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Histological evaluation of cancer extension along the bronchial wall in lung cancer.

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ABSTRACT : The surgical specimens obtained from 39 cases in which primary lung cancers were situated in the central portion proximal to subsegmental bronchi were histologically examined as to how long cancer lesions extend along the bronchial wall, based on grossly visible lesions in the mucosa.

Of 34 cases, 87% showed proximal cancer extension along the bronchial wall. The mode of cancer spread was mainly adventitioal extension and the distence was within 20mm of the sites of grossly visible lesions in the mucosa.

In cases with involvement of the mediastinal lymph nodes and/or carcinoma of undifferentiated histological type, there was a tendency to spread widely. When cancer was located in the orifice of the lobar bronchus, the peripheral cancer spreading was obvious.

Based on these results, it is concluded that the site of resection of the bronchus should be 20mm distant from macroscopically recognizable cancer changes in the mucosa. In most cases (71.4%), however the extent of invasion in the bronchial wall was less than 10mm from such changes.

INTRODUCTION

Indications of surgery in the treatment of primary lung cancer have increased with advances in thoracic surgery, and lobectomy has become popular as a standard procedure. However when the lesion is located either in the main or upper lobe bronchi, pneumonectomy is often the procedure of choice, although cardiopulmonary dysfunction following pneumonectomy is a well recongnized hazard.

To preserve the postoperative pulmonary function, sleeve lobectomy was evolved but it remains unsettled as to how much of the bronchus should be resected. The ultimate purpose of these studies is to determine the extent of resection of the involved bronchus necessary to avoid residual lesions.

MATERIALS AND METHODS

A total of 131 cases of primary lung cancer underwent surgery in our clinics from 1971 to 1977. Of them 34 surgical specimens in which the lesions were situated in the central and hilar portion proximal to the subsegmental bronchus were considered proper candiates for sleeve lobectomy and were eligible for this study.

Age distribution varied from 41 years to 71 and they were 29 males and 5 females, reflecting the overall statistics on lung cancer. These specimens include 3 cases undergoing pneumonectomy and 31 lobectomies. Eleven out of 31 lobectomies were sleeve lobectomies.

The tumors were located on the right side in 22 (64.7%) and on the left side in 12 (35.3%). Twelve were in the right upper lobe, 3 (7.7%) in the right middle lobe, 7 (17.9%) in the right lower lobe, 9 (26.4%) in the left lower lobe. On both sides upper lobe bronchi were more frequently affected.

According to the sites involving the bronchus, 7 were in subsegmental bronchi, 22 in segmental bronchi, 10 in lobar bronchi. In relation to histologic types, squamous cell carcinoma was mainly situated in the subsegmental or the lobar bronchus, adenocarcinoma in the subsegmental bronchus and large cell carcinoma in the segmental bronchus.

Lymph node involvement was seen in 18 (52.9%) out of 34, that is, n_1 involving the hilum was seen in 7, and n_2 involving the mediastinum in 12.

The surgical specimens were fixed in 10% formalin, and sectioned at 5mm intervals along the longitudinal axis of the bronchus and stained with hematoxyline and eosin. In each section prepared for histological examination, the modes of cancer extension were histologically evaluated and their distances from the grossly visible lesions in the mucosa were measured. Furthermore, they were also compared to the findings of the preoperative chest roentogenogram as well as the bronchographic and bronchoscopic examination.

RESULTS

The modes of cancer extension along the bronchial walls were categorized into four types ; mucosal, submucosal, adventitial and extension throughout the bronchial wall, as described by AREY[2] and HAYEK.[3]

Mucosal spread (type I) is a type of sustained cancer extension along the mucosa. In this type, its spread showed patterns of either spreading with defined margin or replacing the intact mucosa with tumor.(Fig. 1)

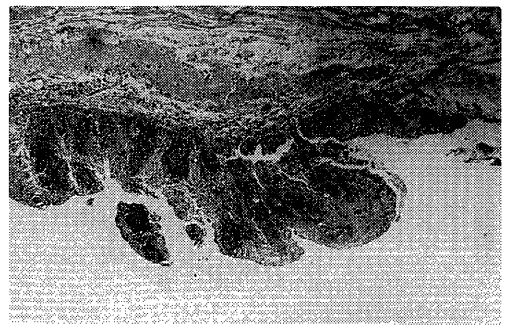

Fig. 1. Type I mucosal cancer spread along bronchial wall.

Submucosal spread (type II) refers to existence of cancer invasion in the submucosal layer. It consists of two types, that is, continuous invasion and discontinuous invasion through lymphatics channels to the submusal layer. (Fig. 2)

Fig. 2. Type II submucosal cancer spread.

Adventitial spread (type III) is a type of cancer extension along the outer layer of the bronchus, not infrequently accompanied by skip lesions. (Fig. 3)

Fig. 3. Type III adventitial cancer spread

Extension throughout the whole coats of the wall (type IV) is a type of uniform extension into the bronchial wall. (Fig. 4) As shown in Table 1, type I was seen in 6, type II in 4, type III in 18 and type IV in 6. Type III was significantly more common.

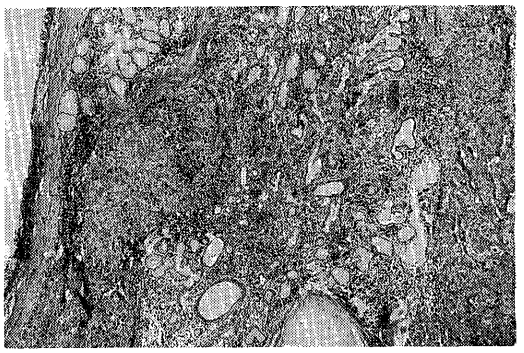

Fig. 4. Type IV cancer spread throughout the shole wall of the bronchus.

According to the histologic type, 20 squamous cell carcinoma cases consisted of 6 type I, 3 type II, 7 type III and 4 type IV. Seven adenocarcinomas consisted of 5 type III and 2 type IV, whereas 6 large cell carcinomas were divided into one type II and 5 type III. In adenocarcinoma and large cell carcinoma, there was a preponderance of type III. The single undifferentiated carcinoma showed type III.

As for the lymph node involvement, 16 among 34 were not involved and the remaining 18 were affected, n_1 in 7 and n_2 in 11. The lymph node metastasis was most fregment in type III, that is, 11 in type III, 4 in type IV, 2 in type II, 1 in type I among 18 involving the lymph nodes.

The distance of extent of cancer from the grossly visible lesion were measured on the basis of the histologic findings. According to the types of cancer extension along the bronchial wall, in type I 2 cases were within 5mm long, 2 within 10mm, 1 within 15mm, 1 within 20mm. Type II included 1 within 5mm long, 1 within 10mm, 1 within 15mm, 1 over 20mm. Type III had 6 within 5mm, 7 within 10mm, 2 within 15mm, 2 within 20mm and 1 over 20mm. Type IV had 1 within 5 mm long, 4 within 10mm and 1 within 15mm respectively. There was a tendency toward the widened proximal extension along the bronchial wall in type IV and less limited in type I and II.

Lymphatic invasion was classified into four groups as follows, lyo : no invasion, ly_1 : slight invasion, ly_2 : moderate invasion and ly_3 : remarkable invasion. As shown in Table 2, there was a propensity toward increased lymphatic invasion in cases with adventitial spread (type III) and with a widened proximal extention. The extent from the grossly visible lesions was analyzed in relation to lymph node metastasis, histologic type and tumor location.

As for lymph node metastases, as shown in Table 3, the greater the extent along the bronchial wall, the more lymph nodes were involved.

In terms of histologic types, there was a tendency toward greater extension by both squamous cell carcinoma and large cell carcinoma whereas it was limited in adenocarcinoma

Table 1. Relationship between modes of cancer extension along the bronchial wall and histology, lymph node metastasis and distance of extent.

modes of cancer extension along the bronchial wall	No. cases	histology				lymph node metastasis			cancer-spreading distance along bronchial wall (mm)				
		sq	ad	large	small	n_0	n_1	n_2	−5	−10	−15	−20	20−
mucosal spread	6	6	0	0	0	5	1	0	2	2	1	1	0
submucosal spread	4	3	0	1	0	2	1	1	1	1	1	0	1
adventitial spread	18	7	5	5	1	7	3	8	6	7	2	2	1
throughout the whole wall	6	4	2	0	0	2	2	2	1	4	1	0	0
total	34	20	7	6	1	16	7	11	10	14	5	3	2

sq : squamous cell carcinoma, ad : adenocarcinoma, large : large cell carcinoma
small : small cell carcinoma

Table 2. Relationship between modes of cancer extension and lymphatic invasion, infiltrative type and differentiation.

Mode of cancer extension	lymphatic invasion				infiltrative			diffentiation		
	ly_0	ly_1	ly_2	ly_3	α	β	γ	well	moderate	poorly
mucosal spread	2	3	1	0	0	6	0	2	4	0
submucosal spread	0	2	1	1	0	2	2	0	2	2
adventitial spread	2	10	6	0	1	11	6	4	6	8
throught the whole wall	0	4	1	1	1	3	2	1	3	2
	4	19	9	2	2	22	10	7	15	12

Table 3. Relationship between distance of extent and lymph node metastasis.

distance of cancer extension (mm)	No.of cases	lymph node metastases n_0	n_1	n_2
− 5	10	7	3	0
−10	14	5	3	6
−15	5	1	0	4
−20	3	1	1	1
20−	2	2	0	0
total	34	16	7	11

Table 4. Relationship between cancer extent and histology.

distance of cancer invasion	No.of cases	histology sq	adeno	large	small
− 5	10	5	3	2	0
−10	14	10	2	2	0
−15	5	3	2	0	0
−20	3	2	0	0	1
20−	2	0	0	2	0
Total	34	20	7	6	1

(Table 4).

As for tumor location, as shown in Table 5 the tumors located in lobar bronchi showed various types of extension although the mucosal or submucosal spread of types I or II predominanted in tumors located distal to the lobar bronchus.

The findings of the chest roentogenogram were divided into five categories, atelectatic, hilar tumor, hilar infiltration, peripheral tumor and peripheral infiltration respectively. With respect to the extent of cancer extension along the bronchial wall as shown in Table 6, extensive cancer spread was observed in cases with atelectatic shadows. Also mucosal spread was more frequently seen in cases with atelectatic shadow whereas adventitial spread was predominant in cases appearing as peripheral tumors.

Table 5. Relationship between tumor location and modes of cancer extension.

bronchus in tumor location	Type of cancer spread Type I	II	III	IV	total
subsegmental		1	4	1	6
segmental	2	1	11	4	18
lobal	4	2	3	1	10
total	6	4	18	6	34

Table 6. Relationship between findings on chest X-ray film and modes of cancer extension, including distance.

finding on the chest xp	modes of cancer invasion mucosal	sub-mucosal	adven-titial	throughout the whole wall	distance of cancer invasion(mm) −5	−10	−15	−20	20−
atelectatic	5		2	1	2	3	2	1	
hilar tumorous	1		1	4	3	3	6		
hilar infiltrative		1	2	1		1	2	1	
periphlral tumorous		2	9	1	5	3	1	1	2
peripheral infiltrative			1			1			
Total	6	4	18	6	10	14	5	3	2

Table 7. Relationship between bronchoscopy findings and modes of cancer extension, including distance.

finding on the bronchography	modes of cancer invasion				distance of cancer invasion(mm)				
	mucosal	sub-mucosal	adven-titial	throughout the whole wall	−5	−10	−15	−20	20−
Obstruction irregular	4	2	5	3	3	8	2	1	
interrupted	2	1	3		4	1	1		
tapering			3	1		2	1	1	
Stenosis simple			5	1	3	1	1		1
irregular			1	1		1		1	
Normal		1	1			1		1	
Total	6	4	18	6	10	14	5	3	2

The bronchographic findings were divided into 6 categories, namely, irregular obstruction, interrupted obstruction, sharp obstruction, simple stenosis, irregular stenosis and normal. The adventitial or submucosal extension was seen in cases with findings of either obstruction or stenosis on bronchography but the types of extent was variable in cases with findings of irregular and interrupted obstruction. (Table 7)

The cancer extent was longer in cases of irregular stenosis, whereas it was limited in those with findings of interrupted obstruction. Even in those with normal bronchographic findings, cancer extended along the bronchial walls to some extent.

Of 34 cases, the bronchographic examinations were performed in 28 cases. Their findings were categorized as follows, direct findings (23 cases 82.1%), indirect (4 cases 14.3%) and normal (1 case 3.6%) respectively. No definite relation could be found between the bronchoscopic findings and the type and distance of cancer extension. In cases of mucosal and submucosal cancer spread, some degree of mucosal changes was recongnized at bronchoscopy, such as the redness in color and granular surface irregularity. However in cases of adventitial spread of cancer, there were few abnormal bronchoscopic findings.

DISCUSSION

It is of great importance to clarify how lung cancer extends along the btonchial wall in the surgical treatment of primary lung cancer. In the central type lung cancer, care must be taken to avold insufficient resection when performing sleeve lobectomy. GRIESS[2] reported in 1945 that the types of cancer development consisted of 1) mucosa, 2) submucosa 3) submucosa and outer fibrous coat 4) outer fibrous coat.

This study showed that the most common type of cancer extension was advential spead. COTTON[4] and MAEDA[5] also reported that the adventitial spread was more common than other types of extension, whereas HOLLAND[6] cited that submucosal spread was the predominant type. No pattern of growth was seen to be related to histological type. The submucosal and adventitial spread were frequently seen in undifferentiated carcinoma by NOSE[7], in squamous cell carcinoma by GRIESS[2] and in adenocarcinoma by SAITO. We concluded that submucosal and adventitial spread are common regardless of histological types.

On bronchography, the findings of irregular or interrupted obstruction were frequently seen in cases with central type lung cancer as described by RINKLER[8]. They show more frequent adventitial cancer invasion.

When the lymph nodes in the mediastinum and hilum are involved, it is assumed that lymphatic flow in the bronchial wall has reversed, precipitating cancer infiltration to spread throughout the bronchial wall. Therefore, the type of cancer invasion varies according to the stage of disease.

The extent of cancer invasion has been evaluated by many investigators. In mucosal invasion, its extent is generally limited within 5 to 15 mm,[2,6,10] but two cases of invasion 25 to 35 mm from the macroscopically recog-

nizable lesion border in squamous cell carcinoma were reported by MIYAZAWA.[9]

Surgeons should be aware of the possibility of extension of cancer along to a wider extent than is visually recognizable. In submucosal or adventitial spread, extensive cancer spread can be prominent in undifferenitated carcinom a,showing a maximum of 3 to 4cm.[10] In the present study it was shown that the maximum cancer extent along the bronchial wall was 33 mm in the case of large cell carcinoma. This study showed that the extent of cancer spread was less than 10mm long in 28 cases (71.4%) among 34. This is an important point in considering the surgical treatment of lung cancer, in particular, when bronchoplasty is projected. Cancer extending beyong 20mm from the macroscopically recongnized bordes is rarely seen, even in undifferentiated carcinoma which tends to exhibit wider extension.

It is difficult to determine macroscopically the distance of cancer invasion along the bronchial wall, according to either mode of cancer spread or grade of the ensuing bronchial stenosis. Intraoperatively microscopic examination would be only required to ensure cancer-free bronchial stump.

It is emphasized that resection of the bronchus should be performed at a distance of 20mm not to leave the remaining cancer lesion from the grossly visible cancer margin in the mucosa if satisfactory resection is attempted. Based on findings of this study, when resection is performed at a 15mm from macroscopic lesion, cancer lesion may be left in 5 out of the 24 cases (20.8%) and when performed at a 10 mm, the remaining lesion may be seen in 10 (41.6%) in advanced cancers.

REFERENCE

1) JENSIK,R, FABER,L.P. MILLY F.J *et al* : Sleeve lobectomy for carcinoma-A ten-year experience. *J. Thorac, Cardiovasc, Surg.*, **64** : 400-412, 1972.

2) GRIESS,D.F. : The proximal extension of carcinoma of the lung in the bornchial wall. *J.Thorac. Surg.*, **14** : 362-368, 1945.

3) AUERBACH,D : Carcinoma occurring in the tracheobronchial tree in cases of bronchial carcinoma, *J. Thorac. Surg.*, **34** : 298-309, 1957.

4) COTTON,R.E. : The bronchial spread of lung cancer. *Brit.Dis. Chest* **53** : 142-150, 1970.

5) MAEDA M, IWAMOTO K, KADOTA, Y *et al* : Histopathological study on metastasis at the bronchial wall of lung cancer, *J.J.A.T.S.* **18** : 148-159, 1970.

6) HOLLAND,R,H. : Carcinoma of the lung treated by lobectomy : the problem of local recurrence. *J.Thorac, Surg.* **35** : 274-278, 1958.

7) NOSE,K : Pathological study in resected long of lung cancer. *Thorac.Surg.* **12** : 254-269 (in Japanese) 1968.

8) RINKLER, C.T. : Bronchography : Diagnostic signs and accuracy in pulmonary carcinoma. *Amer. Roentg.* ; **40** : 802-807, 1968.

9) MIYAZAWA,N : Comparision between the findings of the endoscopy and pathology. *Lung Cancer* **13** : 83-100, 1973.

10) HABEIN, H, C. : Recurrent carcinoma in the bronchial stump. *J.Thorac.Surg.* **31** : 703-717, 1956.