PULMONARY METASTASES: RESULTS OF SURGICAL RESECTION IN 60 CASES: TREATMENT MODALITIES OTHER THAN SURGERY ARE NEEDED

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Abstract- Pulmonary metastases occur in 30% of all oncology patients. Surgical resection of lung metastases is a widely accepted procedure but long-term results are disappointing with a 5-year survival rate of 20-40% and the results vary with the histologic type of the primary tumor. Due to unavailability of any study regarding pulmonary metastasectomy in Iran and emergence of new treatment modalities, reassessment of our current practices is essential. We performed a retrospective study of 60 cases of pulmonary metastasectomy during a 5-year period in one of the major thoracic surgery centers in Tehran (Imam Khomeini Hospital). Bilateral metastases were present in 23% of cases, number of metastases in each patient ranged from 1-12. Average disease-free interval was 12 months, pneumonectomy rate was 21.7% mostly as a second or third attempt and finally, recurrence or death following initial metastasectomy occurred in 12-18 months in most patients. These results confirm that surgery remains unsuccessful in obtaining long-term survival or cure in most patients with pulmonary metastases and treatment strategies other than surgery, such as radiofrequency ablation are needed to avoid performing multiple operations in these patients and improving their quality of life.

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INTRODUCTION

Lung is one of the most frequent sites of hematogenous metastases. Although metastases often represent systemic and uncontrolled tumor growth, patients with resectable metastases isolated within the lung may have more favorable tumor biology and long-term survival (1). However, the fundamental biology of the neoplastic and metastatic process is unchanged by surgery and many patients develop intrathoracic recurrences leading to multiple surgical procedures.

Alternative and new treatment modalities have been emerged to treat these patients more effectively and improving their quality of life such as inhaled interleukin 2 as a biologic therapy, genetic therapy and radiofrequency ablation (2). Results of surgical

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resection of pulmonary metastases in few thoracic surgery centers in Iran are available but not reported.

We retrospectively reviewed the results of surgical interventions for pulmonary metastases in 60 patients to clarify various characteristics such as type of the primary tumors and their location, type of surgery and its extent, disease free interval and whether surgery is effective or other strategies should be considered for our patients.

MATERIALS AND METHODS

This study was a retrospective, descriptive, cross-sectional study, performed during a 5-year period from 1998 to 2003, on patients undergone surgical metastasectomy, eligible for thoracotomy and lung resection in Tehran, Imam Khomeini General Hospital, one of the major and referral thoracic surgery centers. We obtained informed consent from all participants.

Inclusion criteria and indications for pulmonary metastasectomy included: pulmonary nodules consistent with metastases, control of primary tumor, all nodules being potentially resectable with planned surgery, adequate post-operative pulmonary reserve and no extra thoracic metastases. Initial primary tumor histology and location, disease-free interval, laterality and number of metastases, extent and type of surgery, and recurrence or death following metastasectomy were recorded from patients' files.

The collected data was analyzed by SPSS v.11.05 software®, using descriptive indices, such as frequency, frequency percent, mean, median, mode, standard deviation and standard error. In the analytical analysis, Chi Square, independent sample *t* test, and one way ANOVA were used. The significant area was considered 95%.

RESULTS

A total of 60 patients were included in our study, considering the inclusion criteria for pulmonary metastasectomy.

All patients had undergone primary tumor resection and received the required adjuvant therapy by an oncologist. Chest computed tomography (CT) scan and evaluation of pulmonary and cardiac function was performed for all patients. Postero-lateral thoracotomy and sternotomy/or/staged bilateral thoracotomy was performed for unilateral and bilateral metastases, respectively. All nodules were resected with a margin of normal tissue. Lobectomy or pneumonectomy, mostly as the second or third attempt, has been performed at the discretion of operating surgeon.

In the post-operative period, all patients had referred to the primary surgeon/or/oncologist and were also followed by the attending thoracic surgeon at 3 months intervals.

Among 60 cases, there were 35 men (58%) and 25 women (42%), with the mean age of 22.67 ± 2 years. The age range was 14 to 58 years old. There was no significant difference in mean age among males and females ($P = 0.1$).

The primary tumors in decreasing order of frequency were as follow (Table 1): 1) osteosarcoma, 25 cases (41.7%); 2) synovial sarcoma (spindle cell sarcoma), 13 cases (21.7%); 3) teratocarcinoma of the right testis, 5 cases (8.3%); 4) rhabdomyosarcoma of the right arm and chest wall, 3 cases (5%); 5) malignant fibrous histiocytoma of

Table 1. Primary tumor frequency in patients with metastasectomy

Primary Tumor	Frequency	Percent
Osteosarcoma	25	41.7%
Spindle Cell Sarcoma	13	21.7%
Teratocarcinoma	5	8.3%
Rhabdomyosarcoma	3	5%
Malignant Fibrous Histiocytoma (MFH)	3	5%
Askin	3	5%
Fibrosarcoma	1	1.7%
Uterine Leiomyosarcoma	1	1.7%
Embryonal Cell Carcinoma	1	1.7%
Giant Cell Tumor	1	1.7%
Choriocarcinoma	3	5%
Sigmoid Adenocarcinoma	1	1.7%
Total	60	100

the left chest wall, 3 cases (5%); 6) choriocarcinoma, 3 cases (5%); 7) Askin tumor of the left chest wall, 3 cases (5%); 8) fibrosarcoma of the right lower limb, 1 case (1.7%); 9) uterine leiomyosarcoma, 1 case (1.7%); 10) embryonal cell carcinoma of the right testis, 1 case (1.7%); 11) giant cell tumor of the right knee, 1 case (1.7%); and 12) sigmoid adenocarcinoma, 1 case (1.7%).

Pulmonary metastases were diagnosed within 6 months to 3.5 years of the initial treatment of primaries. Average disease-free interval was 12 months. The mean metastases number was 3.71 ± 0.6.

Lung metastases were frequently unilateral (76.7%) and mostly located in the right lung (48%) (Fig. 1). There was a significant difference in metastases number between two groups with unilateral or bilateral lung involvement. There were more metastases in patients with bilateral lung involvement in comparison with unilateral involvement (5.5 vs. 3.1, $P = 0.005$). Right upper lobe and left lower lobe were involved in 25% and 15% of all cases, respectively. Excision was done by means of wedge resection and lobectomy and there was no postoperative mortality. Re-thoracotomy and pneumonectomy, as the second or third attempt for excision of the recurrent lesions, was performed in 21.7% of cases. In most patients, recurrence or death occurred in the following 12-18 months.

In the analytical statistics, there was no significant relationship between sex, metastases location and performing pneumonectomy ($P < 0.05$).

On the other hand there was no significant difference in age and metastases number between two sex groups.

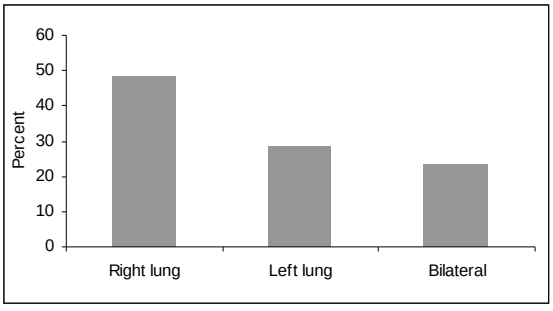

Fig. 1. Location frequency among patients with metastasectomy.

DISCUSSION

Unfortunately, most patients with lung metastases do not benefit from surgery because of one or more of the following reasons: (a) a biologically aggressive tumor characterized by extensive disease (b) a short disease-free interval (DFI) between control of their primary tumor and identification of pulmonary metastases and (c) rapid metastatic growth (1). As the number of metastases increase, the potential for occult micrometastatic disease also increases. The biology of patients with excessive numbers of metastases (but yet still "resectable") is not changed by resection and even with multiple resections, complete eradication of micro metastases may be unachievable.

The relatively short average disease-free interval (12 months) and high incidence of bilateral metastases (23%) in our patients indicate uncontrolled tumor growth which necessitated performance of a major ablative operation such as pneumonectomy in about one-fifth of patients and recurrence or death within 12-18 months. Although our study suffers from lack of a control group treated with new and evolving treatment methods and its retrospective nature, it clearly shows that surgery attempts to solve a biologic problem by mechanical means and remains unsuccessful in obtaining long-term disease-free survival or cure.

Results of surgical resection vary with the histological type of the primary tumor (3) and presence of symptoms and disease-free intervals have significant influence on it (4). On the other hand, isolated and resectable metastases to the lung represent a unique biology among the host and cure in most patients represents a serendipitous occasion in which the host biology, and surgical resection remove all tumor including micro metastases. Is the associated long-term survival the result of surgery or the result of the unique biology of the tumor? This question remains unanswered.

Various strategies have been proposed to treat lung metastases more effectively which include: lung perfusion, inhalation therapy, biologic modifiers and radiofrequency ablation. Isolated lung perfusion is an experimental technique to deliver high-dose chemotherapy to the lung without systemic exposure

(5, 6). Preliminary human studies have shown that it is technically feasible but further clinical research is necessary to determine its effects (7).

Percutaneous radiofrequency (RF) ablation is a minimally invasive technique used to treat solid tumors. In theory, lung tumors are well suited to RF ablation because the surrounding air in adjacent normal parenchyma provides an insulating effect, thus facilitating energy concentration within the tumor tissue (8). It is reported as a good option for those patients who are believed to be at increased risk for resection or who refuse resection (9).

RF ablation might be the treatment of choice for multiple/or/bilateral pulmonary metastases (10). With almost 500 procedures done to date, percutaneous RF ablation appears to be a safe tool with little morbidity (pneumothorax and pleural effusion in less than 30% and 10% of cases, respectively), short hospital stay and gain in quality of life (11).

In conclusion, despite better-refined and more aggressive resection techniques and enhanced selection of patients, better treatment of pulmonary metastases awaits improved adjuvant therapies and new evolving methods.

Conflict of interests

The authors declare that they have no competing interests.

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