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En bloc partial vertebrectomy for lung cancer invading the spine after induction chemoradiotherapy

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Abstract

Objective: The optimal surgical treatment for non-small cell lung cancer (NSCLC) with vertebral body invasion remains both controversial and challenging. We reviewed our experiences of NSCLC with vertebral body invasion, in which we have performed induction chemoradiotherapy followed by lung resection with en bloc partial vertebrectomy. **Methods:** Six NSCLC patients with vertebral invasion underwent an operation following chemoradiotherapy from January 2001 to July 2006. Vertebral invasion was evaluated by the chest CT and MRI findings. Either carboplatin—paclitaxel ($n = 3$) or carboplatin—docetaxel ($n = 3$) was used. Two cycles of chemotherapy were performed with concurrent radiation (50 Gy) treatment. **Results:** In all of the six cases, a complete resection with en bloc partial vertebrectomy was performed with no operative mortality. The histological complete response rate and major response rate were 16.7% (1/6) and 83.3% (5/6), respectively. The 5-year overall survival rate was 67.7%. In addition, no local failure was observed after surgery. **Conclusions:** Surgery after chemoradiotherapy (carboplatin/paclitaxel or docetaxel and 50 Gy radiation) for NSCLC with vertebral invasion could thus be performed with acceptable morbidity.

Keywords: En bloc partial vertebrectomy; Induction chemoradiotherapy; T4 non-small-cell lung cancer

1. Introduction

The treatment of patients for non-small cell lung cancer (NSCLC) with vertebral body invasion remains challenging. Historically, Paulson identified that the invasion of a vertebral body was a contraindication for a surgical resection of superior sulcus tumors [1]. Komaki et al. reported that direct vertebral invasion was considered to be a poor prognostic factor for superior sulcus tumors [2]. Recently, chemoradiotherapy has become the standard treatment for non-resectable stage IIIA and stage IIIB NSCLC [3,4]. Furthermore, the introduction of spinal surgery into lung cancer operations has now made the prognosis of lung cancer with vertebral invasion much better [5—7]. In this study, we review our early results of induction chemoradiotherapy and en bloc surgery (lung resection and partial vertebrectomy) for c-IIIB NSCLC with vertebral invasion.

2. Patients and methods

We reviewed six NSCLC patients with vertebral invasion who were treated by concurrent chemoradiotherapy and surgery from January 2001 to July 2006 at Kagawa university hospital. Vertebral invasion was evaluated by the chest CT and MRI findings. No distant metastasis revealed by chest CT, abdominal CT, brain CT or brain MRI, and bone scan. N factors were three N0, one N1, one N2, and one N3. Mediastinal nodal involvement was evaluated by CT findings (a short-axis diameter of more than 1 cm). For c-N2 disease, positron emission tomography with F-18-fluorodeoxyglucose (FDG-PET) was done before and after induction therapy. For N3 disease, needle biopsy was done before and after induction therapy, and mediastinoscopy were done before thoracotomy. Chemotherapy was conducted during week 1 and week 5, respectively. Concurrent radiotherapy with 50 Gy (2 Gy/day, 5 days/week) was carried out. Re-evaluation was carried out based on the chest CT findings, abdominal CT, brain CT or MRI and bone scans 2—3 weeks after the end of radiation therapy. In N2 and N3, if down-staging of N-factors to N1 or N0 were achieved, thoracotomy was scheduled. There were three carboplatin—paclitaxel and three carboplatin—docetaxel chemotherapy. Carboplatin—paclitaxel chemotherapy

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consisted of carboplatin (AUC = 6 mg/ml/min, 30 min, intravenous infusion) on day 1 and paclitaxel (180 mg/m^2, 3 h, intravenous infusion) on day 1. Premedication for the prevention of hypersensitivity reactions included dexamethasone, diphenhydramine, and cimetidine. Carboplatin—docetaxel chemotherapy consisted of carboplatin (AUC = 6 mg/ml/min, 30 min, intravenous infusion) on day 1 and docetaxel (60 mg/m^2, 3 h, intravenous infusion) on day 1. An area including the hilum of the lung and mediastinum with a 1.5 cm margin from the periphery of the primary lesion was irradiated with 2 Gy per day. The patient's informed consent has been obtained. This study was approved by the Institutional Review Board of the Kagawa University.

2.1. Statistical analysis

A statistical analysis of the data was carried out using the Stat View 4.5 J program. The survival curves were estimated by the method of Kaplan and Meier [8].

3. Results

The median observation time was 4.5 years. Follow-up was available on all six patients. The median age was 60.2 years (range 52—71 years). The group comprised five men and one woman. Three had squamous cell carcinoma and three had adenocarcinoma. The induction therapy was generally well tolerated. The overall response rate of conventional re-evaluation was 66.7% (CR one case and PR three cases) and stable disease was identified in two cases. After induction therapy, nodes status of c-N2 and c-N3 were estimated as negative N2 by PET or mediastinoscopy, respectively. Therefore operation was scheduled for all six patients.

All vertebrectomies were done by one orthopedic surgeon. Pathological examination confirmed the complete margin-free resection of lung cancer invading chest wall and vertebral body. One-incision approach was performed with an enlarged posterolateral thoracotomy [5]. The superior part of the skin incision started at one upper vertebra beyond the invaded vertebra along with a midline posterior vertebral line. A thoracotomy was done through the fifth intercostals space. After the recognition of resectability, an anterior transection of the invaded rib was done. After completing the lung resection, the anterior surface of vertebra was inspected through the thoracic cavity. At that time, the extent of the vertebral resection was determined. After rotating the operation table in an anterior direction, the posterior surface of the ribs and transverse processes were exposed. A transverse resection of the vertebral body without the canal manipulation was performed in two cases (level T2—T3 and level T3) (Fig. 1, upper part). One-third resection of the vertebral body with the canal manipulation was performed in two cases (level T1—T3 and T9) (Fig. 1, middle part). A hemivertebrectomy was performed in two cases (level T2—T3 and level T2—T5) (Fig. 1, lower part). In all cases, no reconstruction of the vertebral body was done. Lobectomies were performed in five patients and a segmentectomy in one patient. The mean duration of the operation was 7.63 h (range 6.05—10.62 h). The mean blood loss was 2327.7 ml (range 415—5412 ml). Major postoperative

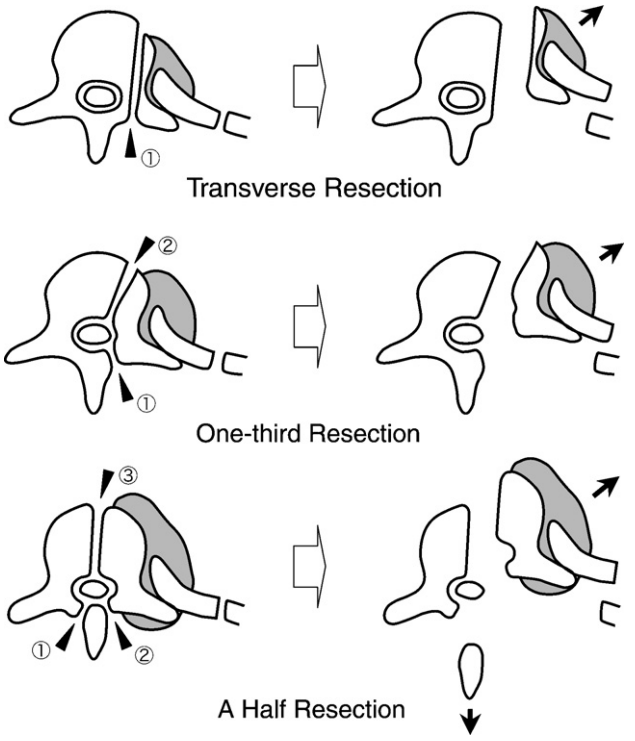

Fig. 1. Techniques of vertebrectomies. Transverse resection (upper part): An oblique osteotomy was done from the posterior (① ▼) to the thoracic cavity. One-third resection (middle part): An osteotomy of the body was performed from posterior to the canal (① ▼) and subsequently from the thoracic cavity to the canal (② ▼). A half resection (lower part): A laminectomy was performed (① ② ▼) first and thereafter an osteotomy of the vertebral body was performed from the thoracic cavity to the canal (③ ▼).

complications were observed in two patients. In one patient, severe pneumonia occurred. In one patient persistent air leakage was observed and a reoperation thus had to be done. He died 4 months after the operation due to empyema and sepsis. The pathological effect of induction therapy was evaluated according to General Rule for Clinical and Pathological Record of Lung Cancer (The 6th Edition, October 2003, The Japan Lung Cancer Society) [9]. A complete pathological response (complete cancer cells death) was achieved in one case (16.7%). A major response (less than one third cancer cells viable) was achieved in five cases (83.3%). In all six cases, no viable cancer cells were found in the resected vertebral body. There were one p-T0N0M0, one p-T3N2M0 and four pT3N0M0. There was no operative mortality (within 1 month after operation).

The 5-year overall survival rate was 66.7 % (Fig. 2). One complete pathological response patient has been alive more than 5 years. Three of five patients with a major response are alive (3—5 years, two without recurrence and one brain metastasis). One died one year after the operation due to lung metastasis but not due to local recurrence. No local recurrence was observed in any of the six cases.

4. Comment

Local control, including a surgical resection, was the significant prognostic factor in the therapy of superior sulcus

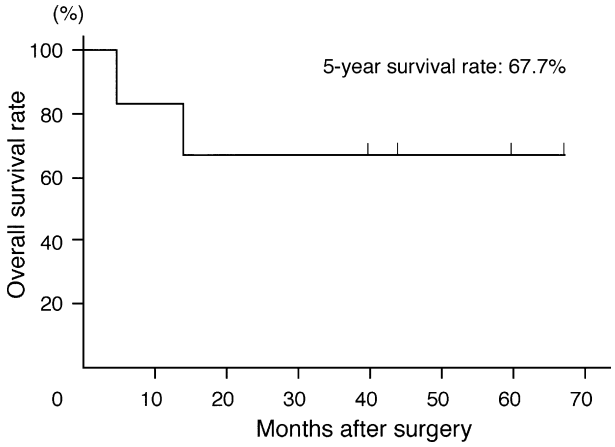

Fig. 2. Overall survival of all six patients.

tumors [2]. Grunenwald and Albain suggest that recent advances in chemotherapy make it possible to control distant metastasis and surgery may be superior to radiation therapy in the treatment of vertebral invasion IIIB NSCLC [10]. Furthermore, with the recent introduction of refined spinal surgery to thoracic surgery, promising results for the surgery of vertebral invasion T4 have been reported. As a result, if definitive surgery is possible after induction chemoradiotherapy, then surgery per se will be the therapy of choice for vertebral invasion T4.

Our study shows that induction chemoradiotherapy followed by a complete surgical resection for vertebral invasion T4 NSCLC could be performed with acceptable morbidity. Our treatments comprise taxanes (paclitaxel or docetaxel)–carboplatin chemotherapy, concurrent 50 Gy irradiation and surgery. Gandhi et al. and Grunenwald et al. reported aggressive multidisciplinary surgical approaches for superior sulcus tumors with vertebral invasion to have favorable survivals [6,7]. Their approaches were heterogenous, including pre or postoperative radiation, pre or postoperative chemotherapy, and induction chemoradiotherapy [6,7]. Our experiences are limited and the number of the patients examined was small. However, our protocol was confirmed and homogeneous. The pathological effects of our patients resulted in one CR and five major effects. The 5-year survival was 67.7% and four of six patients were alive 3–5 years after the treatment. Komaki et al. reported that local control was a significant factor in superior sulcus tumors and that surgery also played an important role in the local control of superior sulcus tumors [2]. In our study, although the number of patients was small, no local recurrence was observed and our induction therapy followed by en bloc partial vertebrectomy may therefore be a useful treatment modality for vertebral body invasion IIIB NSCLC.

We used an enlarged posterolateral thoracotomy [5] as our approach for the IIIB NSCLC with vertebral invasion. This classical approach has some major benefits, i.e. one-incision and no need of a position change. As Grunenwald reported, an en bloc resection of lung cancer invading vertebral body is complex and difficult to perform [7]. In fact, the mean duration of our operation was 7.63 h and the mean blood loss was 2327.7 ml. If the condition of a patient during this type of operation is unstable and serious, then a position change may be dangerous. Another advantage over the prone position is that the surgeon can observe the condition of the invaded vertebra from both inside and outside. As a result, an adequate and safe surgical margin of the vertebral body can thus be selected. If there is no invasion to the subclavian vessels, an enlarged posterolateral thoracotomy is thus a useful approach for IIIB NSCLC with vertebral invasion. There were no events related to the spinal cord by chance, but in case of more than a half vertebrectomy, the reconstruction of the body will be recommended [6,7].

In conclusion, surgery after induction therapy (Taxanes/carbopatin and 50 Gy radiation) for vertebral invasion T4 NSCLC could therefore be performed with acceptable morbidity and mortality. To perform a partial vertebrectomy, an enlarged posterolateral thoracotomy is useful and safe, if there is no invasion to the subclavian vessels.

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