evaluated according to the Response Evaluation Criteria in Solid Tumours (RECIST) guidelines (version 1.1) [22].

All patients had been preoperatively staged using contrast-enhanced CT, FDG-PET and magnetic resonance imaging (MRI) of brain. Routine mediastinoscopy or endobronchial ultrasound with transbronchial needle aspiration to detect occult mediastinal lymph node metastases was not performed.

As a general rule in surgical procedures, we performed a standard surgical procedure, that is, lobectomy with systematic or selective mediastinal lymph node dissection. However, in high-risk patients who were unable to tolerate a lobectomy as assessed by cardiopulmonary function, sublobar resection was selected. Induction therapy was indicated for clinical Stage IIIA patients with resectable mediastinal lymph node metastasis. Adjuvant platinum-based doublet chemotherapy was indicated for pathological Stage II and IIIA patients. On the other hand, adjuvant therapy with oral uracil-tegafur was indicated for pathological Stage IB patients.

In general, a follow-up examination was done every 3 months for the first 2 years, and thereafter every 6–12 months. The follow-up procedures included a physical examination, the serum level of carcinoembryonic antigen and chest radiography. Screening examinations by CT or FDG-PET were done every 6 or 12 months for 5 years.

Recurrent NSCLC was diagnosed based on a physical examination and diagnostic imaging such as CT, MRI and FDG-PET. Histopathological confirmation of the diagnosis was made only when clinically required; as a result, recurrence was histologically confirmed in only 10 of 76 patients.

Written informed consent was obtained from each patient, and the study was approved by the institutional review board of Kawasaki Medical School (IRB no. 1181).

Statistical analysis

The Kaplan–Meier method was used to analyse survival. The χ^2 test was used to compare clinicopathological factors between groups. For univariate analyses of the clinicopathological factors, differences were evaluated using the log-rank test, and a multivariate analysis of independent prognostic factors was conducted using Cox's proportional hazards regression model. Differences were considered significant when the *P*-value was <0.05.

RESULTS

Patient backgrounds

The patient characteristics are given in Table 1. There were 50 men and 26 women. The median age at the time of recurrence was 74.5 (range, 48–87 years). The median disease-free interval from the initial surgery until recurrence was 12.7 months (range 27 days–66.1 months). Regarding the pathological findings, the most common histology was adenocarcinoma in 53 (70%) patients, and the most common pathological Stage was IIIA in 30 cases (39%). Sixty-seven (88%) patients had been screened for EGFR mutation, and EGFR mutations and wild-type EGFR were found in 28 and 39 patients, respectively.

Initial treatment for NSCLC

The initial treatment was surgery alone in 38 patients; multimodality treatment including surgery and preoperative and/or postoperative chemotherapy was performed in the other 38 (50%) patients. Of these, 5 (7%) patients underwent induction chemotherapy or chemoradiotherapy followed by surgery, and 35 (41%) underwent adjuvant chemotherapy, with 2 patients undergoing both preoperative and postoperative chemotherapy. The induction chemotherapy consisted of platinum-based doublet chemotherapy in all 5 patients, with 2 also undergoing concurrent radiotherapy. The adjuvant chemotherapy consisted of platinum-based doublet chemotherapy in 19 patients and oral uracil-tegafur in 16. Twenty-two (29%) patients had been treated with platinum-based doublet chemotherapy either preoperatively or postoperatively.

Recurrence and post-recurrence therapy

Symptoms were evident in 25 (33%) patients at the time of recurrence. The initial recurrence was intrathoracic in 42 patients, extrathoracic in 16 and a combination of intrathoracic and extrathoracic in 18. Forty-seven (62%) patients developed recurrences in multiple organs.

Treatment for recurrence included systemic chemotherapy in 64 (84%) patients and local therapy only in 2 (stereotactic radiosurgery for brain metastases in 2 patients who had only brain recurrences). The remaining 10 patients received only palliative care because of a poor ECOG-PS, an advanced age and so on. Of the 64 patients who underwent chemotherapy, the response to first-line chemotherapy was a complete response (CR) in 4 patients, a partial response (PR) in 23, stable disease (SD) in 8, progressive disease (PD) in 21 and not evaluable (NE) in 8, with a disease control rate for first-line chemotherapy of 55%. EGFR tyrosine kinase inhibitors (TKIs; gefitinib and erlotinib) were used in 36 (47%) patients; none of the patients were treated with a vascular endothelial growth factor inhibitor (bevacizumab).

Post-recurrence survival

The post-recurrence follow-up period ranged from 10 days to 50.1 months (median, 15.0 months), and the 1- and 2-year post-recurrence survival rates were 68.3 and 45.8%, respectively; the median survival time (MST) after recurrence was 17.7 months (Fig. 1). Post-recurrence survival was analysed with respect to clinical factors (age at recurrence, sex, ECOG-PS at recurrence and smoking status), pathological factors (histology, pathological stage and EGFR mutation status), initial treatment (surgical procedure, whether induction chemo/chemoradiotherapy or adjuvant chemotherapy was used and their regimens) and factors related to recurrence (symptoms at recurrence, postoperative recurrence-free period, site and type of recurrence, use of systemic chemotherapy or EGFR-TKIs, response to first-line chemotherapy). Univariate analyses showed that the patient outcome was significantly poorer for patients with an age of ≥80 years at surgery, non-adenocarcinoma, wild-type EGFR, no adjuvant chemotherapy, no preoperative or postoperative chemotherapy, an age of ≥80 years at recurrence, a poor ECOG-PS at recurrence (PS 2–4), a postoperative recurrence-free period <12 months

Table 2: Predictors of post-recurrence survival; baseline and primary lung cancer characteristics

	Post-recurrence survival			*P*-value[a]	
	Patients (%)	MST (months)	2 year (%)	Univariate	Multivariate
Sex					
Male	50 (66)	11.7	37.2	0.2110	
Female	26 (34)	21.6	60.5		
Age at surgery (years)					
≤79	66 (87)	17.7	49.5	0.0128	0.460
≥80	10 (13)	9.2	18.0		
Smoking status					
Smoker	50 (66)	11.7	40.2	0.4185	
Non-smoker	23 (30)	21.6	57.5		
Histology					
Adenocarcinoma	53 (70)	19.8	52.9	0.0060	0.159
Non-adenocarcinoma	23 (30)	8.4	26.5		
Epidermal growth factor receptor mutation status					
Mutation	28 (37)	22.8	64.4	0.0378	0.012
Wild-type	39 (51)	10.5	29.8		
Pathological stage					
IA–IB	28 (37)	13.9	43.2	0.9820	
IIA–IIIB	48 (63)	15.5	47.3		
Initial surgery					
Lobectomy	60 (79)	17.7	51.3	0.1290	
Limited resection	16 (21)	9.8	15.5		
Induction chemotherapy					
Yes	5 (7)	17.7	20.0	0.6514	
No	71 (93)	15.5	48.2		
Adjuvant chemotherapy					
Yes	35 (46)	21.6	64.8	0.0021	0.001
No	41 (54)	9.8	29.0		
Chemotherapeutic regimen					
Paltinum-based	22 (29)	19.0	49.9	0.0082[b]	0.291[b]
Uracil-tegafur	16 (21)	21.6	72.2		
No	38 (50)	9.2	32.3		
Platinum-based chemotherapy					
Yes	22 (29)	13.2	47.0	0.3921	
No	54 (71)	19.0	49.9		

MST: median survival time
[a]Log-rank test for comparison of post-recurrence survival among groups.
[b]*P*-value for Paltinum-regimen and uracil-tegafur vs no perioperative chemotherapy.

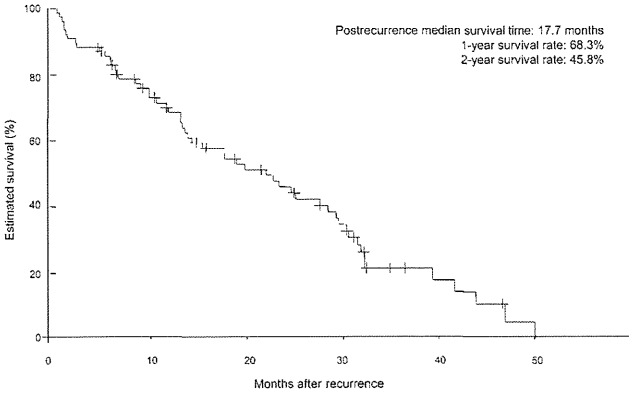

Figure 1: Survival curve illustrating the post-recurrence survival of 76 patients.

and no systemic chemotherapy for recurrence. Multivariate analysis of these factors identified six factors as independent prognostic factors: wild-type EGFR, no adjuvant chemotherapy, an age ≥80 years at recurrence, ECOG-PS 2–4, symptomatic and no chemotherapy for recurrence (Tables 2 and 3, Figs 2 and 3). A multivariate analysis of the 64 patients who underwent systemic chemotherapy showed that the response to first-line chemotherapy for recurrence (P <0.001) and the postoperative recurrence-free period (P = 0.026) were independent prognostic factors (Table 4).

DISCUSSION

In recent years, not only have numerous RCTs established evidence for chemotherapy, but new anti-cancer agents and molecular-targeted drugs have also been introduced, and personalized treatment strategies are now being recommended based on histology and molecular markers [23]. This standardization and personalization of treatment for NSCLC is improving the prognosis of patients with NSCLC. On the other hand, few studies have evaluated treatments for recurrent NSCLC after curative resection. In clinical practice, chemotherapy for recurrence is routinely administered based on the recommended regimen for unresectable advanced NSCLC. However, patients

Table 3: Predictors of post-recurrence survival: recurrent disease characteristics

	Post-recurrence survival			*P*-value[a]	
	Patients (%)	MST (months)	2 year (%)	Univariate	Multivariate
Age at recurrence (years)					
≤79	62 (82)	17.7	49.6	0.0182	0.001
≥80	14 (18)	9.2	20.4		
Performance status at recurrence					
0–1	56 (74)	18.8	58.1	< 0.0001	0.012
2–4	20 (26)	6.3	15.0		
Symptoms					
Yes	25 (33)	6.5	25.1	0.0032	0.003
No	51 (67)	21.5	55.4		
Disease-free interval (months)					
<12	33 (43)	13.3	26.4	0.0084	0.621
≥12	43 (57)	19.8	65.7		
Intra- or extrathoracic recurrence					
Intrathoracic only	42 (55)	15.5	42.8	0.1024	
Extrathoracic only	16 (21)	9.0	23.8		
Both	18 (24)	19.8	56.1		
Initial recurrence					
Single site	29 (38)	18.8	48.0	0.167	
Multiple	47 (62)	13.6	44.7		
Systemic chemotherapy					
Yes	64 (84)	17.7	50.2	<0.0001	0.003
No	12 (16)	1.2	12.5		
EGFR-TKIs (gefitinib and erlotinib)					
Yes	36 (47)	15.5	42.9	0.4205	
No	40 (53)	14.4	48.2		

EGFR-TKI: epidermal growth factor receptor tyrosine kinase inhibitors; MST: median survival time.
[a]Log-rank test for the comparison of post-recurrence survival among groups.

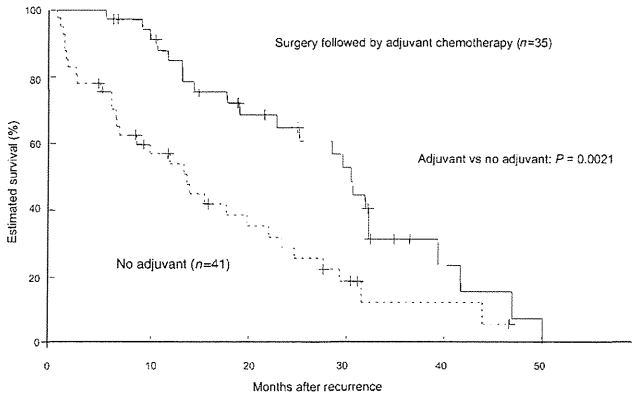

Figure 2: Survival curves illustrating the post-recurrence survival of 35 patients who initially underwent surgery followed by adjuvant chemotherapy and 41 patients who underwent surgery alone. The curves differed significantly for the patients treated with surgery followed by adjuvant chemotherapy vs the patients treated with surgery alone ($P = 0.0021$).

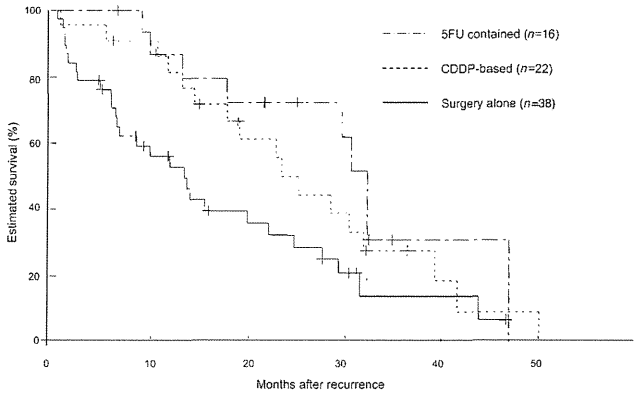

Figure 3: Survival curves illustrating the post-recurrence survival of 22 patients who received platinum-based induction or adjuvant chemotherapy, 16 who received adjuvant chemotherapy with uracil-tegafur and 38 who did not receive pre- or postoperative chemotherapy. The curves differed significantly for patients who received adjuvant chemotherapy with uracil-tegafur vs those who received no perioperative chemotherapy ($P = 0.0089$). However, the curves did not differ significantly for patients who received pre- or postoperative platinum-based chemotherapy vs patients who received no perioperative chemotherapy ($P = 0.1031$) or for patients who received adjuvant chemotherapy with uracil-tegafur compared with those who received pre- or postoperative platinum-based chemotherapy ($P = 0.4231$).

with postoperative recurrent disease can be anticipated to have a poor ECOG-PS and organ function as a result of pulmonary resection or old age. Furthermore, recurrence after pre/postoperative chemotherapy can theoretically be regarded as the proliferation of tumour cells resistant to anti-cancer agents. Therefore, the treatment and prognosis of postoperative recurrence must differ in some aspects from those used for clinical Stage IV NSCLC.

Previous studies of recurrent NSCLC have described a post-recurrence survival rate of 15–20% at 2 years and a post-recurrence MST of 8–13 months [17–19]. In this study, we only investigated patients who had undergone surgery after the mid-2000s, once adjuvant chemotherapy had become established as a standard therapy and found a 2-year post-recurrence

Table 4: Predictors of post-recurrence survival for 64 patients who received systemic chemotherapy

	Univariate *P*-value[a]	Multivariate
Sex		
Male vs female	0.6402	
Age at surgery (years)		
≤79 vs ≥80	0.1273	
Age at recurrence (years)		
≤79 vs ≥80	0.0783	
Performance status at recurrence		
0–1 vs 2–4	0.0010	0.494
Smoking status		
Smoker vs non-smoker	0.7829	
Histology		
Ad vs non-ad	0.2304	
EGFR mutation status		
EGFR mutation vs wild-type	0.1481	
Pathological stage		
IA–IB vs IIA–IIIB	0.4776	
Initial surgery		
Lobectomy vs limited resection	0.4904	
Induction chemotherapy		
Yes vs no	0.8522	
Adjuvant chemotherapy		
Yes vs no	0.0507	0.207
Perioperative chemotherapy		
Yes vs no	0.2780	
Platinum-based chemotherapy		
Yes vs no	0.6443	
Symptoms at recurrence		
Yes vs no	0.0867	
Disease-free interval (months)		
<12 vs ≥12	0.0351	0.026
Recurrent site		
Intra vs extra	0.4756	
Initial recurrence		
Single vs multiple	0.1266	
EGFR-TKIs (gefitinib and erlotinib)		
Yes vs no	0.1566	
Response of initial chemotherapy		
CR/PR/SD vs PD	<0.0001	<0.001

Ad: adenocarcinoma; EGFR: epidermal growth factor receptor; TKI: tyrosine kinase inhibitors; CR: complete response; PR: partial response; SD: stable disease; PD: progressive disease; NE: not evaluable.
[a]Log-rank test for the comparison of post-recurrence survival among groups.

survival rate of 45.8% and a post-recurrence MST of 17.7 months, an improvement in outcome compared with previous reports. This improvement likely reflects the effects of new anti-cancer agents, including EGFR-TKIs. This change in lung cancer chemotherapy can also be expected to have exerted an effect on prognostic factors for recurrent NSCLC. Factors previously reported as affecting the prognosis for recurrent NSCLC include ECOG-PS, whether symptoms are present at the time of recurrence, the postoperative recurrence-free period and pre- or postoperative chemotherapy. Among these, adjuvant chemotherapy has been regarded as a predictor of a poor prognosis for patients with recurrent NSCLC, although this topic has only been addressed by a few studies [15–19]. In our study, 38 (50%) patients received pre- and/or postoperative chemotherapy, with 22 undergoing platinum-based doublet chemotherapy pre- or postoperatively and 16 undergoing adjuvant chemotherapy with oral uracil-tegafur. Among these patients, those who underwent adjuvant chemotherapy had a significantly better outcome than those who did not. This finding differs from that of previous studies. Two possible reasons for this discrepancy can be considered: first, the therapeutic efficacy of EGFR-TKIs and other new anti-cancer agents, and secondly, the use of adjuvant chemotherapy with oral fluorouracil. In Japan, oral uracil-tegafur (referred to as UFT) is routinely used for adjuvant chemotherapy for completely resected pathological Stage IB NSCLC [24, 25]. In our study, oral uracil-tegafur was administered to 16 of the 76 (21%) patients, and the outcomes of these 16 patients were comparatively good (Fig. 3).

Because of the retrospective nature of this analysis, our study has some limitations. First, 33 patients (30% of the recurrent patients) had to be excluded because their post-recurrence course of treatment or outcome could not be analysed. The exclusion of 30% of the patients may have affected our results. Secondly, this study analysed only a small number of patients, and this number was lower than those included in previous studies. So, the conclusions drawn by this study limited the significance of the results obtained. Thirdly, screening for EGFR mutations was not performed in 9 of the 76 (12%) patients. Finally, the response to first-line chemotherapy was not evaluable in 8 of the 64 patients (13%) who underwent systemic chemotherapy for recurrence. These patients discontinued chemotherapy at an early stage because of chemotherapy-induced adverse events or an aggravated general condition caused by disease progression. To resolve these problems, analyse the prognosis of patients with recurrent NSCLC, and establish treatment strategies, multicenter, large-scale, prospective studies are required.

In this study, we investigated the post-recurrence outcome and prognostic factors for patients who had undergone surgery for NSCLC. The prognostic factors included EGFR mutation, adjuvant chemotherapy, ECOG-PS, age, symptoms at the time of recurrence and the use of systemic chemotherapy for recurrence. Although the post-recurrence outcome was better than in previous studies, the outcome for recurrent NSCLC remains poor. The use of adjuvant chemotherapy for initial treatment in accordance with the treatment guidelines is important. Further investigation and standardization of post-recurrence treatment are required.

Conflict of interest: All authors declare that they have no competing interests.

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CASE REPORT

Unknown primary large cell neuroendocrine carcinoma (LCNEC) in the mediastinum

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Abstract Unknown primary large cell neuroendocrine carcinoma (LCNEC) in the mediastinum is extremely rare. In this report, we present a case of a 53-year-old man with superior vena cava (SVC) syndrome who developed LCNEC in the middle mediastinum. His chief complaint was facial edema. Chest X-ray revealed an abnormal shadow in the right upper mediastinum. Computed tomography (CT) scan of the chest revealed a 67-mm mass in the middle mediastinum. Tumor invasion caused constriction of the SVC. The patient underwent induction chemoradiotherapy with vinorelbin and cisplatin and concurrent radiation therapy. After induction therapy, the tumor size decreased remarkably and was resected completely. The pathological diagnosis was LCNEC.

Keywords Mediastinal tumor · LCNEC · Induction chemoradiotherapy · Unknown primary tumor

Introduction

Large cell neuroendocrine carcinoma is a relatively new category of pulmonary neuroendocrine (NE) tumor. Travis et al. proposed a three-grade, four-type scheme for classification of NE tumors of the lung with typical carcinoid (TC) representing a low grade tumor, atypical carcinoid (AC) representing an intermediate grade tumor, and LCNEC and small cell lung carcinoma (SCLC) representing high grade tumors [1, 2]. The prognosis of LCNEC is known to be very poor. Recent clinical studies reported that the 5-year survival rate of patients with LCNEC for all disease stages was 40.3 % [3].

Although LCNEC was first detected in the lung, it appears in various organs. Here we report a very rare case of unknown primary LCNEC in the mediastinum.

Case report

A 53-year-old man was admitted to our hospital for close examination of an abnormal shadow on chest X-ray and computed tomography (CT). His chief complaint was facial edema. He had no other notable examination findings. He had smoked 25 cigarettes per day for 37 years. Chest X-ray revealed a protruding solid mass in the right mediastinum. Enhanced CT revealed a solid mass 67 mm in diameter with severe constriction of SVC and invasion of pulmonary artery in the middle mediastinum (Fig. 1a). PET/CT revealed intense uptake (SUV_{max} 14.5) of the tumor without any evidence of metastasis (Fig. 1c). Preoperative examination of the brain was not performed. He did not have obvious symptoms of brain metastasis.

The levels of tumor markers, such as CEA, CYFRA, Pro-GRP, and IL-2 were normal. The patient subsequently underwent EBUS-TBNA, but there was too little material in the specimen to diagnose. Therefore, we performed thoracoscopic biopsy and interpreted the findings as poorly differentiated squamous cell carcinoma or large cell carcinoma. Thoracoscopic examination revealed that the tumor had not originated in the lung; therefore, we speculated that the tumor had originated in the middle mediastinum. The patient received induction chemoradiotherapy with cisplatin (40 mg/m^2) on days 1 and 8, and vinorelbin (25 mg/m^2) on days 1 and 8, and concurrent radiotherapy

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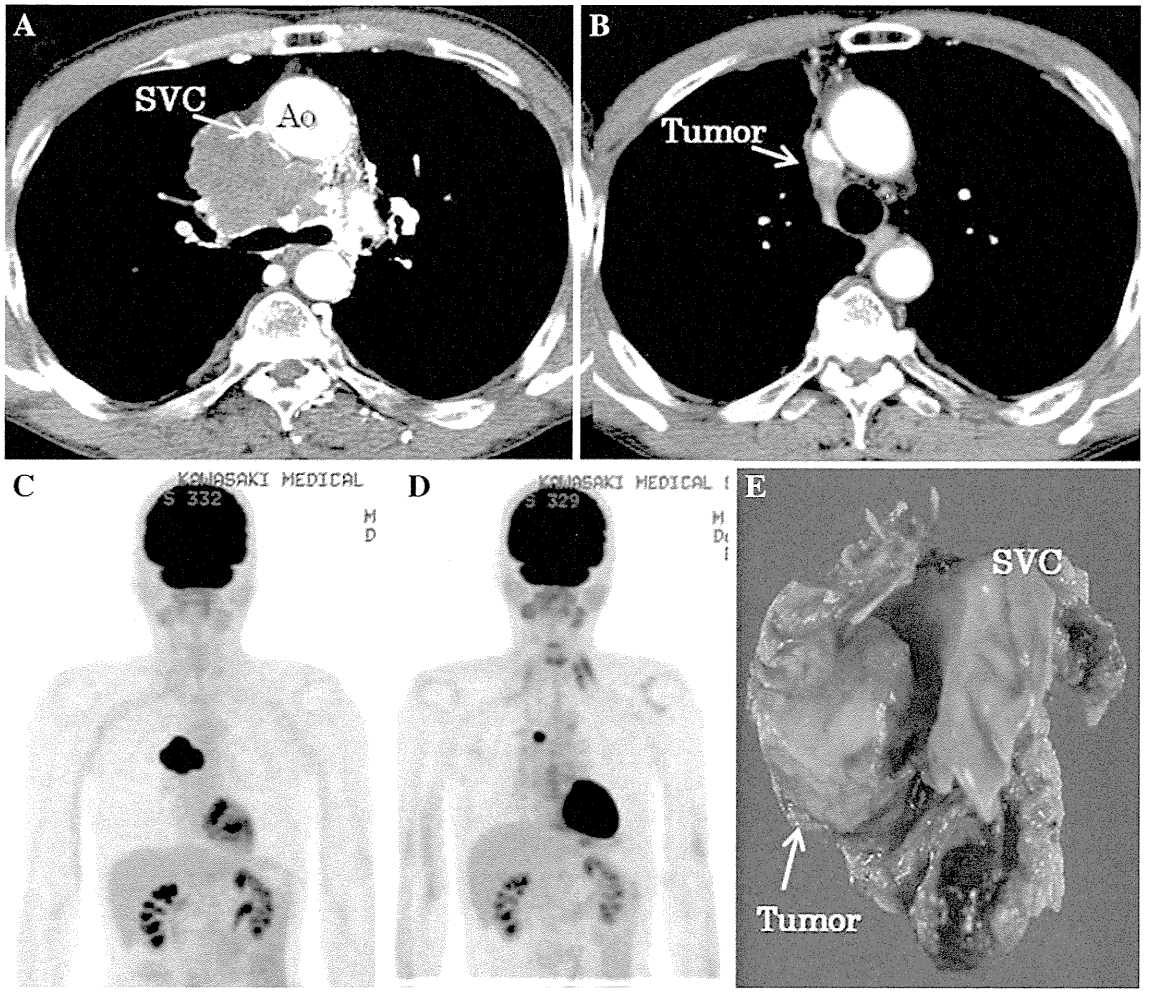

Fig. 1 **a** Enhanced CT revealed a solid mass 67 mm in diameter with severe constriction of SVC in the middle mediastinum. **b** Enhanced CT following induction therapy showed 66 % reduction in tumor size. **c** FDG-PET revealed intense uptake of the tumor without any evidence of metastasis. **d** There was no remarkable change in SUV_{max} after induction therapy. **e** The resected tumor had infiltrated SVC, but not been exposed to the lumen of the SVC

(total dose of 40 Gy). The chemotherapy cycles were repeated every 21 days for two cycles. The venous occlusive symptom disappeared in the early treatment phase. Enhanced CT/FDG-PET following induction therapy showed a partial response (66 % reduction in mass size) (Fig. 1b), but without a remarkable change in FDG activity from maximal standardized-uptake-value of 14.5 pre-therapy to 14.1 post-therapy (Fig. 1d).

After 4 months of initial detection of the tumor, the patient underwent tumorectomy with combined resection of SVC. Vascular reconstruction was performed between the left brachio-cephalic vein and the right auricular appendage, and between the right brachio-cephalic vein and the SVC with ringed polytetrafluoroethylene (PTFE) grafts. The resected tumor was 18 mm in diameter, had infiltrated SVC, but not been exposed to the lumen of the SVC (Fig. 1e). Microscopically, tumor cells were large and polygonally shaped, and had low nuclear to cytoplasmic ratio, coarse nuclear chromatin, and frequent necrosis. The tumor cells were scattered, forming abortive rosette-like structures. Immunohistochemically, the tumor cells were positive for synaptophysin, epithelial membrane antigen (EMA) and cytokeratin, but negative for thyroid transcription factor-1 (TTF-1) and choromogramin A.

Although CT scan revealed more than 66 % reduction in tumor size, most of the residual tumor cells were viable pathologically. Since there was no histological basis to suggest any primary organ of origin in the mediastinum, such as thymic tissue, or any evidence consistent with a lymph node metastasis, we labeled the tumor as an unknown primary LCNEC in the mediastinum.

The patient had an uneventful recovery and was discharged from the hospital on the 14th postoperative day. However, he developed multiple brain metastases with nausea and headache approximately 2.5 months postoperatively and he was treated with whole-brain irradiation.

Unfortunately, he died of extensive brain metastasis 5 months after surgery. At least, there were no other significant recurrences, including in the lung or local recurrence, in the examination conducted 1 month before the patient's death.

Discussion

Large cell neuroendocrine carcinoma is a new category of pulmonary neuroendocrine tumor, whereas LCNEC in the mediastinum is extremely rare. The majority of the reported causes of mediastinal LCNEC originated from thymus. To the best of our knowledge, unknown primary LCNEC in the mediastinum have been reported only 5 cases in the literature including our cases to date [4–7] (Table 1). Patient characteristics, treatments and prognoses are summarized in Table 1. All patients were males. The mean age of the 5 patients was 51.2 years (range 35–65). Three patients were asymptomatic. Induction CDDP-based chemotherapy was performed in 2 cases (nos. 2, 5), showing partial response (PR). Although complete resection was performed after induction chemotherapy, LCNEC recurred shortly postoperatively in both cases. The median overall survival was 11 months (range 2–13 months).

LCNEC is associated with poor prognosis due to high propensity for early distant hematogenous metastases. LCNEC and SCLC are categorized as high grade NE tumours because of their poor prognosis compared with those of other NE tumours of the lung.

Iyoda et al. reported 50 % postoperative recurrence rate of LCNEC in the lung [8]. Since the biological characteristics of LCNEC are similar to those of small cell lung cancer [3], these cases are trend to treat with chemotherapy regimens used for small cell lung cancer.

Previous reports suggest that perioperative chemotherapy is necessary to improve survival in patients with LCNEC of the lung. The 5-year survival rate of patients who underwent perioperative adjuvant chemotherapy was 87.5 %, whereas that of patients who underwent surgery alone was 58.5 % [9].

Some studies suggest that complete resection of pulmonary LCNEC followed by adjuvant chemotherapy using a regimen used to treat small cell lung cancer (platinum plus etoposide) could yield good outcomes [10, 11]. Rossi et al. reported a better survival for the 38 patients who received adjuvant chemotherapy. The multivariate analyses showed a better outcome for patients receiving a regimen of SCLC (platinum-etoposide) than a regimen of NSCLC ($p = 0.0001$) [10].

The role of neoadjuvant/adjuvant therapy for mediastinal LCNEC has not been adequately assessed given the limited number of reported cases. In the present case, induction therapy followed by surgery led to a complete resection of the tumor. However, the patient developed multiple brain metastases soon after surgery. The high biological malignancy grade of mediastinal LCNEC is clear from previously reported cases. We think that adjuvant chemotherapy should be administered to prevent distant metastasis. However, in our case, the patient could not be administered adjuvant chemotherapy because of his emaciation. When considering the severe biological malignancy grade and the frequency of brain metastases, prophylactic whole-brain irradiation may be beneficial. However, there is no evidence of the benefits of postoperative prophylactic irradiation in cases of LCNEC. We should consider postoperative whole-brain irradiation to prevent brain metastasis in the future.

Further study is warranted to determine the efficacy of adjuvant therapy for mediastinal LCNEC.

Table 1 Unknown primary LCNEC in the mediastinum reported in the literature

References	Age Sex	Symptom	Mediastinalsite	Ope	Chemotherapy regimen	RT	Outcome Survival
Natsuhara [4]	50	Asymptomatic	Middle	–	CPA ADM VCR etc.	+	DOD
	M						13 months
Takezawa [5]	35	Asymptomatic	Middle	+	CDDP BLM VP-16 (NA) etc.	–	DOD
	M			CR			12 months
Nojima [6]	65	Asymptomatic	Anterior	–	CDDP + CPT-11	+	AWD
	M						11 months
Lukina [7]	53	Shortness of breath	Posterior	–	NR	NR	DOD
	M						2 months
Maeda	53	SVC syndrome	Middle	+	CDDP + VNR (NA)	+	DOD
	M			CR			9 months

NR not reported, *CR* complete resection, *NA* neoadjuvant chemotherapy, *AWD* alive with disease, *DOD* dead of disease, *CPA* cyclophosphamide, *ADM* adriamycin, *VCR* vincristine, *CDDP* cisplatin, *BLM* bleomycin, *VP-16* etoposide, *CPT-11* irinotecan, *VNR* vinorelbine

Conclusions

We encountered a rare case of unknown primary LCNEC in the mediastinal. It was radically resected following induction therapy. The effect of induction therapy on mediastinal LCNEC has not been adequately assessed. In the present case, concurrent induction chemoradiotherapy with cisplatin and vinorelbin plus radiotherapy was shown to be effective. Induction therapy should be considered as one of the treatment options for radical resection.

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Case Study

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Lung cancer with sarcoid reaction in the lymph nodes following chemoradiotherapy

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Abstract

This report describes a case of lung cancer with sarcoid reaction following chemoradiotherapy, showing false-positive accumulation of ^{18}F-fluorodeoxyglucose on positron-emission tomography in a 55-year-old man. Treatment-related sarcoid reaction should be considered when the accumulation of ^{18}F-fluorodeoxyglucose shows rapid extension in the course of treatment.

Keywords

Adenocarcinoma, Lung neoplasms, Lymphatic metastasis, Positron-emission tomography, Sarcoidosis

Introduction

Positron-emission tomography (PET) with ^{18}F-fluorodeoxyglucose (FDG) plays an important role in the evaluation of response to chemotherapy or chemoradiotherapy, as well as detection of the primary tumor and metastatic lesions in several malignancies. Many reports have indicated that FDG-PET is more reliable and informative than conventional radiologic studies, such as chest computed tomography (CT) or magnetic resonance imaging, for the assessment of nodal status in patients with malignancy. However, FDG uptake is not always specific to malignancies and there are some reports of false-positive FDG accumulation in sarcoidosis and tuberculoma as well as other pathologies characterized by active inflammation.[1] This report describes a case of lung cancer with sarcoid reaction following chemoradiotherapy showing false-positive accumulation of FDG.

Case report

A 55-year-old man was referred to our institute for investigation of an abnormal shadow in the right upper lung field on chest radiography. He had no history of malignancy. The results of a physical examination were normal. Routine hematological and biochemical investigations were almost within normal ranges. Chest CT revealed a mass lesion measuring 55 mm in diameter in the right upper lobe and hilar lymphadenopathy (Figure 1(a)). FDG-PET demonstrated accumulation in the lung tumor and one hilar lymph node (Figure 1(b)). The patient underwent a CT-guided percutaneous needle biopsy, and was diagnosed with adenocarcinoma classified as clinical stage IIIB (T4N1M0). Because it was considered that the tumor had invaded the trachea, we initially performed induction chemoradiotherapy. The patient received 60 mg·m^{-2} of cisplatin on day 1 and 50 mg·m^{-2} of irinotecan on days 1 and 8, concurrent with 2 Gy of thoracic radiation on 5 days per week for a total of 20 Gy. Five weeks later, he received the second cycle of treatment and radiotherapy was restarted. When the radiation dosage reached 40 Gy, CT revealed that the primary tumor had reduced in size to 44 mm and the hilar lymph node had not

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