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Peritoneal relapse from lung adenocarcinoma after a response to EGFR-TKI

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Usefulness of epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKIs) for EGFR-mutated elderly non-small cell lung cancer (NSCLC) patients has been reported (1,2). It is supposed that EGFR-TKIs are increasingly prescribed for them. In NSCLC patients, metastases to meningeal as well as peritoneal space are rare (3,4). However, carcinomatous meningitis, which attracts attention as a recurrence site of the patients who received EGFR-TKIs), is recently a devastating event occurring in NSCLC patients (5). For them, the treatment options currently available are very limited, and the prognosis of them remains poor (3,4). Usefulness of EGFR-TKIs for peritoneal carcinomatosis in two chemo-naive NSCLC patients has recently been reported (6,7), but antemortem diagnosis of carcinomatous peritonitis in NSCLC patients is very difficult (4). We experienced three cases with peritoneal relapse from lung adenocarcinoma after a response to EGFR-TKI. Table 1 showed clinical features of the three lung cancer patients with peritoneal recurrence. They were an 83 year-old woman and a 77 year-old men, and a 72 year-old woman. All of them were non-smokers, and diagnosed as having lung adenocarcinoma pathologically, and they had a point mutation in exon 21 (L858R), respectively. At the time of initial diagnosis, these two women had carcinomatous pleuritis. Gefitinib or erlotinib was prescribed as first line chemotherapy in each patient. All of them responded to the therapy, and progressive free survival was 31, 9, and 8 months, respectively. After these response periods, they complained distension of the abdomen. Abdominal CT scan detected ascites, but there found no other recurrent site than peritoneum. Cytological examination of ascites, lung adenocarcinoma was confirmed. Two patients had isolated peritoneal relapse, and one had peritoneal and meningeal relapse (8). They had supportive care only because of their poor performance status.

Metastatic involvement of the peritoneum in lung cancer patients is not a very rare autopsy finding (9). Based on previous reports, the incidence of carcinomatous peritonitis ranges from 2.7% to 16% in all lung cancer patients (9). Nevertheless, carcinomatous peritonitis from lung cancer is infrequently encountered and clinical reports concerning this distant metastasis are rare. We previously reported that 12 (1.2%) of 1041 patients with lung cancer had carcinomatous peritonitis (6). In our hospital, 3 (2.0%) of 153 consecutive lung cancer developed carcinomatous peritonitis in recent three years, and all of them were recurrent elderly cases after effective therapy with EGFR-TKIs. To our best knowledge, there were two previous cases, who were successfully treated with EFGR-TKI in lung adenocarcinoma patients with carcinomatous peritonitis (6,7). On the other hand, however, there has no patient with peritoneal recurrence after successfully treatment with EGFR-TKIs such as ours. The existence of two different responses, good responded peritonitis with EGFR-TKTs and peritoneal recurrence after good response to EGFR-TKIs, se-

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Table 1. Clinical features of lung cancer patients with peritoneal recurrence

Age*	Sex	Pathology	Stage*	PS*	EGFR mutation	EGFR-TKI	Response	PFS (Months)	OS (Months)	Ascites	Other recurrent sites
83	F	Adenocarcinoma	IV	1	Exon 21, L858R	gefitinib	PR	31	32	Class V (EGFR negative)	None
77	M	Adenocarcinoma	IV	1	Exon 21, L858R	erlotinib	PR	9	10+	Class V	None
72	F	Adenocarcinoma	IV	1	Exon 21, L858R	gefitinib	PR	8	10	Class V	Meninges

* Age, stage, and performance status (PS) of the patient was at the time of diagnosis of lung cancer.
PFS: Progressive free survival, OS: Overall survival, PR: Partial response.

ems to be very similar to what were observed in lung cancer patients with carcinomatous meningitis. In addition, it is interesting to note that genetic change in EGFR gene from mutated type to wild type in cancer cells obtained from ascites in one patient. The mechanisms and relationship between the change and peritoneal relapse are beyond our knowledge.

Although very rare, peritoneum is one of possible sites of relapse in NSCLC patients. In the era of EGFR-TKIs for EGFR mutated patients including the elderly, patients with peritoneal relapse may increase in number. Our results suggest that such recurrence might be related to insufficient concentration of EGFR-TKIs in these sites. Clinicians should be careful about peritoneal recurrence after successful treatment with EFFR-TKIs. Such rare relapse may also be observed in the elderly patients.

CONFLICT of INTEREST

None declared.

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