial mucoepidermoid carcinomas should eliminate any doubt about the unique character of these tumors.
The circuitous saga of mucoepidermoid tumors began in 1945 in New York City [1]. It took 50 years to establish their unparalleled nature. Let us hope that it will not take another 50 years to find the cause of and cure for these often elusive malignant neoplasms.

References