Studies on the Surgery of Bronchiectasis

II. Histologic Study of Changes in the Mucous Membrane of Bronchus

By

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The literature on histologic study of bronchiectasis is abundant, and especially as to chronic inflammation of bronchi, full information is available. In the course of histopathologic studies on this disease, examining serial sections prepared from resected specimens, we found changes indicative of precancerous degeneration in 4 of the 10 cases examined and could obtain several pictures showing varying extents of malignancy, as will be reported in the following.

The age and lesions of patients from whom serial sections were prepared are shown in Table I. The following findings were common to all of the 10 cases studied; 1) an uniform chronic inflammation of bronchial mucosa from bronchi to alveoli; 2) some extent of epithelial hyper trophy and hyperplasia. Most of the pictures of the hypertrophy and hyperplasia seen in the present study represented papillary proliferation toward the bronchial lumen or dendritic invasion into the submucous tissue.

Fig. 1 shows papillary proliferation of several layers of tall cylindrical cells in more proximal parts of respiratory bronchioles; Fig. 2 represents papillary proliferation of low cylindrical cells toward the lumen in more distal parts of respiratory bronchioles; and Fig. 3 shows several layers of low cylindrical cells dendritically invading the submucous tissue in distal parts of respiratory bronchioles.

In some cases, pictures showing more advanced stages of hyperplasia were seen. Thus, in Okuyama’s case (Fig. 4, bronchogram; Fig. 5, resected lung) there were observed a hyperplasia toward the lumen at the seemingly transitive parts between respiratory bronchioles and alveolar passages. The hyperplasia was made up of a few layers of cuboidal cells
with hyperchromatic nuclei and a small amount of interstitial tissue (Fig. 6).

In Endo’s case (Fig. 7, bronchogram; Fig. 8, resected lung) it was noted at alveolar passages that cuboidal cells, with hyperchromatic nuclei and unaccompanied by interstitial tissue, made a papillary proliferation toward the lumen, as shown in Fig. 9. In some respiratory bronchioles, several layers of cuboidal cells with pale cytoplasm and round chromophobic nuclei showed particularly active proliferation, and these cells superposed like a stone wall and projected into the lumen (Fig. 10).

From these findings obtained with Okuyama’s and Endo’s cases it is clear that the hyperplasia in these cases had advanced beyond those stages such as shown in the first 3 pictures (Figs. 1 to 3) toward precancerous degeneration, but at the same time it cannot be asserted that the changes had become precancerous. We obtained, however, the following 2 cases, which gave pictures indicating undoubtedly precancerous degeneration:

Chiba’s case (Fig. 11, bronchogram; Fig. 12, resected lung): There were found, in respiratory bronchioles, cell nests of hyperplastic epithelium being formed insularly in the lumen as shown in Fig. 13. The cells in outer part of these nests were cylindrical and the cells in the centers of these nests were cuboidal containing hyperchromatic nuclei. No basement membrane was perceived in these nests. These nests seem to have been formed by very active growth of the hyperplastic epithelium of the mucous membrane. It was also found in parts of respiratory bronchioles that the hyperplastic epithelium of the mucous membrane partly formed cell nests in the submucous tissue, as shown in Fig. 14. As can be seen from a picture of high magnification of one of these areas (Fig. 15), many

<table>
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cells were polymorphous, not clearly outlined, and their nuclei were large, round or oval, and chromophobic. The basement membrane became rough and showed a tendency to destruction. A mitotic figure was found in the cell nests. These findings may be asserted to represent precancerous change.

Another case of precancerous degeneration was observed: In Igari's case (Fig. 16, bronchogram: Fig. 17, resected lung), solid cell nests were found to have been formed by epithelial cells of the mucous membrane in some areas of respiratory bronchioles or alveolar passages. The cells of the nests were cuboidal and had hyperchromatic nuclei, as shown in Fig. 18.

DISCUSSION

Cases in which carcinoma of the lung developed from bronchiectasis have been reported by several authors\textsuperscript{1,2}, including Bass and Singer,\textsuperscript{3} Löhlein,\textsuperscript{4} Womack and Graham,\textsuperscript{5} and Siegmund.\textsuperscript{6} We\textsuperscript{7} too have communicated a combined case of bronchiectasis and pulmonary carcinoma, in which it was ascertained that the two diseases are very closely related with each other.

Microscopic examination of serial sections prepared from 10 resected lungs of our 10 cases of bronchiectasis gave the following findings: In the cases of Okuyama, Endo, Chiba and Igari there were obtained histologic pictures indicating active epithelial proliferation in the mucous membrane of the bronchioli; in the first 2 cases pictures revealing a proliferation near a precancerous state were found, while the tendency to malignancy on the part of epithelium of the mucous was much stronger in the last 2 cases than in the first 2. Thus, in Chiba's case a mitotic figure was recognized, and in Igari's case the occurrence of precancerous change was demonstrated in that atypically proliferated cells with hyperchromatic nuclei formed solid cell nests.

According to Aschoff,\textsuperscript{8} primary bronchial carcinoma is liable to originate in respiratory bronchioles (the first to third orders). It is to be noted in our cases that precancerous changes were often seen in the transitive parts between the respiratory bronchioles and the alveolar passages. Siegmund etc.\textsuperscript{4,6} state that pulmonary carcinoma is produced by epithelial metaplasia of the mucous membrane, while our findings suggest the possibility that pulmonary carcinoma takes its origin from epithelial hyperplasia of the mucous membrane.

The fact obtained by our researching that the precancerous changes were not rare in bronchiectasis may be considered to furnish a basis for an early operation.
Summary

Microscopic examination was made of serial sections from 10 resected lungs to study changes in the epithelium of the mucous membrane, with the results that precancerous changes were recognized in 4 of the 10 cases.

References

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5) Womack & Graham, Am. J. Pathology, 1941, 17, 645.
6) Siegmund, Virchow’s Arch, 1922, 236, 191.
7) Honda, Unpublished.
Fig. 1. Papillary proliferation of several layers of tall cylindrical cells in more proximal parts of respiratory bronchioles.

Fig. 2. Papillary proliferation of low cylindrical cells toward the lumen in more distal parts of respiratory bronchioles.

Fig. 3. Several layers of low cylindrical cells dendritically invading the submucous tissue in distal parts of respiratory bronchioles.

Fig. 4. Bronchogram of Okuyama’s case.
Fig. 5. Resected lung of Okuyama's case.

Fig. 6. Microscopic picture of Okuyama's case. There were observed hyperplasia of epithelium toward the lumen at the seemingly transitive parts between respiratory bronchioles and alveolar passages.

Fig. 7. Bronchogram of Endo's case.

Fig. 8. Resected lung of Endo's case.
Fig. 9. Microscopic picture of Endo's case. It was noted at alveolar passages that cuboidal cells, with hyperchromatic nuclei and unaccompanied by interstitial tissue, made a papillary proliferation toward the lumen.

Fig. 10. Microscopic picture of Endo's case. Several layers of cuboidal cells with pale cytoplasm and round chromophobic nuclei showed particularly active proliferation.

Fig. 11. Bronchogram of Chiba's case.

Fig. 12. Resected lung of Chiba's case.
Fig. 13. Microscopic picture of Chiba's case. Cell nests of hyperplastic epithelium being formed insularly in the lumen of respiratory bronchioles.

Fig. 14. Microscopic picture of Chiba's case. The hyperplastic epithelium of mucous membrane partly formed cell nests in the mucous tissue.

Fig. 15. Microscopic picture of Chiba's case. Many cells were polymorphous, not clearly outlined, and their nuclei were large, round or oval, and chromophobic. A mitotic figure was found in the cell nests.

Fig. 16. Bronchogram of Igari's case.
Fig. 17. Resected lung of Igari's case.

Fig. 18. Microscopic picture of Igari's case. Solid cell nests in some areas of respiratory bronchioles or alveolar passages. The cells of the nests were cuboidal and had hyperchromatic nuclei.