

Complete Resection of Pulmonary Metastatic Melanoma

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Background: The prognosis of melanoma metastasized to other organs is very poor. There have been many studies on metastatic melanoma in Western society, but there have been few studies done in Korea because of the small number of cases. **Materials and Methods:** A retrospective review of 7 patients who underwent complete resection of pulmonary metastases from melanoma from January 2005 to December 2009 was performed. When the primary lesion was controlled or simultaneously controllable and no other metastatic lesion was found, pulmonary resections were performed. We analyzed the clinical prognoses after the initial melanoma diagnosis. **Results:** Of the seven patients, one was male and six were female. The mean age was 58.2 years (range 45~71). Six patients had a single pulmonary lesion and one patient had three lesions confined to the same lobe. The mean disease-free interval was 43.5 months (0~146 months). Before pulmonary resection, 4 patients had received systemic therapy. After pulmonary resection, 6 patients received systemic therapy. Complete resection was confirmed histologically. The metastasectomy was performed by wedge resection (6 patients) or lobectomy (1 patient). There were no mortalities or complications. After pulmonary resection, 1 patient had recurrent multiple lesions in the lung and 4 patients had metastases to other organs. The organs were the liver, brain, pleura, and lymph nodes. The mean observation time was 31.6 months and 3 patients died during observation. The mean survival was 27.7 months (14~60 months) and the 1-year and 3-year survival rates were 100% and 42%, respectively. **Conclusion:** When patients were selected carefully, the complete resection of pulmonary metastatic lesions was considered a major therapeutic tool.

Key words: 1. Metastasectomy
2. Melanoma
3. Prognosis

INTRODUCTION

The prevalence of melanoma is rapidly increasing because of the spread of the Westernized lifestyle and diet. It has been reported that 55,100 people in the United States were diagnosed with melanoma in 2004, and that melanoma constituted 0.2% of all cancer cases in Korea, according to 2007 Korean Ministry of Health and Welfare statistics [1,2]. After the treatment of melanoma at the primary site, melanoma can

recur locally and can metastasize to any organ. 30% of all melanoma patients will have metastases [3]. Metastatic melanoma is usually associated with a dismal prognosis. The mean survival is only 6 to 8 months, and the 5-year survival rate is about 5% [4-6]. In general, the prognosis depends on the initial site of metastasis. More than 80% of patients with metastatic melanoma initially show only one distant organ site involved. The most common metastatic organ is the lung, and about 40% of patients with metastatic melanoma initially

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Table 1. Patient characteristics for primary melanoma

| Patient | Age/Gender | Primary site | Postoperative systemic therapy |
|---------|------------|---------------------|--------------------------------|
| 1 | 63/F | Chest wall | Yes |
| 2 | 58/F | Right heel | Yes |
| 3 | 45/F | Right maxilla | No |
| 4 | 71/F | Right middle meatus | No |
| 5 | 59/F | Right heel | Yes |
| 6 | 59/M | Right hand thumb | No |
| 7 | 53/F | Vulva | Yes |

show isolated pulmonary metastasis. Progress of the disease can be attenuated by complete pulmonary metastatectomy [5].

Complete response to systemic therapy is very rare (10~15%), making complete resection a very effective treatment modality in pulmonary metastatic melanoma [5,7]. Complete resection has been shown in many studies to be associated with a 5-year survival rate as high as 39%, compared to a 3% to 5% 5-year survival rate for systemic therapy patients [3,4,8].

We retrospectively analyzed the clinical outcome of complete resection performed in patients with pulmonary metastatic melanoma.

MATERIALS AND METHODS

A retrospective clinical review was performed of the medical records of 7 patients who underwent complete surgical resection of pulmonary metastases from melanoma between January 2005 and December 2009 after the primary melanoma had been controlled. The indications for metastasectomy included a curable or cured primary tumor, no evidence of extra-pulmonary metastases, complete resectability of the pulmonary metastasis, and the patient being in a condition to tolerate surgery. We obtained information regarding the disease-free interval (DFI) and other organ metastasis after metastasectomy from medical records. Pulmonary metastatic melanoma was diagnosed when the HMB 45 and the S-100 immunohistochemistry stain of the specimen were positive. One of the 7 patients with coincidental lesions at the lung and the primary site underwent pulmonary metastasectomy and primary melanoma resection simultaneously. The DFI was de-

Table 2. Patient characteristics for pulmonary metastasis

| Patients | DFI (months) | Location | Tumor number and size (largest) | Performance status (ECOG) |
|----------|--------------|----------|---------------------------------|---------------------------|
| 1 | 54 | RUL | One/0.7 cm | 1 |
| 2 | 29 | RLL | One/0.6 cm | 1 |
| 3 | 30 | LLL | One/1.2 cm | 0 |
| 4 | 0 | LLL | One/1 cm | 2 |
| 5 | 24 | RLL | One/1.2 cm | 0 |
| 6 | 22 | LLL | Three/2.9 cm | 1 |
| 7 | 146 | LLL | One/2.5 cm | 0 |

DFI=Disease free interval; ECOG=European Cooperative Oncology Group; RUL=Right upper lobe; RLL=Right lower lobe; LLL=Left lower lobe.

defined as the time between the occurrence of pulmonary metastasis and resection of the primary melanoma. The survival curves were calculated by the Kaplan-Meier method and differences were tested by the log-rank test.

RESULTS

There was one male and six female patients. The mean age was 58.2 years (range 45~71). Six patients had a single pulmonary lesion and one patient had three lesions confined to the same lobe. The pulmonary metastasectomy was performed by wedge resection (6 patients) or lobectomy (1 patient). Complete resection was performed in all patients and confirmed histologically. There were no mortalities or complications after operation. The mean DFI was 43.5 months (0~146 months). Before pulmonary resection, 4 patients had received systemic therapy. After pulmonary resection, 6 patients received systemic therapy. After pulmonary resection, 1 patient had recurrent multiple lesions in the lung and 4 patients had metastases to other organs. The organs were the liver, brain, pleura, and lymph nodes. The mean observation time was 31.6 months and 3 patients died during observation. The mean survival was 27.7 months (14~60 months) and the 1-year and 3-year survival rates were 100% and 42%, respectively (Table 1~3, Fig. 1).

Table 3. Characteristics of pulmonary metastasectomy

| Patients | Surgical procedure | Survival time (month) | Post-operative systemic therapy | Survival |
|----------|--------------------|-----------------------|---------------------------------|----------|
| 1 | Wedge resection | 60 | Yes | Alive |
| 2 | Wedge resection | 24 | Yes | Dead |
| 3 | Wedge resection | 14 | Yes | Alive |
| 4 | Wedge resection | 36 | No | Alive |
| 5 | Wedge resection | 29 | Yes | Dead |
| 6 | Lobectomy | 15 | Yes | Dead |
| 7 | Wedge resection | 16 | Yes | Alive |

DISCUSSION

Melanoma is a malignant tumor of melanocytes from the neural crest. Melanocytes are found predominantly in the skin, but are also found in all part of body [9,10]. The prevalence of melanoma is rapidly increasing because of the spread of the Westernized lifestyle and diet in the Republic of Korea. Melanoma constituted 0.2% of all cancer cases in Korea according to a 2007 report by the Korean Ministry of Health and Welfare [6,10]. After the primary melanoma is controlled, recurrence may develop. About 30% of patients have metastasis. More than 80% of patients with metastatic melanoma initially show only one distant organ site involved. The lung is the most common organ involved, with about 40% of patients showing isolated pulmonary metastasis [3,5, 11-13]. Metastatic melanoma is usually associated with a dismal prognosis. The mean survival of patients with metastatic melanoma is 6 to 8 months [4,5,8,11,14]. There are many studies for metastatic melanoma in Western society but there are few studies in Korea because of the small number of cases. Many studies have shown that systemic chemotherapy and immune therapy have little effect on metastatic melanoma, especially on lesions over 2 cm in size [4,5,8,11,12,14, 15]. Unlike systemic therapy, surgery can provide a patient with immediate disease-free status from metastatic melanoma with little morbidity and improved long-term survival [15,16]. Only complete resection can improve the long-term survival of the patient, especially those with a single metastatic lesion [14]. Among all distant metastases from malignant melanomas of the skin, pulmonary metastasis occurs most frequently. Patients are usually asymptomatic, so PET-CT and chest CT

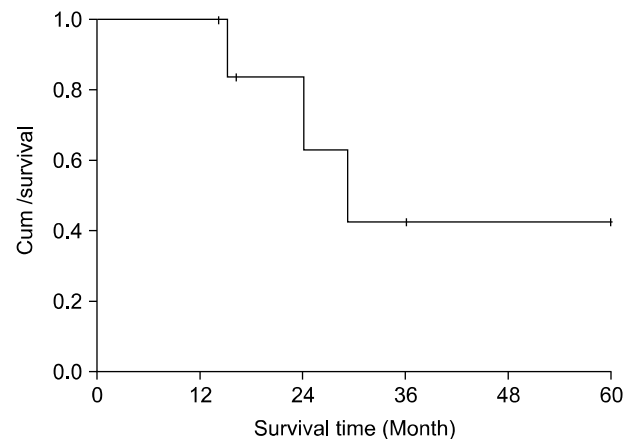


Fig. 1. Overall survival of patients. The mean survival was 27.7 months and The 1-year and 3-year survival rates were 100% and 42%, respectively.

are needed in follow-up after the primary site is controlled. Studies combining PET-CT and conventional chest CT show 88% sensitivity, 91% specificity, 15% false negative, and 10% false positive. This process can be used to define metastatic lesions with a size of 5 mm [3,5,6,8,14,17,18]. A previous study (IRLM, International Registry of Lung Metastasis) has suggested some significant prognostic factors for metastatic melanoma. Factors included the number of pulmonary nodules, the DFI, the site of metastasis (visceral vs. non-visceral), and the completeness of resection. The completeness of resection is the most important of these factors [3,5,7,15, 16]. One study showed that the patients with complete resection had a 5-year survival of 29% and a mean survival of 40 months [18]. Another study showed that the patients with incomplete resection had a 5-year survival of 13% and a mean survival rate of 11 months [12]. The 5-year survival rate of patients with a DFI over 36 months was 30%, compared to 17% in the patients with a DFI below 36 months. The DFI in our study was 45.5 months, but the 5-year survival could not be calculated using the DFI because of the small number of cases. Although the prognosis of metastatic melanoma is poor, complete resection can improve long-term survival. Even incomplete resection can provide longer survival than systemic therapy, which means resection itself can attenuate the tumor burden and improve immunity [3,5,11,12]. By mechanical reduction of the immunosuppressive factors of the tumor, surgery can restore immunity to a level that con-

trols the progression of metastases and ensures a durable clinical response. The current AJCC staging system categorizes the M stage by metastatic site because of different prognosis. Skin, subcutaneous tissues, and distant lymph node metastases are categorized as M1a. Pulmonary metastases are identified as M1b. Metastases to other visceral sites, or patients with skin, soft tissue, or lung metastases have M1c disease [7,11]. Patients with pulmonary melanoma metastases tend to survive longer than patients with other visceral metastases, so they may need aggressive treatment [3,10,14]. Surgical therapy for pulmonary metastasis is not a new treatment modality, as the first metastasectomy was performed more than 50 years ago [15]. In Korea, the surgery is usually limited to the occasional complete resection of a solitary visceral metastasis, or for palliative resection for symptomatic metastases causing bowel obstruction and brain hemorrhage, because of little insight and attention [10,11,18]. The Korean clinical protocol for defining the pathology of a malignant melanoma is different from that of Western clinicians. The 1-year and 5-year survival rates in our study were 100% and 42%, respectively. Although our study involved few cases, we observed the effectiveness of complete resection in metastatic melanoma. Melanoma is not yet a commonly encountered cancer in Korea. Because there were only 7 cases in our study, further studies will be needed.

CONCLUSION

The prognosis of melanoma metastasis to other organs is very poor. But when the patients were selected carefully, the complete resection of pulmonary metastatic lesions can improve survival of the patients with pulmonary metastatic melanoma.

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