Resection of Pulmonary Metastasis

Carlos A. Rueda, MD
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University of Colorado Health Sciences Center
Department of Surgery
Grand Rounds
Introduction

- The lung is a common site for metastasis.
- Pulmonary metastasis occur in 30% to 40% of patients who have cancer.
- Presence of pulmonary metastasis may or may not contribute to clinical outcome.
Pathogenesis

Several routes for spread to the lungs

- Hematogenous dissemination
- Lymphogenous dissemination
- Direct invasion
- Intra-bronchial dissemination
Hematogenous Dissemination

- Angiogenesis allows cancer cells to invade the vascular space.

- Malignant cells may passively come to rest in lung capillaries.

- Malignant cells may also actively invade through the capillary endothelium.
Lymphogenous Dissemination

Two lymphogenous routes:

- Cancer cells from involved lymph nodes may access larger lymphatics such as the thoracic duct.

- Mediastinal or hilar node involvement may result in retrograde dissemination of malignant cells into the pulmonary lymph channels.
Direct Invasion

Direct invasion by malignancies into the lungs come from cancer originating in:

- The chest wall
- The mediastinum
- Abdominal viscera
- Retroperitoneum
Intra-bronchial Dissemination

- Original malignancies in the aerodigestive tract.
- Direct implantation.
- Attempt at explanation of high frequency of second carcinomas (usually squamous cell) in patients treated for aerodigestive cancers.
- Needs careful molecular analysis of both tumors to prove or disprove.
Metastasectomy

- Historically, first long-term survivor after pulmonary metastasis resection for renal cell was reported in 1939 by Barney and Churchill.
- First large series of pulmonary metastasis resection done in 1965.
  - N=205
  - Overall 5 year survival rate 30.3%
  - Almost as good as that for primary lung cancer resections.

Indications for Pulmonary Metastasectomy

- Thomford et al. (1965).
  - Patient must be a good risk for surgical intervention
  - Primary malignancy is controlled
  - No evidence of metastatic disease anywhere else
  - Radiographic evidence of metastasis is limited to one lung

Indications for Pulmonary Metastasectomy

Current Major Criteria

- Patient must be a good risk for surgical intervention

- Primary site is controlled

- No other, extrapulmonary metastases; or, if present, they can be controlled by surgery or other modalities

- Pulmonary metastases are thought to be completely resectable
Indications for Pulmonary Metastasectomy

Current Additional Criteria

- Existence of effective systemic chemotherapy as a combined modality
- Difficulty of differential diagnosis from primary lung cancer
- No other effective treatment, except resection
- Symptomatic pulmonary metastasis
Surgical Approaches

- **Wedge resection** is the most frequent procedure.
  
  - Ercan et al. (2004) reported the incidence of lymph node involvement being 28.6% in metastatic lung cancer.
  
  - Okumura et al. (1996) in a retrospective report showed better survival with wedge resection than with lobectomy and poor survival with lymph node involvement in pulmonary metastasis of colorectal cancer.


VATS

Disadvantages
- Loss of bimanual palpation

Advantages
- Less adhesion than with thoracotomy.
- Minimal invasiveness
Pneumonectomy

Central lesions such as proximal endobronchial or with lesions with hilar node metastasis

Patients requiring pneumonectomy must have sufficient pulmonary reserve, controlled primary disease, no evidence of other metastatic disease, and lack better alternative therapy.
Pneumonectomy

Koong et al. (1999) International Registry of Lung Metastasis

- 20% 5-year survival rate after successful complete resection; operative mortality of 4%
- Incomplete resection operative mortality of 19%
- Lower than the 5-year survival rate of 36% for all pulmonary metastasectomies, it is superior to no resection.

Pneumonectomy

Outcomes

Osteosarcoma

- Retrospective multi-institutional study from the Japanese Musculoskeletal Oncology Group
- 280 patients with metastatic osteosarcoma.
- Divided into four groups
  - Group 1: Lung mets identified at initial presentation
  - Group 2: Lung mets identified during initial chemotherapy
  - Group 3: Lung mets identified after initial chemotherapy
  - Group 4: Lungs mets identified after completion of initial therapy

Osteosarcoma

Results, 5-year survival rates:

- Mets identified at initial presentation 18%
- Mets identified during initial chemo 0%
- Mets identified after initial chemo 6%
- Mets identified after completion 31%

P<0.0001

Conclusions

- Patients with detected metastasis after completion of initial treatment had better 5-year survival than those in which initial treatment had not been completed.

- Pulmonary metastasectomy is the most effective treatment for lung metastasis in osteosarcoma.

Outcomes

Colorectal cancer
- Many retrospective studies
- Overall 5-year survival 35-45%
- Overall 10-year survival 20-30%
- Many prognostic factors have been investigated
  - Pre-thoracotomy CEA level
  - Number of pulmonary metastases
  - Regional lymph node involvement

### Table 2. Survival and Prognostic Factors for Pulmonary Metastasectomy for Colorectal Cancer

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>No. of patients</th>
<th>5-Year survival</th>
<th>10-Year survival</th>
<th>Favorable Prognostic Factors</th>
<th>Nonsignificant Prognostic Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>McCormack</td>
<td>1979</td>
<td>35</td>
<td>22%</td>
<td>–</td>
<td>Dukes’ A &amp; B</td>
<td>DFI, number</td>
</tr>
<tr>
<td>Manse</td>
<td>1986</td>
<td>66</td>
<td>38%</td>
<td>–</td>
<td>Solitary</td>
<td>Age, sex, size, location</td>
</tr>
<tr>
<td>Goya</td>
<td>1989</td>
<td>62</td>
<td>42%</td>
<td>22%</td>
<td>Solitary, size</td>
<td></td>
</tr>
<tr>
<td>McCormack</td>
<td>1992</td>
<td>144</td>
<td>40%</td>
<td>30%</td>
<td>CR</td>
<td></td>
</tr>
<tr>
<td>van Halteren</td>
<td>1995</td>
<td>38</td>
<td>43%</td>
<td>–</td>
<td>Number, DFI</td>
<td></td>
</tr>
<tr>
<td>Okumura</td>
<td>1996</td>
<td>159</td>
<td>40.5%</td>
<td>27.7%</td>
<td>Number, LN</td>
<td>Age, sex, location</td>
</tr>
<tr>
<td>Girard</td>
<td>1996</td>
<td>86</td>
<td>24%</td>
<td>–</td>
<td>CR, CEA, number</td>
<td>Age, sex, size, DFI</td>
</tr>
<tr>
<td>Inoue</td>
<td>2000</td>
<td>25</td>
<td>39.2%</td>
<td>20%</td>
<td>CEA, LN</td>
<td></td>
</tr>
<tr>
<td>Saito</td>
<td>2002</td>
<td>165</td>
<td>39.6%</td>
<td>–</td>
<td>CEA, LN</td>
<td>Liver</td>
</tr>
<tr>
<td>Pfannschmidt</td>
<td>2003</td>
<td>167</td>
<td>32.4%</td>
<td>–</td>
<td>Number, CEA</td>
<td></td>
</tr>
</tbody>
</table>

Outcomes

Renal cell carcinoma

– Lungs are the second most frequent site for metastases and often the only location
– First resection of a pulmonary metastasis, an en bloc resection of the chest wall and adjacent lung metastases was performed by Weinlecher in 1882.
– The first report of pulmonary metastasectomy in renal cell carcinoma was by Barney and Churchill in 1939.
Renal Cell Carcinoma

- Most conventional antineoplastic drugs or radiation therapy have little or no efficacy.
- Immunotherapy has shown promise but prospective controlled clinical studies are pending.
- Surgery remains the only effective treatment.
- The 5-year survival rate with unresected disease is only 2.7%.

Renal Cell Carcinoma

Pfanschmidt et al (2002)
- 191 patients underwent resection for pulmonary metastasis
- Primary tumor treated with radical nephrectomy.
- No extrapulmonary disease at the time of metastasectomy.

Renal Cell Carcinoma

<table>
<thead>
<tr>
<th>Prognostic Factor</th>
<th>p Value</th>
</tr>
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<tbody>
<tr>
<td>Age</td>
<td>NS</td>
</tr>
<tr>
<td>Gender</td>
<td>NS</td>
</tr>
<tr>
<td>Redo surgery for recurrent disease</td>
<td>NS</td>
</tr>
<tr>
<td>Number of metastases</td>
<td>0.0002</td>
</tr>
<tr>
<td>Complete resection</td>
<td>0.049</td>
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<tr>
<td>Lymph node metastases</td>
<td>0.0038</td>
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<tr>
<td>Disease-free interval</td>
<td>0.012</td>
</tr>
</tbody>
</table>

Renal Cell Carcinoma

Breast cancer

- Lanza et al. (1992)
  - 5-year survival about 50%
  - Survival influenced by
    - Estrogen receptor status
    - Disease free interval


- Ludwig et al. (2003)
  - Prognosis was not correlated with
    - Number of pulmonary metastases
    - Disease free interval
    - Lymph node involvement
    - Receptor status

Outcomes

- Uterine cancer
    - Squamous cell carcinoma 46.8%
    - Cervical adenocarcinoma 40.3%
    - Endometrial adenocarcinoma 75.7%
    - Choriocarcinoma 86.5%

Outcome

Disseminated non-seminomatous testicular cancer

- Initially cisplatin-based chemotherapy
- Surgical resection of pulmonary metastasis indicated even if there are extrapulmonary metastases.
- Pathologic results of necrosis in resected specimen have a good prognosis
- Relapse rate of 5-10%

Testicular Cancer

Outcomes

Head and Neck Cancers
  - Squamous cell carcinoma 34%
  - Glandular tumors 64%
  - Adenoid cystic carcinoma 84%

Conclusion

- Encouraging outcome of pulmonary metastasectomy, as good as 40% at 5 years.
- Consider that surgery is merely a local treatment.
- Most studies are retrospective reports.
- Biases:
  - Patients in good physical condition
  - Slow growing tumors
  - Early detection by intensive follow up
Conclusion

The future

- Further analysis of various prognostic factors

- Special reference to each primary malignancy

- Multi-institutional study

- Randomized prospective studies