Metachronous adrenal masses in resected non-small cell lung cancer patients: therapeutic implications of laparoscopic adrenalectomy

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Abstract

Objective: In literature only few reports focused on the resection of solitary adrenal gland metastasis in patients operated on for non-small cell lung cancer (NSCLC). We report our experience on laparoscopic adrenalectomy for suspected or confirmed metachronous solitary adrenal metastasis from NSCLC and discuss its therapeutic role.

Methods: From June 1993 to March 2003, 14 patients (pts), who had been undergone lung resection for NSCLC, with suspected or confirmed solitary adrenal gland metastasis at the follow-up, underwent 15 laparoscopic adrenalectomy (in 1 patient it was bilateral). All the patients had enlarged adrenal glands at the abdominal ultrasound or CT. All but 2 pts underwent at least 1 adrenal fine needle aspiration. All the patients underwent a careful staging to exclude other sites of metastasis. The adrenal gland was in 6 cases the right, in 9 cases the left.

Results: In 7 cases we had a preoperative cytological diagnosis of metastasis. In 1 case adrenalectomy was not performed because of infiltration of vena cava and in 1 case it was necessary to perform a small laparotomy because of bleeding. The pathologic examination confirmed in 11 cases a NSCLC metastasis while in 4 cases it was a cortical adenoma. Regarding the 10 patients with NSCLC metastases, 3 are still alive and well at 37–80 months from the lung resection. One patient (who underwent bilateral adrenalectomy) is still alive at 44 months with local relapse. Two patients died 5 and 6 months after the adrenalectomy for other causes, 1 died at 14 months for local and systemic relapse and the remaining 3 patients died at 12 to 38 months for systemic relapse.

Conclusions: Laparoscopic adrenalectomy in patients resected for NSCLC is a safe mini-invasive procedure. Even though this series is still too small, laparoscopic adrenalectomy should be considered an effective therapeutic tool in case of progressive adrenal gland enlargement, also with negative cytological examinations. A bigger series and other institution experiences will clarify its oncological value.

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1. Introduction

Even though it is commonly accepted that laparoscopic adrenalectomy is the treatment of choice for benign adrenal lesions [1], still controversial are the indications to adrenalectomy in case of primary or metastatic adrenal cancer and the opportunity of approaching malignant lesions by this mini-invasive procedure [2-3]. Moreover, it has been claimed that a laparoscopic exploration can also be necessary in order to confirm both the neoplastic nature of the lesion and the feasibility of the operation [4]. Adrenal gland is a common site of metastasis from lung carcinoma but rarely the patients are suitable to a surgical resection [5-6]. Despite that some long-term survivors of resection of a solitary adrenal metastasis from NSCLC are reported in the literature [7-11]. Since 1993, we started a planned policy on patients, resected for a NSCLC, with the suspicion or cytological diagnosis of solitary adrenal metastasis. We present our data, aiming to debate the role of laparoscopy in the treatment of solitary adrenal metastasis from NSCLC.

2. Materials and methods

From June 1993 to March 2003, out of 197 patients who underwent a laparoscopic adrenalectomy for various pathologies, 14 were treated (1 patient bilaterally) with the diagnosis or suspicion of a solitary adrenal metastasis from NSCLC. There were 13 males and 1 female. Mean age was 65.7 (50-78) years. All the patients had been radically resected for lung carcinoma and the characteristics of the tumors are listed in Table 1.

All patients presented at the follow-up enlargement of an adrenal gland suspicious for metastasis and underwent an accurate work-up consisting of: a chest and upper abdomen CT scan, an abdominal ultrasonography, a complete staging
### Table 1
Characteristics of the resected NSCLC patients who underwent laparoscopic adrenalectomy

<table>
<thead>
<tr>
<th>No</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>TNM</th>
<th>Histology</th>
<th>Sideact</th>
<th>Size (cm)</th>
<th>Adrenalectomy</th>
<th>Diagnostic Tool</th>
<th>Pathology</th>
<th>Interval (thor/lap)</th>
<th>Survival (months)</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PS 71</td>
<td>m</td>
<td>T2N0</td>
<td>Adenoca</td>
<td>Left</td>
<td>4.7</td>
<td>Laparoscopic</td>
<td>FNAB +</td>
<td>Metastasis</td>
<td>12</td>
<td>18</td>
<td>Dead for cerebrovascular disease free of disease</td>
</tr>
<tr>
<td>2</td>
<td>MA 55</td>
<td>m</td>
<td>T2N0</td>
<td>Squam.</td>
<td>Right</td>
<td>3</td>
<td>Laparoscopic</td>
<td>FNAB +</td>
<td>Metastasis</td>
<td>9</td>
<td>14</td>
<td>Dead for heart disease (IMA) free of disease</td>
</tr>
<tr>
<td>3</td>
<td>MA 67</td>
<td>m</td>
<td>T2N0</td>
<td>Large cell</td>
<td>Right</td>
<td>3</td>
<td>Laparoscopic</td>
<td>FNAB (&gt; volume)</td>
<td>Metastasis</td>
<td>26</td>
<td>80</td>
<td>Alive and well</td>
</tr>
<tr>
<td>4</td>
<td>QA 77</td>
<td>m</td>
<td>T3N0</td>
<td>Adenoca.</td>
<td>Left</td>
<td>3.8</td>
<td>Laparoscopic</td>
<td>FNAB (&gt; volume)</td>
<td>Adenoma</td>
<td>7</td>
<td>98</td>
<td>Alive and well</td>
</tr>
<tr>
<td>5</td>
<td>TG 69</td>
<td>m</td>
<td>T2N0</td>
<td>Squam.</td>
<td>Right</td>
<td>4.1</td>
<td>Laparoscopic</td>
<td>FNAB (&gt; volume)</td>
<td>Adenoma</td>
<td>10</td>
<td>96</td>
<td>Dead for second primary contralateral lung cancer</td>
</tr>
<tr>
<td>6</td>
<td>BA 63</td>
<td>m</td>
<td>T2N0</td>
<td>Adenoca.</td>
<td>Left</td>
<td>2.5</td>
<td>Laparoscopic</td>
<td>FNAB+</td>
<td>Adenoma</td>
<td>9</td>
<td>14</td>
<td>Dead for systemic disease</td>
</tr>
<tr>
<td>7</td>
<td>CD 52</td>
<td>m</td>
<td>T1N2</td>
<td>Adenoca.</td>
<td>Right</td>
<td>3.5</td>
<td>Explorative (Cava involved)</td>
<td>FNAB+</td>
<td>Adenoma</td>
<td>19</td>
<td>90</td>
<td>Alive and well</td>
</tr>
<tr>
<td>8</td>
<td>CD 52</td>
<td>m</td>
<td>T1N2</td>
<td>Adenoca.</td>
<td>Right</td>
<td>3.5</td>
<td>Explorative (Cava involved)</td>
<td>FNAB+</td>
<td>Adenoma</td>
<td>11</td>
<td>14</td>
<td>Dead for systemic disease</td>
</tr>
<tr>
<td>9</td>
<td>EF 63</td>
<td>m</td>
<td>T2N0</td>
<td>Large cell</td>
<td>Left</td>
<td>4</td>
<td>Laparoscopic</td>
<td>FNAB+</td>
<td>Metastasis</td>
<td>6</td>
<td>12</td>
<td>Dead for heart disease (IMA) free of disease</td>
</tr>
<tr>
<td>10</td>
<td>ZC 64</td>
<td>m</td>
<td>T2N1</td>
<td>Squam.</td>
<td>Left</td>
<td>3</td>
<td>Laparoscopic</td>
<td>FNAB (&gt; volume)</td>
<td>Metastasis</td>
<td>17</td>
<td>46</td>
<td>Alive and well</td>
</tr>
<tr>
<td>11</td>
<td>LL 78</td>
<td>m</td>
<td>T3N0</td>
<td>Adenoca.</td>
<td>Left</td>
<td>3.5</td>
<td>Laparoscopic</td>
<td>FNAB (&gt; volume)</td>
<td>Metastasis</td>
<td>14</td>
<td>43</td>
<td>Alive and well</td>
</tr>
<tr>
<td>12</td>
<td>VB 76</td>
<td>m</td>
<td>T3N0</td>
<td>Adenoca.</td>
<td>Left</td>
<td>10</td>
<td>Laparoscopic</td>
<td>FNAB+</td>
<td>Metastasis</td>
<td>34</td>
<td>38</td>
<td>Alive for systemic disease</td>
</tr>
<tr>
<td>13</td>
<td>CM* 50</td>
<td>m</td>
<td>T3N0</td>
<td>Large cell</td>
<td>Left</td>
<td>6</td>
<td>Laparoscopic</td>
<td>FNAB+ (PET)</td>
<td>Metastasis</td>
<td>17</td>
<td>44</td>
<td>Alive with local relapse</td>
</tr>
<tr>
<td>14</td>
<td>CM* 51</td>
<td>m</td>
<td>T3N0</td>
<td>Adenoca.</td>
<td>Left</td>
<td>6</td>
<td>Laparoscopic</td>
<td>FNAB+ (PET)</td>
<td>Metastasis</td>
<td>31</td>
<td>44</td>
<td>Alive with local relapse</td>
</tr>
<tr>
<td>15</td>
<td>BL 68</td>
<td>m</td>
<td>T2N0</td>
<td>Squam.</td>
<td>Right</td>
<td>10</td>
<td>Laparoscopic</td>
<td>FNAB+</td>
<td>Metastasis</td>
<td>9</td>
<td>37</td>
<td>Alive and well</td>
</tr>
</tbody>
</table>

*Patient who underwent bilateral adrenalectomy.

**3. Results**

The statistical analysis has been performed using the StatSoft software. Results are expressed as mean ± standard deviation. Survival was evaluated from the date of surgery until death. Survival curves were estimated by the Kaplan-Meier product-limit method and were compared by the log-rank test.

The exeresis was always preceded by a laparoscopic intraoperative ultrasonography to exclude other abdominal metastatic nodules or an extra-capsular invasion of the adrenal gland which would have been a contraindication for adrenalectomy. The interval of laparoscopic adrenalectomy was 4–34 months. The adrenal lesion was on the left in 9 cases and on the right in 6 cases. No adrenal mass was symptomatic. Mean steroid of the lesion was 4,6 (range: 2, 5–10) cm. Median time of the adrenal gland was necessary in only one case for an intra-operative bleeding in the patient who underwent staged bilateral adrenalectomies. We did not experience any important post-operative complication. The pathologic examination for the adrenal mass was necessary in only one case for an intra-operative bleeding in the patient who underwent staged bilateral adrenalectomies. We did not experience any important post-operative complication. The pathologic examination was performed in 6 cases.

Among the cases submitted to FNAB, 7 were true positive, 3 false negative, and 3 false positive. The adrenal lesion was on the left in 9 cases and on the right in 6 cases. No adrenal mass was symptomatic. Mean steroid of the lesion was 4,6 (range: 2, 5–10) cm. Median time between thoracic surgery and adrenalectomy was 13 (range: 4–34) months. The exeresis was always preceded by a laparoscopic intraoperative ultrasonography to exclude other abdominal metastatic nodules or an extra-capsular invasion of the adrenal gland which would have been a contraindication for laparoscopic adrenalectomy. The interval of laparoscopic adrenalectomy was 4–34 months. The adrenal lesion was on the left in 9 cases and on the right in 6 cases. No adrenal mass was symptomatic. Mean steroid of the lesion was 4,6 (range: 2, 5–10) cm. Median time between thoracic surgery and adrenalectomy was 13 (range: 4–34) months.
confirmed in 11 cases a NSCLC metastasis while in 4 cases it was a cortical adenoma. One patient underwent a left adrenalectomy for a solitary adrenal gland metastasis and 14 months later the contralateral adrenalectomy for a new solitary metastasis. Regarding the 10 patients with NSCLC metastases, 3 are still alive and well at 37-80 months from the lung resection. One patient (who underwent bilateral adrenalectomy) is still alive at 44 months with local relapse. Two patients died 5 and 6 months after the adrenalectomy for other causes, 1 died at 14 months for local and systemic relapse and the remaining 3 patients died at 12-38 months for systemic relapse. Survival curves from thoracic operation and laparoscopic adrenalectomy are shown in Fig. 1. We did not observe any significant difference of survival according to the interval between the thoracic operation and laparoscopic adrenalectomy (Fig. 2).

4. Discussion

Even before the introduction of laparoscopic adrenalectomy the opportunity of operating patients presenting with a solitary metastasis to the adrenal gland from lung cancer had been explored [7,8]. However, laparoscopic adrenalectomy, providing a quicker and better surgical outcome, contributed to extend the current indication to adrenalectomy in case of patients resected for lung cancer and the experiences of some institutions have been recently published [14-16]. In some way, we may formulate a similitude with what happened for metachronous single brain metastasis from lung cancer which is now always evaluated for surgical exeresis [17-18]. Similarly to what happened for solitary brain metastasis also for solitary adrenal metastasis from lung cancer, we are moving from reports of some long-term survivors [7,10] to trials showing a better outcome in patients who underwent adrenalectomy compared to chemotherapy alone [19], looking at some interesting trials combining chemotherapy and surgery [20].

Before focusing on the therapeutic value of adrenalectomy in case of solitary metastasis we should debate on the indication to surgery when an adrenal mass is discovered during the follow-up of patients resected for NSCLC. A preoperative diagnosis of the adrenal mass may be a difficult goal to achieve and the differential diagnosis between adenoma and metastasis is critical [21]. If, on one hand, the conservative approach, consisting of follow-up with the CT and ultrasonography of the adrenals, may lead to a delay in the treatment, on the other hand, surgery in case of...
adenoma may be considered an over treatment. Unfortunately FNAB, in most of the reported experiences, is quite disappointing in terms of accuracy of the technique with a sensitivity as low as 57% [4]. Though in our series we had no complications related to FNAB its sensitivity was quite low because the rate of false negative appeared to be too high (3 out of 6 cases); fortunately it did not exclude patients from surgical treatment because of other considerations (significant mass growth at follow up). In one patient (no. 14), who previously underwent a left adrenalectomy, after 3 negative FNAB we also performed a PET scan which showed the right adrenal gland as the only site with ipermetabolic activity. It is our opinion that in case of negative FNAB a PET scan may give further informations and help us in the decision making. Unfortunately when we treated the patients of our series a PET scan was not disposable and we could not test its diagnostic accuracy. We used MRI only in two cases but it did not add useful informations, and, consequently, we do not use it anymore for the differential diagnosis. Nowadays, at our institution, all the patients, with a confirmed or suspected solitary adrenal metastasis, undergo a PET scan with the aim of confirming that it is really a solitary metastasis. In any case it is our opinion that an adrenal mass (> 3 cm), appearing during the follow-up of a patient resected for NSCLC and not present before, whose nature is not clarified by the diagnostic tools (including FNAB and PET scan), deserves at least a laparoscopic exploration.

Unfortunately, only 7% of the patients developing metastatic disease from NSCLC have a solitary metastasis [5], so that only selected cases may be suitable to laparoscopic adrenalectomy and benefit from that. Moreover the dismal results provided by the chemotherapy and radiotherapy, emphasize the surgical resection as the best option for a potential cure [19,22]. As it was demonstrated with solitary brain metastasis [18] the stage of lung cancer (N0 vs N1-2) and the interval between the lung resection and the adrenalectomy may be prognostic factors. Our series is still too small to define possible prognostic factors, however, the 2 patients with N2 disease died 3 and 4 months after the adrenalectomy with systemic disease. As regards the disease free interval, it was identified as a prognostic factor by some authors [15,19]. Our data do not support this thesis, in agreement with other authors [14], even if we observed a trend of better survival in patients with longer disease free interval.

In conclusion, laparoscopic adrenalectomy in patients resected for NSCLC proved to be a safe mini-invasive procedure. Laparoscopic adrenalectomy should be considered an effective therapeutic tool in case of metachronous solitary adrenal metastasis or progressive adrenal gland enlargement, highly suspected for metastasis. A bigger series and other institution experiences will clarify its oncological value.

References