

# Late Recurrent Pulmonary Typical Carcinoid Tumor:

## Case Report and Review of the Literature

ARI CIMENT, M.D.<sup>1</sup>, JOAN GIL, M.D., PH.D.<sup>2</sup>, AND ALVIN TEIRSTEIN, M.D.<sup>3</sup>

### Abstract

Carcinoid tumors are uncommon pulmonary neoplasms. They are classified histologically as either atypical or typical. Atypical carcinoids are aggressive malignancies that require radical surgical resection and have a guarded prognosis with a propensity to metastasize and recur. Typical carcinoids are low-grade malignancies with relatively less metastatic or recurring potential and are usually treated with simple excision. Recurrence of a typical pulmonary carcinoid tumor more than a decade after initial resection is very rare. A patient with recurrence of a typical carcinoid tumor 11 years after resection of the primary lesion with one involved lymph node is reported here. Late recurrences are rare in both atypical and typical varieties, but are much more common in atypical carcinoids. The patient reported here represents the fifth case of recurrence of a typical carcinoid tumor more than ten years after resection. This suggests that, after resection of a typical carcinoid neoplasm, patients should be monitored carefully, especially if lymph node metastases are present at the time of surgery.

**Key Words:** Carcinoid, typical, atypical, recurrence, metastases, monitoring.

---

### Late Recurrent Pulmonary Typical Carcinoid Tumor

PULMONARY CARCINOID TUMORS represent 2% of all primary lung neoplasms. They are usually classified as either atypical or typical. Most authorities agree that atypical carcinoids are malignancies that are treated as carcinomas with radical surgery (1). They have a guarded prognosis with a propensity to recur and metastasize. The typical variety has been regarded as a low-grade malignancy with less metastatic or recurring potential and is treated with simple excision. Recurrence of a typical pulmonary carcinoid tumor more than a decade after initial resection is rare. The following is a report of a patient who had a rare late recurrence of a typical carcinoid tumor 11 years after complete primary resection. This represents one of the latest known recurrences after surgery.

---

<sup>1</sup>Second-year Pulmonary Fellow, <sup>2</sup>Pathology Attending, and <sup>3</sup>Pulmonary Attending, Pulmonary Disease, Mount Sinai School of Medicine, New York, NY.

Address all correspondence to Ari Ciment, M.D., 1245 Park Avenue, Apt. 2K, New York, NY 10128; e-mail: airciment@aol.com and ari.ciment@mssm.edu

Accepted for publication January 2006.

### Case Report

In October 2004, an 80-year-old male presented with a one-month history of right-sided chest discomfort. Although a nonproductive cough had been present for many years, he denied wheezing, orthopnea, anorexia, weight loss, fever, chills or hemoptysis. In 1993, he had undergone a right lower lobectomy for an endobronchial typical carcinoid tumor. One positive hilar lymph node had been found. The patient had stable angina pectoris and medication-controlled diabetes. He denied exposure to known toxic inhalants except for a brief smoking history 50 years previously. Physical examination was normal except for a well-healed right thoracotomy scar. Spirometry was consistent with slight obstructive dysfunction. Oxygen saturation was 95% while breathing room air. A CT scan of the patient's chest revealed a large packet of mediastinal lymph nodes involving the pretracheal and subcarinal areas, and measuring 5 × 5.8 cm (Fig. 1). Positron emission topography (PET) scan revealed adenopathy exhibiting a standardized uptake value (SUV) of 4.9 and 11.9, respectively. After a non-diagnostic bronchoscopic needle aspiration, cervical mediastinoscopy yielded lymph nodes with typical carcinoid tumor, histo-



**Fig 1.** The CT scan of the chest revealed a large packet of mediastinal lymph nodes involving the pretracheal and subcarinal areas, and measuring 5 × 5.8 cm.

logically identical to the primary tumor resected 11 years previously.

### Discussion

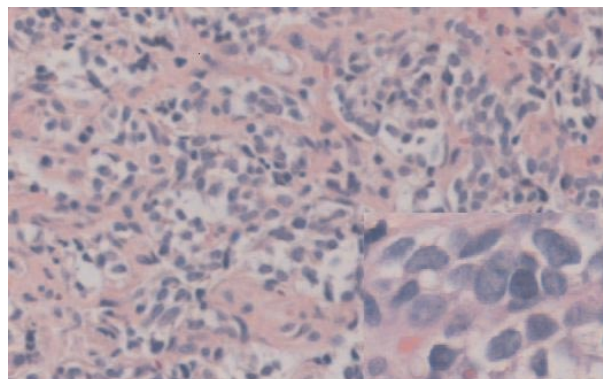
A majority of carcinoid tumors are located in the gastrointestinal tract, usually in the colon, rectum and small intestine. But 25% of them occur in the thorax, with two different clinical presentations:

1. An endobronchial lesion that causes hemoptysis, atelectasis and/or recurrent obstructive pneumonias.
2. A growing peripheral nodule, often discovered incidentally by a routine chest radiograph. CT examination often demonstrates vascular, circumscribed masses, which enhance with contrast. Though PET scanning is rarely positive in carcinoid tumors, there are reports demonstrating PET positivity, as in the patient reported here (2).

Carcinoid tumors are neuroendocrine malignancies arising from bronchial Kultchitsky cells, with less aggressive potential than large cell neuroendocrine carcinomas and small cell carcinomas. Histologically they consist of round cells with a recognizable nuclear chromatin pattern referred to as “salt and pepper,” which frequently develops into an organoid pattern with a fine connective cell stroma and rich vascularization. By electron microscopy these tumors exhibit diagnostic neuroendocrine cytoplasmic “dense core” inclusions (3). Immunohistochemistry for standard neuroen-

dochrine markers (neuron-specific enolase, chromogranin, synaptophysin) has been used by many to corroborate the histologic diagnosis (4). In 1972 Arrigoni et al. emphasized the entity of “atypical” carcinoid, a more aggressive form with biologic behavior and prognosis comparable to that of a carcinoma (5). Whether typical or atypical, these malignancies are characterized by small areas of necrosis, nuclear pleomorphism, absence of organoid or trabecular pattern, and areas of increased cellularity (Fig. 2). Currently, the sole diagnostic feature that distinguishes typical from atypical carcinoid is the number of mitoses. The diagnosis of typical carcinoid is supported only if the mitotic rate is equal to or lower than 2 mitoses/10 high power fields (HPF). The diagnosis of atypical carcinoid is established when there are 2–10 mitoses/HPF or in the presence of any necrosis. High mitotic rates above 10/10 HPF indicate a small cell carcinoma. Staining for the antigen Ki67 using the antibody MIB-1 has been used to determine the fraction of proliferating cells and to help ascertain the grade of the tumor (4).

Recurrence of carcinoid tumors after surgical resection varies between 2–9% and 5–30% for typical and atypical histologies, respectively. Froudarakis et al. found a statistical difference in survival between typical and atypical carcinoids. They noted no recurrences (6). Halevy et al. found no recurrences or distant metastases in 14 patients with bronchial adenomas after a 4–17 follow-up (7). One report of 95 patients who underwent lung resection revealed 10 recurrences. Seven of these had atypical histology. Lymph node metastases were more common in the atypical variety (8). Ferguson et al. analyzed 139 patients with resected pulmonary carcinoids (9). Recurrent carcinoid de-



**Fig. 2.** The histological pattern of the mediastinoscopy biopsy specimen showed an organoid structure with characteristic rounded cells. These rounded cells (inset) demonstrated a “salt and pepper” pattern characterizing the fine intranuclear granular appearance of chromatin, consistent with the diagnosis of typical carcinoid tumor.

veloped in eight patients at postoperative intervals of  $43 \pm 25$  months. The authors concluded that the only significant predictor of recurrence is atypical histology, with a relative risk of recurrence of 7.9. Kaplan et al. noted a locoregional failure rate of 8.4% for typical carcinoids and 22.7% for atypical carcinoids (10). A study of 27 patients with atypical carcinoids showed a recurrence rate of 18.5% (11). Thomas et al. concluded that patients with atypical pulmonary carcinoid tumors with regional lymph node metastases have a high likelihood of developing recurrent disease if treated with surgical resection alone. Many of the atypical carcinoid patients (63.6%) developed systemic metastases at a median time of 17 months after diagnosis (12).

Recurrences more than ten years after lung resection, whether of the typical or atypical histological varieties, are uncommon. A 1978 case report detailed a case of recurrent carcinoid 32 years after initial resection (13). In all, there have been 4 reported typical carcinoid recurrences more than 12 years after surgical intervention. In a report of 82 cases, 65 "benign" and 17 "malignant," 1 of 2 recurrences in the typical group occurred 12 years after surgery (14). Another typical carcinoid occurred 16 years after primary resection in a group of 57 patients (15). A review of 60 patients with pulmonary carcinoids revealed that 1 out of 42 patients with typical carcinoid had recurrence 14 years after resection (16). And among 93 patients with typical carcinoid tumors, one had disseminated metastatic bone and liver disease 17 years after the resection. (17). These 4 cases, and the fifth reported here, highlight the rarity of recurrence and emphasize the need for close surveillance of resected typical carcinoids for many years after resection, especially if local lymph node involvement is present at the time of the original resection.

### References

1. Kosmidis PA. Treatment of carcinoid of the lung. *Curr Opin Oncol* 2004; 16(2):146–149.
2. Wartski M, Alberini JL. Typical and atypical bronchopulmonary carcinoid tumors on FDG PET/CT imaging. *Clin Nucl Med* 2004; 29(11):752–753.
3. Robbins R, Kumar V. The lung. Chapter 15. Pathologic basis of disease. 7th ed. 2005. pp. 764–765.
4. Rusch V. Molecular markers help characterize neuroendocrine lung tumors. *Ann Thorac Surg* 1996; 62(3):798–809; discussion 809–810.
5. Arrigoni MG, Wollner LB, Bernatz PE. Atypical carcinoid tumors of the lung. *J Thorac Cardiovasc Surg* 1972; 64(3):413–421.
6. Froudarakis M, Fournel P, Burgard G, et al. Bronchial carcinoids. A review of 22 cases. *Oncology* 1996 53(2):153–158.
7. Halevy A, Schachner A, Nili M, et al. Bronchial adenoma: surgical experience with long-term follow-up (4–17 years). *J Surg Oncol* 1985; 29(1):66–68.
8. McCaughan BC, Martini N. Bronchial carcinoids. Review of 124 cases. *J Thorac Cardiovasc Surg* 1985; 89(1):8–17.
9. Ferguson MK, Landreneau RJ, et al. Long-term outcome after resection for bronchial carcinoid tumors. *Eur J Cardiothorac Surg* 2000; 18(2):156–161.
10. Kaplan B, Stevens C, Allen P, et al. Outcomes and patterns of failure in bronchial carcinoid tumors. *Int J Radiation Oncol* 2003; 22(1):125–131.
11. Marty-Ane CH, Costes V. Carcinoid tumors of the lung: do atypical features require aggressive management? *Ann Thorac Surg* 1995; 59(1):78–83.
12. Thomas CF Jr, Tazelaar HD, Jett JR. Typical and atypical pulmonary carcinoids: outcome in patients presenting with regional lymph node involvement. *Chest* 2001; 119(4):1143–1150.
13. Altschuler M, Warner R, Kirschner P. Resection of Mediastinal Metastasis of Malignant Carcinoid 32 Years After Pneumonectomy. *N Y State J Med* 1978; 78(14):2205–2010.
14. Bertelsen S, Aasted A, et al. Bronchial carcinoid tumours. A clinicopathologic study of 82 cases. *Scand J Thorac Cardiovasc Surg* 1985; 19(1):105–111.
15. Hurt R, Bates M. Carcinoid tumours of the bronchus: a 33 year experience. *Thorax* 1984; 39(8):617–623.
16. Rea F, et al. Bronchial carcinoids: a review of 60 patients *Ann Thorac Surg* 1989; 47(3):412–414.
17. Schreurs, AJ, Westermann, CJ, Van den Bosch, JM, et al. A twenty-five-year follow-up of ninety-three resected typical carcinoid tumors of the lung. *Thorac Cardiovasc Surg* 1992; 104:1470–1475.