Resection of Pulmonary Metastases from Malignant Melanoma: Results of a 16-Year Experience

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ABSTRACT Between 1970 and 1986, 49 patients had resection of presumed pulmonary metastases from malignant melanoma. Sixteen patients were found to have benign disease only despite the appearance of a new nodule in 13. Patients with benign disease had a significantly longer mean survival (169 months) compared with the group with malignant disease (22 months). Median survival for all patients with malignant disease was 13 months. Survival after resection did not correlate with the Clark level of the original lesion, lymph node status, disease-free interval, or number of nodules on preoperative tomograms. Two of 10 patients with 1 nodule resected are long-term survivors (88 and 120 months). Exploration in patients with presumed pulmonary metastases from melanoma is justified to rule out benign disease even if a new solitary nodule is detected. There are no prognostic indicators predicting survival after resection of melanoma metastases, and a significant number of patients will have benign disease.

The use of thoracotomy for the resection of metastatic tumors has been shown to prolong survival when used selectively in patients with favorable histologies. Three-year survival of more than 30% has been reported in patients undergoing metastasis removal with primary histologies of osteogenic sarcoma [1], soft tissue sarcoma [2], and urinary tract cancers [3]. Not all histologies have given favorable results; the unfavorable or less favorable histologies include colorectal disease, breast cancer, and uterine or cervical cancer [4]. Metastatic melanoma has generally been considered an unfavorable histology, yet the number of patients reported is significantly less in all series than the number with other histologies.

Mathisen and associates [5] presented a series of 33 patients who were proven to have metastatic melanoma resected at the National Cancer Institute from 1957 to 1978, with no 5-year survivors reported. This report updates and reexamines the efficacy of excision of pulmonary melanoma metastases at the same institution. Particular attention is given to the possible prognostic factors of survival including the original lesion of the Clark level of lymph node involvement, number of nodules on preoperative studies, and number of nodules resected.

Material and Methods

Between 1970 and 1986, 971 patients were admitted to the Clinical Center, National Cancer Institute, with a diagnosis of malignant melanoma. During that time, 49 patients had thoracic exploration through thoracotomy or median sternotomy for the resection of presumed pulmonary metastases for melanoma. There were 31 male and 18 female patients with a median age of 50 years (range, 17 to 67 years). All patients had extensive preoperative staging prior to attempted resection including bone scan, computed tomography of the head or brain scan, computed tomography or scan of the liver, full linear tomograms, or, most recently, computed tomography of the chest (22 patients). Only 5 patients seen prior to January, 1978, underwent computed tomography of the chest, and these scans were performed on a first-generation computed tomographic (CT) scanner.

Patients were considered eligible for thoracic exploration if the primary tumor was controlled, the presence of new pulmonary lesions was consistent with metastases in the absence of extrapulmonary metastases at the time of thoracotomy, and the resection would leave the patient with sufficient pulmonary parenchymal reserve. The operative procedure was performed as described previously [1, 2].

The Clark level of the original melanoma was available for 36 patients, and nodal status at the time of the original primary operation was available for all patients. Patients were examined in regard to long-term survival with respect to the original Clark level, original nodal status, disease-free interval from the time of original melanoma resection to diagnosis of thoracic disease, completeness of thoracic resection, number of nodules on preoperative roentgenographic studies, and number of nodules resected at the time of operation. Survival curves were estimated by the method of Kaplan and Meier. Most comparisons between groups were made by means of the generalized Wilcoxon test of Gehan. All p values resulted from two-sided tests.

Results

Operative Findings

A total of 59 explorations, 55 thoracotomies and 4 median sternotomies, were performed in the 49 patients. The majority of patients (32/49, 65%) had metastatic disease at exploration, and 16 (33%) had benign
disease. One patient was found to have a primary lung cancer. Three patients had a repeat thoracotomy for recurrent disease. There were no operative deaths.

A total of 197 nodules were removed, 111 of which were metastatic melanoma. The histologies of the benign disease included granulomatous disease, anthracotic nodules, lymphoid aggregates, hematoma, histiocytosis, pericardial disease, and pneumocystis and nonspecific pneumonitis. Of the 16 patients with benign disease, 13 had the appearance of a new nodule on preoperative roentgenographic studies. Only 74 (38%) of the 197 nodules resected were visualized on preoperative linear tomograms. Eighteen of the patients had both preoperative computed tomograms and linear tomograms. Of 90 resected nodules in these patients, preoperative computed tomograms revealed 41 (46%) compared with 24 (27%) visible on linear tomograms (p < 0.05).

Actuarial Survival Following Resection

Long-term survival data were available on 47 (96%) of the 49 patients. The actuarial median survival following thoracotomy for 31 patients with histologically documented metastases was 13 months. Of these 31 patients, 20 had complete resection of metastatic disease and 11 had incomplete resection either because of the inability to remove all nodules or the presence of histologically documented thoracic lymph node metastatic disease at the time of exploration. Patients found to have benign disease (N = 16) (none of the excised nodules revealing melanoma) had significantly longer survival than patients with malignant disease (mean survival of 169 months versus 22 months, respectively; p ≤ 0.001). There was no difference in survival between patients who had complete and those with incomplete resection (Fig 1).

Possible Influence of Prognostic Variables

CLARK LEVEL. Of the 20 patients who had complete resection of the metastatic nodules, no difference in actuarial survival was noted when lower Clark levels were compared with higher levels. Similarly, the Clark level of the original lesion had no prognostic implications when all patients (those with complete resection, incomplete resection, and benign disease) in this series were examined.

NODAL STATUS. The pathological status of the lymph nodes at the time of resection of the original melanoma was examined in all patients as well as in the patients who were found to have pulmonary metastatic disease only. In no patient did the status of the lymph nodes correlate with actuarial survival after resection of metastasis.

DISEASE-FREE INTERVAL. Survival following thoracotomy did not correlate with disease-free interval, that is, time from resection of the primary tumor to recurrence of pulmonary metastases. Specifically, there was no correlation for survival in a comparison between disease-free intervals of 12 months or less versus more than 12 months.

NUMBER OF NODULES ON PREOPERATIVE LINEAR TOMOGRAPHY. Twenty-nine of the 31 patients proven to have metastatic melanoma at resection underwent preoperative linear tomography, and the number of nodules detected by linear tomography in these patients was correlated with survival after nodule excision. The number of nodules on preoperative linear tomograms was not a significant predictor of survival after thoracotomy (Fig 2). It should be noted, however, that no patient with 2 or more nodules seen on preoperative tomography lived longer than 3 years after resection while 2 patients with 1 nodule or more on preoperative tomograms lived...
A detailed analysis of the prognostic factors including characteristics of the primary tumor was not helpful in predicting survival. Neither the Clark level of the original lesion nor the nodal status could predict survival. The inability of nodal status to predict long-term survival after resection of melanoma metastasis has been hinted at in the literature. Two of the 5-year survivors in the study of Cahon [6] actually had positive hilar lymph nodes found on examination of the specimen. Takita and colleagues [8] reported no correlation between survival and disease-free interval in 17 patients undergoing resection of metastases from melanoma, and this is confirmed by our data. Finally, no cutoff point in the number of nodules present on preoperative workup could be found to have prognostic significance in regard to survival, unlike studies of metastasis resection in soft tissue and osteogenic sarcomas. Moreover, the correlation between the number of nodules on preoperative studies and the number of resected nodules was poor. Although not significant, the only group of patients with long-term survival were those with 1 nodule seen on preoperative studies and 1 nodule resected. No patient with more than 1 nodule resected lived more than 3 years.
The variable biological behavior of melanoma makes it impossible to predict with certainty who will benefit from metastasis removal, and these results seem to call for heightened patient selectivity. The disappointing results, however, in our opinion, must be weighed against the background of failure in treating these patients with chemotherapy and radiation therapy. In the future, the role of melanoma metastasis excision may need further redefining in light of the favorable reported responses of metastatic melanoma to newer immunotherapeutic manipulations including the systemic use of lymphokines [9].

Hence, we favor exploration of patients with new pulmonary lesions and a past history of malignant melanoma when complete staging reveals no other site of disease and there is control of the primary lesion. Exploration of patients with solitary nodules is justified, in our opinion, to rule out the presence of benign disease to prevent further adjuvant therapy, and, in a select group of patients, may be associated with prolonged survival. Those patients who have multiple nodules resected will be in a poor prognostic category and on recurrence, may be eligible for newer immunotherapy regimens. Those patients found to have unresectable disease or who are left with objective disease that can be followed roentgenographically, could possibly graduate immediately to innovative therapies including the use of interleukin-2 [9], interferon [10], or monoclonal antibody treatment [11, 12].

References