KAWASAKI MED. J. VOL. 14 : NO. 1, 23-31 (1988)

Epithelial Mucinosis in Exophytic Endobronchial Squamous Cell Carcinoma

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Accepted for publication on February 3, 1988

ABSTRACT. Three cases of exophytic squamous cell carcinoma of the lung in which an unusual epithelial change with intercellular mucin deposit; namely epithelial mucinosis, was present in variable degree are reported here. As either exophytic variant of lung carcinomas or its mucinotic change is rare, the general concept of this lung carcinomas is summarized and the significance of epithelial mucinosis is discussed.

Key words : lung — endobronchial tumor — exophytic tumor — squamous cell carcinoma — epithelial mucinosis

An exophytic variant of squamous cell carcinoma of the bronchus has been rarely reported in the literature.[1—10] Exophytic tumor is a polypoid or papillary tumor which protrudes toward and sometimes occludes the bronchial lumen. Generally, it is confined to the bronchial wall without deep penetration of the pulmonary parenchyma.

The present communication describes three cases of exophytic squamous cell carcinoma in which an unusual change of epithelial mucinosis was present in variable degree. The general concept of this variant of lung carcinomas is reviewed and the significance of its mucinotic change is discussed.

CASE REPORTS

CASE 1. A 50-year-old man had been in good health until about a year ago, when he experienced hemoptysis of a week's duration. Since one month prior to admission, hemoptysis developed every morning. He was admitted to the Kurashiki Daiichi Hospital, where a bronchoscopy, done on January 22, 1986, disclosed a polypoid tumor in the left B 10 of the bronchial tree. Although bronchial brushing was suggestive of adenocarcinoma, punch biopsy was reported to be a squamous cell carcinoma. Survey for the metastasis was negative and left lower lobectomy was performed on January 27, 1986. Postoperative course was unremarkable and he is free of recurrence.

Pathology : The specimen received was a left lower lobe of the lung. Resection margin of the left lower bronchus was free of tumor. B 10 was completely occluded by a polypoid brown tan tumor (Fig. 1) which protruded toward main bronchus to slight degree. On cut sections, the tumor was confined within the boundary of the bronchus and measured 1.5×1.0 cm in greatest dimension. Its cut surface was grey white and gave some mucinous appearance.

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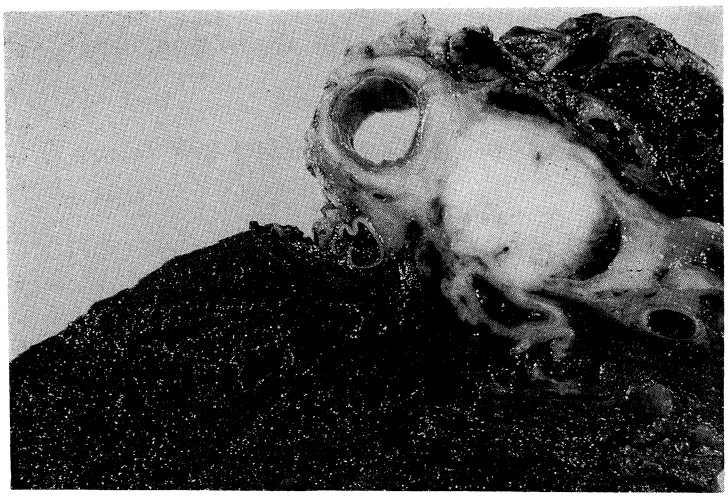

Fig. 1. Gross photograph showing a cut surface of the tumor in the B 10 (case 1).

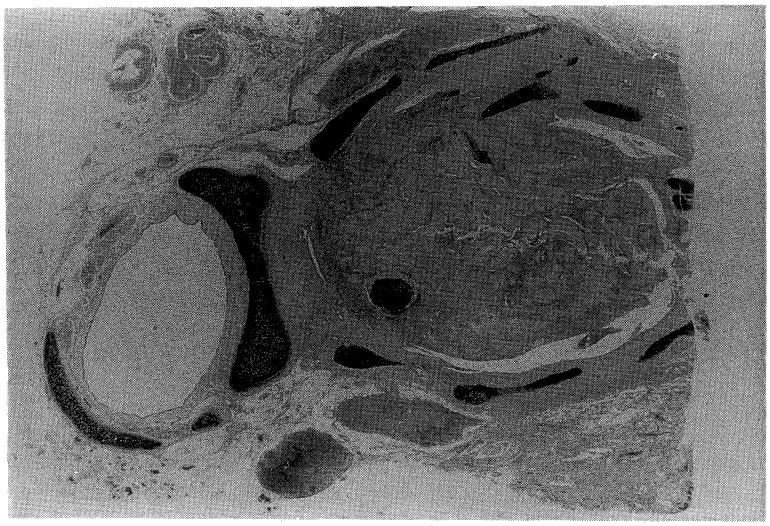

Fig. 2. Scanning photomicrograph of the exophytic tumor. (H-E, ×2.5)

The rest of the lung showed atelectasis. Histologically, the tumor grew in papillary fashion, formed large cell nests, and protruded to almost completely occlude the bronchial lumen (Fig. 2). The midportion of the tumor surface was hemorrhagic and its periphery was covered by remaining ciliated columnar epithelium. It tended to infiltrate into the lamina propria, but did not extend beyond the boundary of cartilages. The tumor was a squamous cell carcinoma showing large cell nest, stratification (Fig. 3), prominent intercellular bridge formation (Fig. 4), and occasional and scattered keratinization. Intercellular spaces were markedly widened with basophilic mucinous material and the cellular cohesion was preserved at the sites of intercellular bridge so that it gave an appearance of reticular network (Fig. 5). Mucinous cysts were also present in

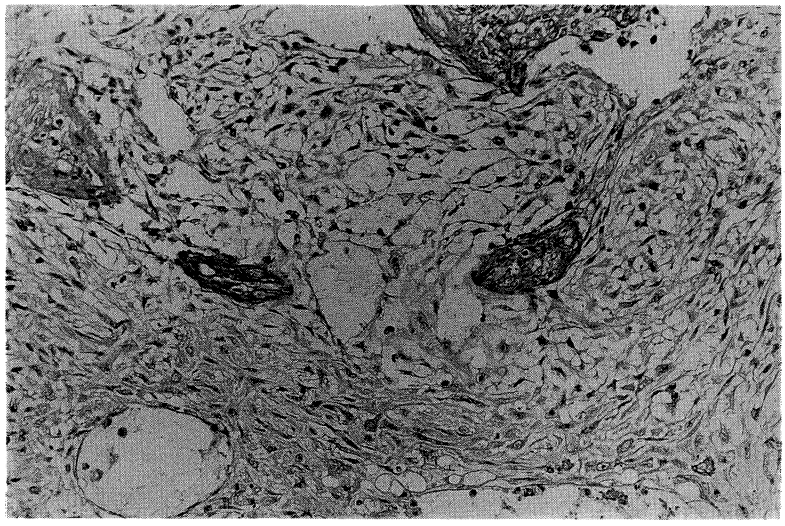

Fig. 3. Reticular network formed by neoplastic squamous cells within the mucinous substance. (H-E, ×200)

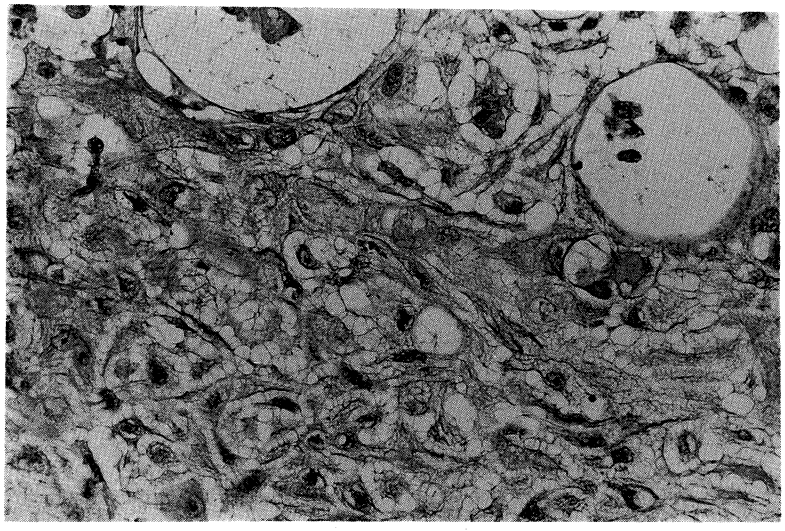

Fig. 4. Tumor cells show characteristic features of squamous cells, but intracellular vacuolization is also discernible. (H-E, ×500)

places (Figs. 3-5). Intracellular fine vacuolization was occasionally discerned (Fig. 5). A few lymphocytes and neutrophils were scattered among the tumor cell nests, and the interstitium was infiltrated by a number of lymphocytes, plasma cells and a few neutrophils. This mucinous substance was PAS-negative, alcian blue-positive and hyaluronidase digestible. Lymph nodes were free of metastasis.

CASE 2. A 57-year-old man with a history of asthmatic attacks at winter time for the past 6 years came to the Kawasaki Medical School Hospital for shortness of breath of 3 months' duration. Bronchoscopy, performed on August

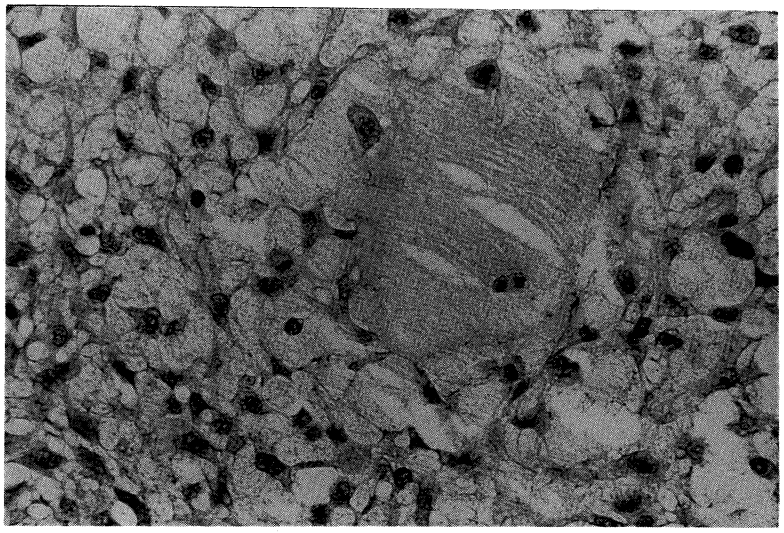

Fig. 5. Intercellular spaces are filled with mucinous substance which has been revealed to be hyaluronic acid by histcchemical study. (H-E, ×500)

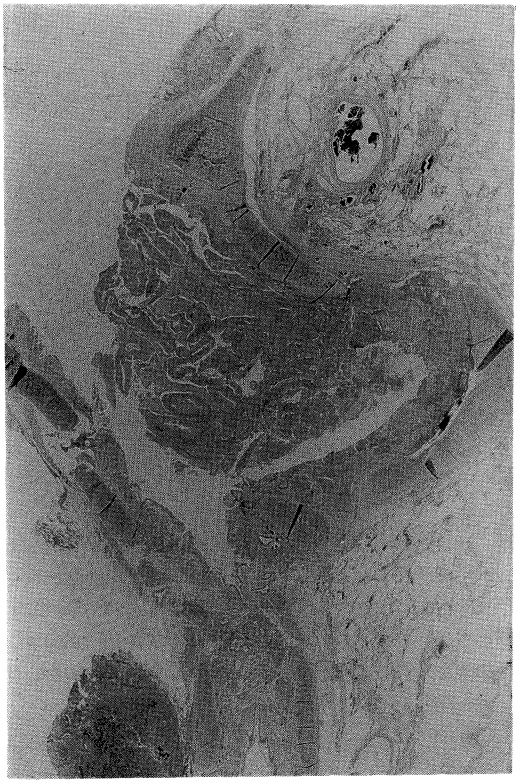

Fig. 6. Scanning view of an exophytic papillary tumor in case 2. (H-E, ×2.5)

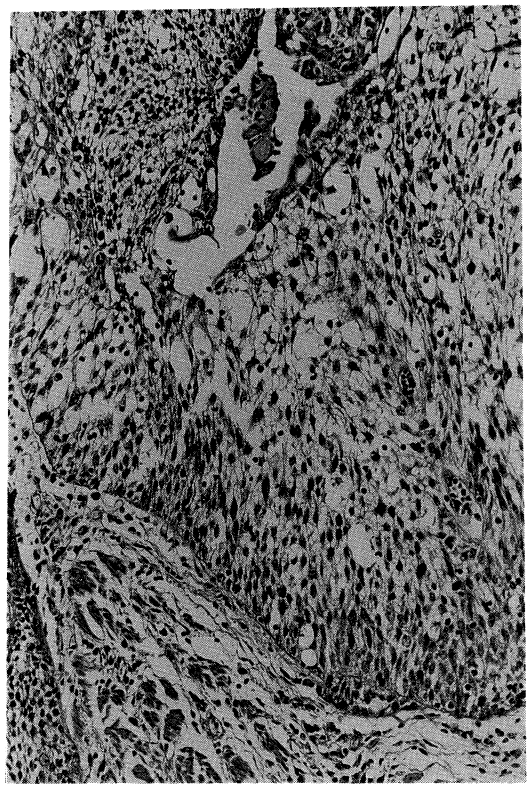

Fig. 7. Intercellular spaces are widened with occasional lymphocytes.

10, 1984, disclosed squamous cell carcinoma of the left upper bronchus and obstructive pneumonia peripheral to this tumor. Left upper lobectomy was done on September 4, 1984. The postoperative course was uneventful.

Pathology : The specimen was the left upper lobe which had been resected at 11 mm above the bifurcation. At the orifice of B 1 + 2 one cm diameter polypoid and califlower-like tumor had almost completely occluded the lumen. Histologically, the tumor was a moderately differentiated papillary squamous cell carcinoma with keratinization and intercellular bridge formation (Fig. 6). In places, there was a stromal infiltration extending down to the level of the cartilage. Adjacent non-polypoid portion of the mucosa was also covered by tumor cells, representing so-called "carcinoma in situ". Latter portion and small areas of polypoid portion of the tumor showed widening of intercellular spaces with mucinous material (Fig. 7). A few lymphocytes were rather frequently seen not only in those spaces but also in the lamina propria below the tumor. Mucinous material was PAS-negative, alcian blue-positive, and hyaluronidase sensitive.

CASE 3. This is the case that one of the authors experienced at the Hospital of Albert Einstein College of Medicine, New York. The patient was a 54-year-old Caucasian man who was undergone a right lower lobectomy. A detailed clinical history is not available. Resected was a left lower lobe of the lung.

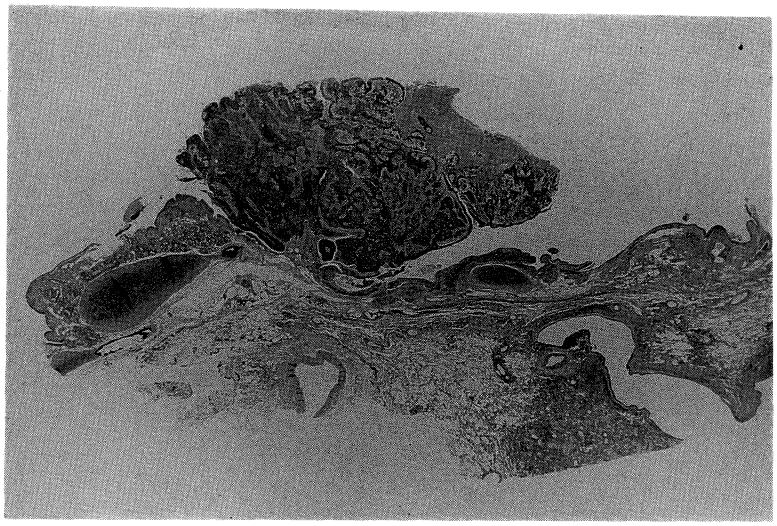

Fig. 8. Scanning view of the exophytic tumor in case 3. (H-E, ×2.5)

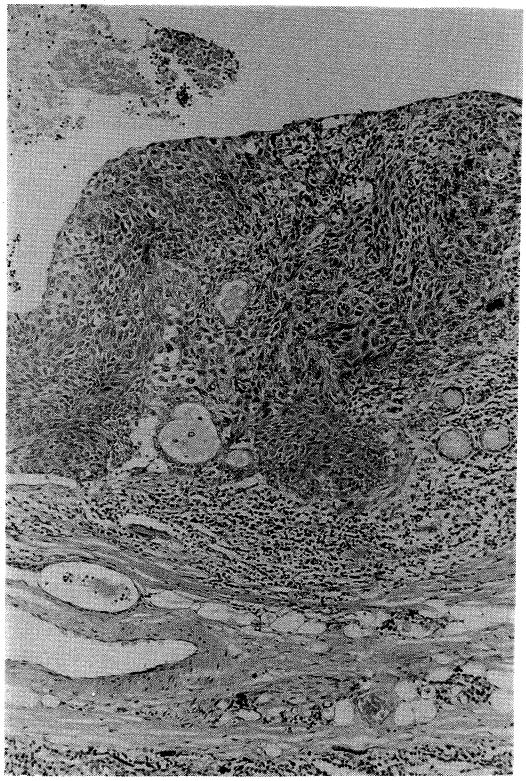

Fig. 9. Epithelial mucinosis in this case is focal and minimal, and is accompanied by a few lymphocytes. (H-E, ×100)

The main lower lobe bronchus was occluded by a tumor measuring 1 cm in the longest dimension. It was an exophytic tumor with questionable stromal invasion (Fig. 8). In situ carcinoma was seen in the adjacent mucosa. There was no apparent invasion anywhere in the polypoid portion of the tumor. Histologically it was a moderately differentiated squamous cell carcinoma with occasional keratinization. Cell atypism with some pleomorphism was present. Generally, tumor cells showed tight cohesion, but focally intercellular spaces were widened (Fig. 9). There, slight lymphocytic infiltration was accompanied. Rest of the lung showed areas of marked obstructive and organizing pneumonia.

DISCUSSION

Exophytic endobronchial squamous cell carcinoma has been reported to be rare,[1–10] but its real frequency is not well established. Dulmet-Brender *et al.*[10] commented that they encountered about one case per year. The mean ages so far reported are 60.1,[1] 59.9,[2] 57.8,[10] and 56.9[3] years, respectively. There is no known occupational cause of this tumor. Smoking habits have rarely been implicated as a cause in the past reports. As seen in our patients, the presenting symptoms are either persistent cough, recurrent hemoptysis or less frequently relapsing pulmonary infection. Usually, the tumor is not seen on routine chest x-ray, and bronchoscopy appears to be the key examination. Histologically, the tumor is a squamous cell (epidermoid) carcinoma; sometimes with a resemblance to a transitional cell tumor.[9] Even though transitional cell appearance may be seen, a term of transitional cell carcinoma should not be used because this is, in fact, composed of squamous cells with the presence of tonofilaments in abundance and desmosomes but without any tight junctions. All the patients studied so far received surgical treatment and were of T1N0 type except for one patient who had T1N1 disease. The general prognosis for this type of carcinomas is said to be better than that of all surgically removed lung carcinomas. However, it seems to be no better than that reported for the early detected stage I carcinoma. Exophytic endobronchial squamous cell carcinomas may be in situ or mucosal carcinomas. According to Dulmet-Brender *et al.*,[10] it does not indicate the initial stage of an infiltrating carcinoma, but probably constitutes a special form of bronchogenic carcinomas.

Mucinosis is defined as the deposit of mucin in epithelial or connective tissue. This change is sometimes seen in a variety of skin lesions,[11] and may be divided into three forms according to its location; namely epidermal mucinosis, follicular mucinosis and dermal mucinosis. Although first two types are inclusively designated as epithelial mucinosis, the epithelial mucinosis per se is not limited to the lesions in the skin. In the skin, epidermal mucinosis can be seen in conditions such as basal cell carcinomas, keratoacanthomas, squamous cell carcinomas, verruca vulgaris and spongiotic dermatitides.[11] However, squamous cell carcinomas of the aerodigestive tract, for example, may show similar mucinotic changes. Review of literature on exophytic endobronchial squamous cell carcinoma[1–10] failed to reveal such mucinotic changes in the tumor. To our knowledge, in addition, there are no previous reports describing mucinosis in any other types of lung carcinomas. In our cases, the histochemical study showed hyaluronic acid to be the major component of the mucin deposit. This

mucin composition is quite similar to that present in alopecia mucinosa of the scalp.[12] It should be noted, however, that mucin produced in the epithelial mucinosis is not that type of so-called epithelial mucin which is produced by the glandular epithelium and is secreted into the glandular lumen, but of non-epithelial mucin which is usually present in the stroma.[13] Evidence[14] suggests that so-called non-epithelial (stromal) mucin can be produced by epithelial cells. Reed[15] has speculated that T-lymphocytes may stimulate follicular keratinocytes to produce stromal mucin in lesions such as follicular mucinosis. In fact, inflammatory cell infiltrates composed predominantly of lymphocytes were present within the affected epithelium of follicular structures. In our lung carcinoma cases, epithelial mucinosis was also associated with lymphocytic infiltration. This may indicate that similar mechanism might have been operative. Consequently, we speculate (1) that inflammatory cells are a requisite for the development of epithelial mucinosis even in the tissue other than skin; (2) that stratified squamous epithelia and squamous carcinoma cells in the sites other than skin may be the source of mucin, the major component of which is hyaluronic acid, and (3) that squamous cell carcinoma of the lung may be accompanied by reactive lymphoid cell infiltrates in some cases and finally (4) that infiltrating lymphocytes may stimulate mucin production of neoplastic squamous cells. The presence of intracellular vacuolization in one of our cases further indicates that neoplastic squamous cells may in fact produce and secrete hyaluronic acid. On the other hand, this intracellular vacuolization may give a false impression of adenocarcinoma when exfoliated carcinoma cells are examined in routine cytological specimens like in our first case. Lastly, it remains to be elucidated whether infiltrating lymphocytes represent a response to the tumor itself or not, and whether either the presence of lymphocytes among the tumor cells or epithelial mucinosis is related to the patient's prognosis.

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