Ultra-Late Relapse with a Single Cerebellar Metastasis 10 Years after Complete Surgery for Stage IIA Non-small Cell Lung Cancer (Bronchioalveolar Carcinoma)

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The prognosis for non-small cell lung cancer (NSCLC) is generally poor, but relapse-free survival exceeding 5 years is often considered proof of cure. This report compares prognostic factors influencing long-term overall survival and progression-free survival in NSCLC with a case of ultra-late relapse 10 years after initial treatment.

METHODS

Literature search using PubMed database and Cochrane Library with no limitation concerning time period was updated until September 12. Only English literature was searched and the following keywords were used: NSCLC, non-small cell lung cancer, late relapse, and late recurrence.

CASE REPORT

A 60-year-old man with smoking cessation 10 years previously had left lower lobe lobectomy in October 2000. Histologic examination revealed highly differentiated bronchioalveolar carcinoma without vascular or pleural invasion and with spread to 2 intrapulmonary N1 lymph nodes out of 10 resected. Negative for EGFR mutation. CT scan was without signs of metastasis or mediastinal gland involvement, and mediastinoscopy was negative.

The operation was micro- and macroscopic complete, and the surgical-pathological TNM classification was T2aN1M0 (stage IIA). No adjuvant chemotherapy was applied as this was not a standard treatment at that time. The patient developed vertigo and headache in July 2010, and cerebral magnetic resonance imaging scan revealed a cerebellar metastasis which was incompletely removed by neurosurgery. Whole brain irradiation was given. Histopathological examination with immunohistochemistry revealed the metastasis being similar to the bronchioalveolar carcinoma treated 10 years earlier. Examination with positron emission tomography-computed tomography fused imaging and cerebral magnetic resonance imaging scan showed no other relapse sites or sign of other primary tumor. The patient died in January 2011 due to intracranial progression.

DISCUSSION

The literature search revealed that the risk of recurrence 5 years after initial complete surgery varies from 3.8 to 15.0% (Table 1). Only one published study has been found with data on ultra-late relapse 10 years or more after treatment.[1] These numbers should be interpreted carefully because there is no consensus between definition of late relapse and newly developed malignant disease in the literature.

Maeda et al.[2] reported the most important prognostic factors for development of recurrence to be lymph node involvement, intratumoral vascular invasion, smoking habits, carcinoembryonal antigen, histologic condition, pleural invasion, and pathologic stage.

Similarly, Wang et al.[3] observed correlation between resectable lymph nodes and 5-year survival, while Martini et al.[1] found age, sex, histologic condition, or stage, including N-status, to not influence 5-year survival.

Likewise, Okada et al.[4] reported that for patients alive 5 years after initial treatment, neither age, nodal status, sex, or histologic condition affected subsequent survival. In contrast, these factors were found to have prognostic value before 5 years. Also, Pasini et al.[5] found no correlation between vascular or lymphatic invasion and 5-year survival or 5-year progression-free survival.

These findings support that lung cancer is very heterogeneous in outcome and more individual, targeted treatment is obviously needed to improve long-term survival. The case also supports this, as the patient developed a cerebellar metastasis 10 years after initial treatment despite positive prognostic factors. This may suggest that other factors may be of influence, e.g., presence of oncogenic driver mutations or other biological factors.

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REFERENCES

1. Martini N, Rusch VW, Bains MS, et al. Factors influencing ten-year survival in resected stages I to IIIA non-small cell lung cancer. *J Thorac Cardiovasc Surg* 1999;117:32–38.

TABLE 1. Frequency and Sites of Late Relapse in NSCLC

	Maeda et al. (2010)	Wang et al. (2010)	Okada et al. (2003)	Pasini et al. (2002)	Martini et al. (1999)
Total population, *n*	1358	846	848	241	686
Recurrence free >5 yr, *n* (%)	819 (60.3)	56 (6.6)[a]	421 (49.6)[a]	150 (62)	686 (100)
Late recurrence after 5 yr, *n* (%)	87 (10.6)	[b]	[b]	22 (15)	26 (3.8)[c]
Initial stages	IA–IIIB	IIIA–IV	IA–IIIB	I (T1–2N0M0)	IA–IIIA
Histology					
Adenocarcinoma	585 (43.0)	[b]	245 (58.2)	99 (41.0)	412 (60.0)
Squamous cell	179 (13.2)		160 (38.0)	130 (54.5)	244 (36.0)
Large cell	33 (2.4)		8 (1.9)	10 (4.0)	29 (4.0)
Others	22 (1.6)		8 (2.0)	2 (0.8)	1 (0.1)
Treatment	Surgery	Surgery RT Chemotherapy	Surgery	Surgery	Surgery
Site of late recurrence after 5 yr, *n* (%)					
Locoregional	38 (43.7)	[b]	[b]	[d]	6 (23.1)
Contralateral lung	—				3 (11.5)
Brain	4 (4.6)				9 (34.6)
Bone	4 (4.6)				2 (7.7)
One site	22 (25.3)				4 (15.4)
Other	19 (21.8)				2 (7.7)

[a] Study does not elaborate whether the patients are disease free or not but only if they are alive.
[b] Is not calculated or specified in the study.
[c] Study composes of population who have survived the first 5 yr. Therefore, this number represents 10 yr after initial treatment. Study has distinguished local recurrence from secondary malignant tumors. Hence, this number is lower than that of Pasini et al.
[d] 14/20 of the late recurrences were inside the thorax.

2. Maeda R, Yoshida J, Hishida T, et al. Late recurrence of non-small cell lung cancer more than 5 years after complete resection. *Chest* 2010;138:145–150.
3. Wang T, Nelson RA, Bogardus A, et al. Five-year lung cancer survival: which advanced stage nonsmall cell lung cancer patients attain long-term survival? Cancer 2010;116:1518–1525.
4. Okada M, Nishio W, Sakamoto T, et al. Long-term survival and prognostic factors of five-year survivors with complete resection of non-small cell lung carcinoma. *J Thorac Cardiovasc Surg* 2003;126: 558–562.
5. Pasini F, Pelosi G, Valdugo F, et al. Late events and clinical prognostic factors in stage I non small cell lung cancer. *Lung Cancer* 2002;37:171–177.

