Bronchial Carcinoid Tumor: a Retrospective Analysis of 62 Surgically Treated Cases

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OBJECTIVE: To evaluate the results of surgical treatment for lung carcinoid tumor.

PATIENTS AND METHOD: The medical records of 62 patients who underwent surgical intervention for lung carcinoid tumor between May 1985 and October 2000 were reviewed.

RESULTS: Fifty-two patients had typical carcinoid tumors and 10 had atypical carcinoid tumors. Hilar or mediastinal lymph node metastases were present in 9 patients. Distant metastasis occurred in 5 patients and was significantly more frequent in those with the atypical carcinoid histological subtype. The overall survival rate at 15 years was 70%, with a mean survival rate of 138 (SD 11) months, calculated with the Kaplan-Meier method. We found no statistically significant correlation between smoking and the development of carcinoid tumors.

CONCLUSIONS: Although carcinoid tumors behave like low-grade malignant tumors, they should be treated in the same way as other malignant lung tumors. Curative surgical resection is the technique of choice whenever possible.

Key words: Carcinoid tumor. Carcinoid syndrome. Surgical treatment.

Tumor carcinoide bronquial. Análisis retrospectivo de 62 casos tratados quirúrgicamente

OBJETIVO: Evaluar los resultados del tratamiento quirúrgico del tumor carcinoide pulmonar.

PACIENTES Y MÉTODO: Se han revisado las historias clínicas de 62 pacientes intervenidos quirúrgicamente por un tumor carcinoide pulmonar entre mayo de 1985 y octubre de 2000.

RESULTADOS: Cincuenta y dos pacientes tenían un carcinoide típico y 10 un carcinoide atípico. Nueve pacientes presentaban metástasis ganglionares hiliares o mediastínicas y 5 presentaban metástasis a distancia. Estas últimas fueron más frecuentes en el subtipo histológico carcinoide atípico con diferencias estadísticamente significativas. Cinco pacientes tenían clínica de síndrome carcinoide. La supervivencia global a los 15 años fue del 70% y la supervivencia media de 138 ± 11 meses. No encontramos asociación estadística entre el hábito tabáquico y el desarrollo de tumor carcinoide.

CONCLUSIONES: Aunque el tumor carcinoide se comporta como un tumor de bajo grado de malignidad, su tratamiento debe realizarse de modo similar al del resto de los tumores malignos pulmonares; la resección quirúrgica con intención curativa es la técnica de elección siempre que sea posible.

Palabras clave: Tumor carcinoide. Síndrome carcinoide. Tratamiento quirúrgico.

Introduction

Lung carcinoid tumor is a neuroendocrine neoplasm that arises from the enterochromaffin cells of the amine precursor uptake and decarboxylation system of the bronchial mucosa. They represent 2% of all lung tumors, are endobronchial in 90% of the cases, and lead to nodal involvement in 10%.

Previously, lung carcinoid tumors were called "bronchial adenomas" and were not considered malignant, although the potential for atypical carcinoids to become malignant was recognized. The World Health Organization's current histologic classification of pleuropulmonary tumors defines carcinoids as malignant tumors of epithelial origin with various growth patterns (organoid, trabecular, insular, palisading, or rosette) that suggest neuroendocrine differentiation. In addition, they are subclassified into typical and atypical carcinoids according to the number of mitoses per high power field and the presence or not of necrosis.

Compared to other malignant tumors, carcinoid tumors have a high rate of resectability and a better prognosis. The prognosis depends principally on factors such as the size of the tumor, histologic type, nodal involvement, and the presence of metastasis.

We present a retrospective study of 62 patients treated for lung carcinoid tumor between May 1985 and October 2000 at the Thoracic Surgery Unit of the Hospital Clínic

in Barcelona, Spain. The following parameters were recorded: sex, smoking history, carcinoid syndrome, surgical indication, nodal involvement, and presence of metastasis. The relation between these factors and long-term survival was studied.

Patients and Methods

The clinical records of 62 patients treated for carcinoid tumor between May 1985 and October 2000 were reviewed. We recorded 8 parameters: sex, smoking habit (pack-years), carcinoid syndrome (defined as the presence of facial flushing, hypertensive crisis, or diarrhea), location of tumor as determined by computed tomography (CT) and fiberoptic bronchoscopy, hilar or mediastinal lymph node involvement in the excised tissue, distant metastasis (found by thoracoabdominal CT scan and/or abdominal ultrasound), histopathology (of the biopsy obtained during fiberoptic bronchoscopy and of the resected tumor), surgical technique used, and postsurgical complications.

The overall survival rates were computed at 15 years (telephone or outpatient follow up). Survival rates were studied with respect to tumor size, histology, nodal involvement, and presence of metastasis.

Results

Of the 62 patients, 35 were male (56%) and 27 female (44%). The patients ranged in age from 15 to 81 years, with a mean age of 49.1 (SD 17.4) years. Thirty percent of the patients (n=19) were smokers or former smokers. It was impossible to document postoperative follow up of 15 patients treated before 1990.

A preoperative fiberoptic bronchoscopy was performed on all patients. Endoscopy revealed intrabronchial lesions in 44 cases (71%); findings were normal in 18 cases. In 20 of the 44 cases with intrabronchial lesions, the lesion was highly suggestive of carcinoid tumor or it was well vascularized; as a result, no biopsy was performed. A needle aspiration was carried out in the remaining cases.

Histologic diagnosis was made prior to surgery in 26 cases (42%); of these, diagnosis was obtained by endoscopic biopsy in 24 cases and by CT-guided transparietal fine-needle aspiration in 2. Diagnosis was established intraoperatively in 32 cases and postoperatively in 4 after analysis of the resected tissue.

Five patients (7.9%) had carcinoid syndrome—2 in the atypical carcinoid group (20%) and 3 in the typical carcinoid group (5.8%). The lower right lobe was the most common location (Table 1).

Lung resection with lymph node biopsy was the technique chosen for 53 patients. For 9 patients, open surgery was contraindicated because of poor lung function or comorbidity. In these cases, a laser photoresection of the endoluminal portion of the tumor was performed (Table 2).

Fifty-two patients (84%) had typical carcinoids and 10 (16%) atypical carcinoids. Nine patients (15%) had lymph node metastasis, which was more common in the

atypical carcinoids (n=3; 33%) than in the typical carcinoids (n=6; 12%).

Five patients (8%) had distant metastasis, 4 in the liver area and 1 within the lungs. Of the 4 patients with liver metastasis, the diagnosis was established postoperatively in 2 cases and preoperatively in 2 (in these cases, no change was made to the planned surgical intervention because, in the first patient, the liver metastasis was resectable and, in the second, the carcinoid tumor caused recurrent episodes of obstructive pneumonitis requiring multiple hospital admissions).

Six patients (10%) developed complications that required specific treatment: vesicular edema, hydro-pneumothorax requiring chest tubes, infection of the surgical incision, hypertensive crisis, hyperglycemia, and hemothorax requiring a second intervention.

The mortality rate of the series at 15 years was 13% (6 of 47 patients with postoperative follow up). The mortality rate from tumor-related causes was 11% (5 cases: 3 typical and 2 atypical carcinoids). No postoperative intrahospital deaths occurred. The overall survival rate for the series was 70%, with an average of 138 (SD 11) months (Figure).

No significant differences were found in survival with respect to the presence of nodal involvement; the presence of metastasis was, however, a factor for which significant differences were found. Likewise,
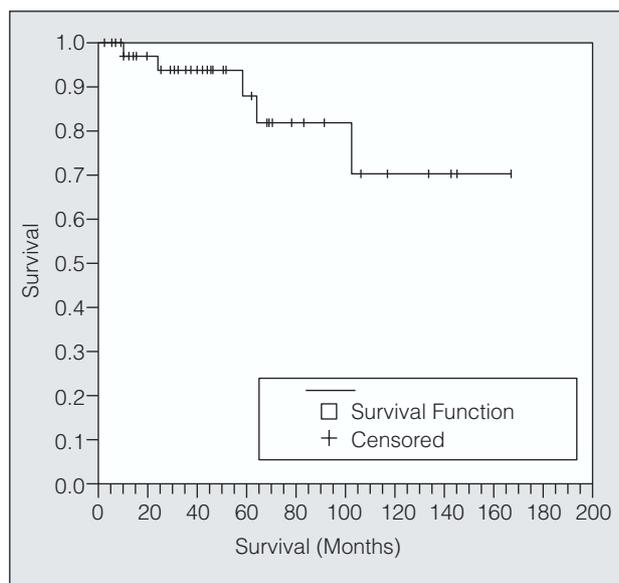
TABLE 1
Tumor Location

Location	Number	Percentage
Lower right lobe	11	17.7
Lower left lobe	9	14.5
Upper right lobe	8	12.9
Upper left lobe	7	11.3
Middle lobe	6	9.7
Bronchus, right superior lobe	5	8.1
Bronchus, left superior lobe	4	6.4
Right main bronchus	3	4.8
Left main bronchus	3	4.8
Middle lobar bronchus	2	3.3
Left inferior lobar bronchus	2	3.3
Intermediate bronchus	1	1.6
Right inferior lobar bronchus	1	1.6

TABLE 2
Surgical Technique Used

Type of Resection	Number	Percentage
Upper right lobectomy	10	16.1
Lower right lobectomy	9	14.5
Photoresection with Nd:YAG laser	9	14.5
Lower left lobectomy	7	11.3
Upper left lobectomy	6	9.7
Middle and lower bilobectomy	6	9.7
Left pneumonectomy	4	6.6
Middle lobectomy	3	4.8
Atypical segmentectomy	3	4.8
Segmentectomy	3	4.8
Upper and middle bilobectomy	1	1.6
Right pneumonectomy	1	1.6

Figure. Actuarial survival curve (Kaplan-Meier) according to histologic type.

significant differences in presence or absence of metastasis (*P*=.027) were found in function of tumor type diagnosed after histology, with metastasis being more common in atypical carcinoid tumors. No significant relation was found between the emergence of complications and the surgical technique used, the location of the tumor, or the existence of carcinoid syndrome. We observed no significant correlation between smoking and tumor histology. Patients who smoked had a higher mortality rate from nontumor causes than nonsmokers, although the difference was not significant.

Discussion

Carcinoid tumors have an incidence of 1% to 2%.[1-4] In some series, this incidence is higher in the male population (2:1), while in other series it is higher among females (3:2).[4] In our series, we found no significant differences in distribution by sex (55.6% men and 44.4% women). We found no relation between sex and tumor histology or survival rates.

The age of presentation is quite variable. In our series, the mean age was 49 years—similar to that of other series—and the range was from 15 to 81 years.[1-4] Some authors report that the emergence of carcinoid tumor occurs, on average, about 10 years before the emergence of bronchial carcinoma.[4]

Preoperative fiberoptic bronchoscopy performed on all of the patients found lesions in 71% of the cases. Domingo et al[5] have asserted that the macroscopic image of the lesion often suggests the diagnosis, although they support needle aspiration of the lesion because it has a diagnostic yield of 80%.

Carcinoid syndrome, defined as the presence of facial flushing, hypertensive crisis, or diarrhea is described in 6.7% to 10% of cases.[4,6-8] Its emergence is more common in carcinoids restricted to the intestine, in which the presence of liver metastasis is necessary to confirm diagnosis. Liver metastasis is not a requisite in the case of bronchial carcinoids, however. In our series, 7.9% of the patients (n=5) had carcinoid syndrome and, of these, 60% had typical carcinoid tumor. We found no significant relation between histology and the emergence of carcinoid syndrome. Moertel et al,[7] in a series of 209 patients, found carcinoid syndrome in 6.7%, a figure that rose to 15% when metastasis was present.[9] In our study, we found no significant relation between the presence of metastasis and carcinoid syndrome.

Some studies report that carcinoid tumors are located in the left hemithorax in up to 75% of the cases.[3] In our series, the lower right lobe of the right hemithorax was the most common location (Table 1).

Jamal et al[1] observed that 16% of the patients with carcinoid tumor had nodal involvement; this percentage increased to 28% for atypical carcinoids. Other studies have found mediastinal lymph node involvement in up to 30% to 50% of the cases of atypical carcinoids.[10,11] In our study, nodal involvement was present in 15% (n=9). We observed no significant correlation between nodal involvement and cancer-related mortality, a finding consistent with reports from Froudarakis et al[12] that the prognosis was no worse for patients with nodal involvement. We also found no relation between nodal involvement and the type of tumor.

In some series, up to 30% of cases involve the presence of distant metastasis, mainly in cases located in the colon, small intestine, or bones. In atypical carcinoid tumors, cases with cerebral and thyroid involvement have been described.[4] In our series, 8% of the cases (n=5) had distant metastasis. We found a significant relation between the presence of metastasis and the atypical carcinoid histologic subtype (*P*=.027) and between the presence of metastasis and mortality (*P*=.002).

The most common surgical treatment was lobectomy.[4,3,13] Segmentectomy was considered valid for high risk surgical patients with a small tumor located in the periphery of the lung parenchyma and without mediastinal or hilar lymph node involvement.

Authors such as El Jamal et al,[1] citing the slow growth of carcinoid tumors,[14,15] have argued in favor of conservative resection regardless of the tumor type; on the other hand, others favor routine excision of the lobe or lung and the area around the lymph nodes.[16-18]

Endoscopic resection of endobronchial tumors has been described, although recurrence—later requiring excision according to usual practice—has been observed after this procedure.[1] For this reason, most authors reserve this treatment for patients ineligible for surgery.[19]

The role of chemotherapy in treating carcinoid tumors is still not clear. The cause-effect relation between tobacco use and carcinoid tumor is not clear either.

In conclusion, bronchial carcinoid tumors are malignant neoplasms with a good long-term prognosis after surgical treatment. The survival of patients with

carcinoid tumor depends basically on the histologic type and the presence of distant metastasis. Routine resection is the treatment of choice whenever possible. Palliative measures such as laser photoresection should be reserved for high risk patients with contraindications for surgery.

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