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Intraoperative Detection of Lung Cancer by Octreotide Labeled to Indium-111

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The contribution of radio surgery (RGS) using octreotide labeled with Indium-111 (In^{111}) has been studied for surgical treatment of lung cancer. Thirteen patients were administered 111 Mbq of In^{111} octreotide intravenously. Scintigraphic images were preoperatively taken at 4, 24, and 48 hours after the tracer injection. Pulmonary resection and intraoperative evaluation by RGS technique were then performed to set the section limits. Histological staining of all the resected specimens and resection margins were assessed and their results were used as a confirmation of the RGS intraoperative findings. RGS is a simple method that can help the surgeon in the intraoperative assessment of bronchial, parenchymal, and parietal resection margins. Further research is needed to verify whether this method also may be useful in the intraoperative definition of the extent of mediastinal lymph node dissection. ***Semin. Surg. Oncol. 15:220–222, 1998.***

KEY WORDS: lung neoplasms; radioimmunodetection; intraoperative care; sensitivity and specificity; false positive reactions; false negative reactions; octreotide; iodine radioisotopes; indium radioisotopes; lymph node excision; monoclonal antibodies; neoplasm metastasis; carcinoembryonic antigen

INTRODUCTION

Current interest in radio surgery (RGS) is based on the necessity to perform more radical resections in cancer surgery. As with colorectal surgery [1–6], the method also has been extended to the surgical treatment of lung cancer to improve preoperative staging which, despite current sophisticated techniques, is still inadequate [7–10].

In our previous experience, the use of the monoclonal antibody B72.3 radiolabeled with Iodine-125 (I^{125}) did not yield expected results because the method is too complex, does not provide preoperative images, and has poor specificity [9,10].

The use of anti-carcinoembryonic antigen (CEA) monoclonal antibodies (MoAbs) labeled with ^{99m}Technetium (Tc) in parahilar lung cancer is unsuitable for discriminating tumors from normal tissue because of high blood-pool radioactivity [10–12]. Thus, we tested octreotide labeled with Indium-111 (In^{111}) which was already in use for small cell lung cancer diagnosis [13–15].

MATERIALS AND METHODS

Sixteen patients, ranging from 28 to 80 years of age, were administered an injection of 111 Mbq of In^{111}-octreotide intravenously. Total body scintigraphic images were taken at 4, 24, and 48 hours after the injection; three patients with metastases were excluded from the study. Pulmonary resection by RGS technique was performed on the 13 remaining patients from 1 to 6 days after injection of the tracer. Three left pneumonectomies, one superior bilobectomy, eight lobectomies, and one wedge resection were performed. One pneumonectomy and two lobectomies required an extension of the resection to the thoracic wall by a two-rib thoracectomy.

During each operation, the presence of radiolabeled octreotide was assessed by means of a gamma-detecting probe (GDP) with a tip made on natrum iodide crystal. The radioactivity uptake value of each evaluated site, expressed as counts per second (cps), was defined by the average of three consecutive counts performed at the same site. Counts were made at the following sites: 1) latissimus dorsi; 2) healthy pulmonary tissue; 3) mediastinal blood pool background (pericardium and/or large intrathoracic vessels); 4) neoplastic pulmonary tissue; 5) hilar

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and mediastinal lymph nodes; 6) bronchial, parenchymal and parietal resection margins.

RESULTS

Preoperative scintigraphic imaging confirmed a good tracer uptake by cancer primary lesions and, in all cases, allowed a satisfactory definition of the extension of the neoplastic tissue at the parenchymal seat.

With GDP ratio counts between neoplastic and normal tissue—which was higher than 2/1—intraoperative probing detection allowed a clear differentiation of cancer from normal lung tissue in 12 out of 13 patients (92.3%; Table I). One patient who underwent a median lobectomy had a negative ratio of 1.90/1. In three thoracotomies, RIGS findings allowed resection in clearly healthy tissue as confirmed by pathologic examination of the margins of resection.

Eighty lymph nodal groups have been evaluated following mediastinal lymph node dissection. Pathologic examination confirmed RGS intraoperative lymph nodal status assessment in six out of eight lymph node dissections. We observed one RGS false positive (a large, right inferior paratracheal lymph node with high counts that was found negative at hematoxylin-and-eosin [H&E] staining), and one RGS false negative (a clinically enlarged carenal lymph node with captation ratio lower than 2/1 also found to be pathological at H&E staining).

DISCUSSION

Octreotide is a somatostatin analogue that can target some neoplastic lesions such as neuroendocrine cancers and small cell lung cancers [16]. By labeling octreotide to In^{111} it is possible to obtain preoperative scintigraphic images of tumor [17,18]) and intraoperatively detect the tracer at the tumor sites by a revealing system based on the use of the GDP. Lung small cell cancers have several somatostatin receptors [19,20], while non-small-cell lung cancers have no receptors, although octreotide has been shown to link activated leukocytes or neuroendocrine cells surrounding neoplastic tissue [21]. Through these properties, octreotide can be used for RGS purposes. Moreover, the thorax seems to be the ideal zone for radioguided intraoperative scanning, given its distance from the liver and spleen which are organs with a high In^{111} uptake.

When ratio counts between cancer and healthy tissue were higher than 2/1, it constituted the main criterion for obtaining a correct intraoperative staging. It is noteworthy that we observed ratios ranging from 1.90/1 to 6.69/1. These values can assist the surgeon in better defining parenchymal, bronchial, and chest wall safety of the resection margins.

The RGS assessment of lymph node status, especially for N2 level (TNM classification), is controversial because of the close proximity of large vessels with elevated background radioactivity as well as the possibility of false negative and false positive RGS findings. It appears of higher value in pretracheal, upper parortracheal, carenal, and paraesophageal groups.

TABLE I. Intraoperative Gamma-Detecting Probe Findings in 13 Patients Operated for Lung Neoplasms*

Patient/surgery	Radioactivity (counts/10") at tumor tissue	Normal tissue radioactivity (counts/10")	Tumor to normal tissue counts ratio
1. Upper bilobectomy	693	136	5.09
2. Right lower lobectomy	475	71	6.69
3. Right upper lobectomy	65	20	3.24
4. Left pneumonectomy + thoracectomy	118	28	4.13
5. Wedge resection	175	32	5.4
6. Left pneumonectomy	192	34	5.62
7. Right upper lobectomy	47	14	3.35
8. Left pneumonectomy	120	33	3.63
9. Median lobectomy	105	55	1.90
10. Right upper lobectomy + thoracectomy	173	54	3.20
11. Left upper lobectomy + thoracectomy	175	32	5.40
12. Right upper lobectomy	280	90	3.11
13. Left upper lobectomy	170	3	5.6

*Tumor-to-normal-tissue counts ratio >2/1 were considered positive findings for malignant tissue assessment. Normal tissue evaluation was performed only at the latissimus dorsi muscle.

CONCLUSIONS

We believe that further research is needed to establish the real clinical contribution of RGS in mediastinal lymph node intraoperative assessment. Moreover, follow-up of the patients who underwent RGS will assist us in determining whether it can be considered a valid approach to the management of lung cancer.

This diagnostic approach to lung cancer appears to be a simple method that provides preoperative images, completes data of other standard diagnostic procedures, and has a high resolution in intraoperative staging assessment.

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