症 例

Peripheral adenoid cystic carcinoma of the lung

—a case report—

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Adenoid cystic carcinoma of the lung occurs commonly in the trachea and main bronchi and rarely occurs as a peripheral lung mass. A case of peripheral adenoid cystic carcinoma of the lung is reported. The patient was a 67-year-old Japanese female who had the complaint of cough for one and half months. On admission to the hospital, she was found to have a left abnormal lung mass. She was transferred to the Surgical Department of Kanazawa University Hospital for further examination and surgery. A tumor was located in the left superior lingula segment (S-4 b), and was resected. The cut surface of the tumor was yellow-white and measured 2.3×3.0×2.6 cm with a well-defined margin. There was no relationship between the tumor and the trachea or main bronchus. Histologic and electron microscopic examination revealed the tumor to be an adenoid cystic carcinoma. Histologically, there was no involvement of the main bronchi in the tumor, but bronchi without cartilage were found at the periphery of the tumor, which indicated that the tumor might arise from the fifth or sixth order bronchus.

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I. Introduction

Adenoid cystic carcinoma is an uncommon and specific variant of adenocarcinoma that occurs most frequently in the major and minor salivary glands⁷⁾. This tumor also occurs in the breast, uterine cervix¹²⁾, larynx⁹⁾, Bartholin's gland¹⁾ skin⁵⁾

and trachea and bronchus⁴⁾. However, the occurrence of a primary adenoid cystic carcinoma as a large peripheral lung mass is extremely rare, and few cases have been reported to date^{2,3,10)}. We report a case of peripheral adenoid cystic carcinoma of the lung along with electron microscopic and cytological findings.

II. Case report

A 67-year-old woman with a complaint of cough for one and half months, was admitted to a hospital where she was found to have an abnormal shadow in the left lung. She was transferred to the Department of Surgery, Kanazawa University Hospital, for further examination. She had no history of smoking. Physical examination revealed a well-nourished woman without superficial lymphadenopathy. Laboratory data were within the normal range. Preoperative chest films revealed a 3.5 cm mass with a rather clear demarcation in the left upper lobe. The sputum culture was normal. Tumor aspiration cytology was performed but no tumor cells were found. Exploratory thoracotomy was performed on February 10, 1988. The pathologic examination during surgery by frozen section revealed an adenoid cystic carcinoma, and an upper lobectomy was performed.

III. Pathologic findings

A resected lung specimen was fixed in 10% buffered formalin. A routine histologic examination was performed after paraffin embedding and staining with hematoxylin-eosin (H & E), Alcian blue, periodic acid Schiff (PAS), and elastica van Gieson stain. Tumor imprint specimens were fixed in 95% ethanol for Papanicolaou stain, or air-dried and fixed in 95% methanol for May-Grünwald-Giemsa stain.

For electron microscopy, fresh samples of the lung tumor were minced into small cubes and fixed in 2.5% glutaraldehyde in phosphate-buffered saline (PBS), postfixed in 1% osmium tetroxide in

Fig. 1 Macroscopic appearance of the lung tumor located in the peripheral lung parenchyma, showing a yellow-white cut surface with well-defined margin. The arrowhead indicates a small pulmonary artery located in the periphery of the tumor

PBS, and embedded in Epon 812. Ultrathin sections were stained with uranyl acetate-lead citrate, and examined under a transmission electron microscope.

Macroscopically, the tumor was located in the left superior lingula segment (S-4 b). The cut surface of the tumor was homogeneously yellow-white with a well-circumscribed border, and measured $2.3 \times 3.0 \times 2.6$ cm (Fig. 1). The tumor was located in the periphery of the lung parenchyma. No particular relationship was observed between the tumor and the main bronchus. The small pulmonary artery and bronchus were seen at the periphery of the tumor.

Microscopically, the main bronchus was not entrapped in the tumor, but two small bronchi without cartilage were found at the periphery of the

Fig. 2 Microscopic appearance of the tumor, showing small, round cells arranged in characteristic strand, tubular, or cribriform pattern. H-E stain. Original magnification (a : $\times 200$, b : $\times 400$)

tumor. The tumor cells were rather small and uniform with round or ovoid nuclei and formed strands or clumps with varying numbers of cystic or alveolar spaces forming an interlacing cylinder or cribriform pattern. Tubular and solid patterns also were found in varying degrees in the tumor (Fig. 2). The center of the cylinder or tubule was filled with mucin positively stained with PAS and Alcian blue. The stroma was also positively stained with Alcian blue to varying degrees. There was no metastases in the regional lymph nodes.

Fig. 3. shows the cytologic features of the tumor imprint specimen. The tumor cells in ball-like clusters were small and rounded with little variation in size, and showed a low degree of atypia. The nuclei of the tumor cells had fine granular chromatin and small but prominent nucleoli. A characteristic feature was the presence of a central core of homogeneous mucinous substance corresponding to the material filling the cystic spaces. The size of the central core was various. The small one gave an appearance of a rosette-like structure with central acellular area.

Examination by electron microscopy revealed a tumor composed of islands of polygonal cells surrounded by basal lamina, and containing scattered spaces through the islands (Fig. 4). Some of the

Fig. 3 Cytologic features of the tumor imprint specimen (a, b), showing ball-like clusters (a) with a core of homogeneous mucinous substance (a, arrow). Higher magnification shows that tumor cells are small and round with little variation in size, and show a low degree of atypia (b). Original magnification (a : $\times 400$, b : $\times 800$)

spaces were filled with basal laminar material and the others were composed of epithelial-type lining with junctional complexes and microvilli at their luminal surfaces (Fig. 5), each corresponding to pseudolumens and true lumens, respectively. In addition, the tumor cells tended to be separated from one another and to have lateral cytoplasmic processes projecting into the intercellular spaces (Fig. 4).

IV. Clinical course

After establishing the tumor histology, an extensive survey for the presence of another tumor was performed to exclude the possibility of this tumor being a metastasis, but no tumor was found outside the lung. Furthermore, no recurrence or other

Fig. 4 Electron microscopic features of the tumor, showing islands of polygonal tumor cells with cystic spaces containing basal laminar materials (asterisks) and irregular intercellular spaces with lateral cytoplasmic projections ($\times 3,400$)

Fig. 5 Tumor cells on the left are separated by cystic space filled with basal laminar material (large asterisk) and the ones on the right form the true lumen (small asterisk) with microvilli and junctional complexes ($\times 17,000$)

primary tumors have been found during the follow-up period for 4 years and 6 months after surgery, and the patient remains free of recurrence.

V. Discussion

Primary lung tumors are generally classified according to the type of lung tissue they originate from; bronchial epithelial, mucous gland, and mesenchymal origin¹¹⁾. Adenoid cystic carcinoma is a histopathologically distinct tumor which originates from the mucous glands. In a large series of primary lung tumors, adenoid cystic carcinoma constituted only 3 out of 1,500 cases (0.2%)¹⁴⁾. Adenoid cystic carcinoma of the lung occurs commonly in the trachea and main bronchus^{11,14)}. Occurrence of adenoid cystic carcinoma in the peripheral lung tissue is extremely rare and only a few cases have been reported so far^{2,3,10)}. Gallagher et al. reported a case of a 48-year-old female with peripheral adenoid cystic carcinoma of the lung who had had multiple nodules 11 years after resection of the original tumor³⁾. Dalton et al. reported a case of peripheral adenoid cystic carcinoma, presenting as a large peripheral lung mass, measured about 10×9×6 cm in a 63-year-old female²⁾. Okura et al. reported a 70-year-old Japanese woman who had an adenoid cystic carcinoma measuring 1.5×1.5 cm in the left upper lobe of the lung (S1+2)¹⁰⁾. Bronchial glands have been reported present in the bronchi down to a diameter of about 1.0 mm and reach their greatest development in the second to the fifth order bronchi¹³⁾. Mitani studied the occurrence of human bronchial glands in bronchi of different orders and reported that all studied cases had both bronchial glands and cartilage from the first to fourth order, whereas bronchial glands were found in 79% of the fifth order bronchi but only in 11% of the sixth order. Cartilage was seen in 89% of the fifth order bronchi and 44% of the sixth order bronchi. No bronchi more than the seventh order had bronchial glands or cartilage⁸⁾. Therefore, adenoid cystic carcinoma may occur in bronchi of up to the sixth order. In

the present case, the relationship of the tumor to the trachea and main bronchus was not demonstrated but bronchi without cartilage were found at the periphery of the tumor. Therefore, the tumor might arise from the bronchus of fifth or sixth order bronchus.

Adenoid cystic carcinoma is believed to grow slowly and to have a high rate of invasiveness and local recurrence, and a definite but low potentiality for distant metastasis. The tumor is composed of two cell types, duct-lining cells and cells of myoepithelial type, forming a characteristic cribriform pattern^{6,15)}. This tumor is histologically and ultrastructurally identical to the salivary gland, breast, or uterine cervix tumor of same name^{6,7,14)}.

Electron microscopically, the tumor was characterized by islands with polygonal cells with numerous sieve-like spaces scattered through the islands. Some cystic spaces were composed of epithelial-type lining cells with microvilli and junctional complexes, and the others were filled with basal laminar material, which indicated the continuity between the interstitium and the cystic space^{6,7)}. The former is the true lumen, and the latter the pseudocyst. The presence of both pseudolumen and true lumen is considered to be a characteristic ultrastructural finding for adenoid cystic carcinoma^{6,7)}. In addition, irregular intercellular spaces were frequently found in the myoepithelial islands, as described previously^{6,7)}. All of these electron microscopic features were seen in the present case.

要 旨

肺の腺様嚢胞癌は主に太いレベルの気管支に発生し、末梢肺組織に発生することはきわめてまれである。最近、われわれは末梢肺組織に発生した腺様嚢胞癌の1例を経験したので、その臨床病理所見について報告する。症例は67歳、男性で約1ヵ月半の咳嗽を主訴に近くの病院を訪れた。X線検査の結果、左肺野に異常陰影を指摘され、精査、治療のため当病院に紹介された。腫瘍は左肺舌区に存在し、肺癌を疑い、切除を行った。切除された肺腫瘍は約2.3×3.0×2.6

cm大, 断面は淡黄白色で, 境界は明瞭であった。肉眼的に腫瘍と大きな気管支との間に明確な関連はみられなかった。組織学的に, 腫瘍は腺様嚢胞癌であった。他の部位に原発巣は発見されなかった。組織像にても腫瘍と太い気管支との間に関係を認めなかったが, 腫瘍の辺縁部に軟骨を欠く細気管支が存在していることから, おそらく5ないし6次分枝の細気管支より発生したものと推定された。

References

- 1) Addison, A., Parker, R.T. : Adenoid cystic carcinoma of Bartholin's gland ; A review of the literature and report of a patient, *Gynecol. Oncol.*, 5 : 196~201, 1977.
- 2) Dalton, M.L., Gatling, R.R. : Peripheral adenoid cystic carcinoma of the lung, *South Med. J.*, 83 : 577~579, 1990.
- 3) Gallagher, C.G., Stark, R., Teskey, J., Kryger, M. : Atypical manifestations of pulmonary adenoid cystic carcinoma, *Brit. J. Dis. Chest.*, 80 : 396~399, 1986.
- 4) Hajdu, S.I., Huvo, A.G., Goodner, J.Y., Foote, F.W., Beattie, E.J. : Carcinoma of the trachea. Clinicopathologic study of 41 cases, *Cancer*, 25 : 1448~1456, 1970.
- 5) Herbst, E.W., Utz, W. : Multifocal dermal-type basal cell adenomas of parotid glands with co-existing dermal cylindromas, *Virchows Arch. Pathol. Anat.*, 403 : 95~102, 1984.
- 6) Hoshino, M., Yamamoto, I. : Ultrastructure of adenoid cystic carcinoma, *Cancer*, 25 : 186~198, 1970.
- 7) Lawrence, J.B., Mazur, M.T. : Adenoid cystic carcinoma : A comparative pathologic study of tumors in salivary gland, breast, lung, and cervix, *Hum. Pathol.*, 13 : 916~924, 1982.
- 8) Mitani, S. : Studies on distribution and histological observation of mucus gland in the bronchial tree of adult human lungs. *Lung Cancer.*, 14 : 21~29, 1974. (in Japanese with English abstract)
- 9) Olofsson, J., Van Nostrand, A.W.P. : Adenoid cystic carcinoma of the larynx : a report of four cases and a review of the literature, *Cancer*, 40 : 1307~1313, 1977.
- 10) Okura, T., Shiode, M., Tanaka, R., Furukara, A., Kukita, H. : A case of peripheral adenoid cystic carcinoma, *Jpn. J. Thrac. Dis.*, 30 : 773~776, 1990. (in Japanese with English abstract)
- 11) Payne, W.S., Ellis, F.H., Woolner, L.B., Moersch, H. J., Minn, R. : The surgical treatment of cylindroma (adenoid cystic carcinoma) and muco-epidermoid tumors of the bronchus, *Thorac. Cardiovasc. Surg.*, 38 : 709~726, 1959.
- 12) Prempre, T., Villasanta, U., Tang, CK. : Management of adenoid cystic carcinoma of the uterine cervix (cylindroma) : report of six cases and reappraisal of all cases reported in the medical literature, *Cancer*, 46 : 1631~1635, 1980.
- 13) Spencer, H. : The anatomy of the lung. In "Pathology of the lung", Spencer H, ed. pp 17~77, 1985. Pergamon Press, Oxford.
- 14) Sweeny, W.B., Thomas, J.M. : Adenoid cystic carcinoma of the lung, *Contemp. Surg.*, 28 : 97~100, 1986.
- 15) Thackray, A.C., Lucas, R.B. : Tumors of the major salivary glands. In : Atlas of tumor pathology. Second series, fascicle 10. pp 91~90, Armed Forces Institute of Pathology, Washington D.C., 1974.