

Case Report

Spontaneous Partial Regression of a Carcinoid Tumor: Radiology May Not Capture the Real Picture

Ashok Kuwal¹ , Nishant Chauhan² , Naveen Dutt³ , Poonam Elhence⁴ , Manish Advani⁵ , Sunil Kumar⁶ 

¹Department of Pulmonary Medicine, Pacific Institute of Medical Sciences, Udaipur, Rajasthan, India

^{2,3}Department of Pulmonary Medicine, All India Institute of Medical Sciences, Jodhpur, Rajasthan, India

⁴Department of Pathology, All India Institute of Medical Sciences, Jodhpur, Rajasthan, India

⁵Department of Pulmonary Medicine, Pacific Institute of Medical Sciences, Udaipur, Rajasthan, India

⁶Department of Pulmonary Medicine, Pacific Medical College and Hospital, Udaipur, Rajasthan, India

Cite this article as: Kuwal A, Chauhan N, Dutt N et al. Spontaneous Partial Regression of a Carcinoid Tumor: Radiology May Not Capture the Real Picture. Turk Thorac J 2019; DOI: 10.5152/TurkThoracJ.2018.18059

Abstract

A partial or complete resolution of the neoplastic lesion, either spontaneously or in the presence of therapy that is considered inadequate to exert significant influence on the growth of the neoplastic lesion, is considered a spontaneous regression. This phenomenon is extremely rare in lung neoplasms. A close follow up with imaging along with bronchoscopy and a biopsy of the lesion is essential, as they may have potential for distant spread even during radiological regression. Here, we report a case of a partial resolution of a bronchial carcinoid tumor that had a high mitotic activity and was resected.

KEYWORDS: Carcinoid, mitotic activity, spontaneous regression

Received: 06.05.2018

Accepted: 08.08.2018

Available Online Date: 31.01.2019

INTRODUCTION

Carcinoid tumors are rare endocrine tumors that represent less than 1% of all pulmonary tumors [1]. They can develop in various organs in the body, most commonly in gastrointestinal tract followed by the bronchopulmonary region. Three fourth of pulmonary carcinoids are located in the central airways and present with recurrent pneumonia, hemoptysis, or cough [2]. Endobronchial biopsy with immunohistochemical stains for chromogranin and synaptophysin is usually diagnostic of pulmonary carcinoids.

Spontaneous regression (SR) of cancer refers to a partial or complete resolution of the malignant neoplasm in the absence of treatment or in the presence of a treatment that is considered inadequate to exert a significant influence on tumor growth [3]. SR is very rare phenomenon in thoracic malignancies, particularly pulmonary carcinoids, and only few cases has been reported in literature [4-6]. Here, we present a case of pulmonary carcinoid tumor that showed partial regression on imaging but found to have high proliferative potential on followup and was surgically resected.

CASE PRESENTATION

A 19 years old male, non-smoker, student presented with complaints of dry cough and dyspnea on exertion for 2 years. He underwent chest radiography, which was normal. A contrast enhanced computed tomography (CECT) scan of the thorax was done, which revealed a 1.7 x 2.1 x 2.2 cm well defined, mildly enhancing lesion in the right lower lobe just after the division of the superior segment with coarse calcifications (Figure 1). Diagnostic bronchoscopy was performed and a biopsy from the lesion was taken. A histopathological examination of the lesion was suggestive of bronchial carcinoid tumor. The patient was lost to follow up and again presented with persistent cough along with episodes of blood tinged sputum and dyspnea after an interval of 24 months.

The general physical examination was unremarkable. On auscultation, there were diminished lung sounds over the right hemithorax, particularly the right subscapular area, and there was localized wheezing over same area.

The patient was advised a repeat CECT scan of the thorax, which revealed a decrease in the size of the lesion (1.5x1.9x1.8 cm) with no associated parenchymal lesions (Figure 2). Bronchoscopy showed an exophytic mass lesion completely occluding the lumen of the right lower lobe bronchus after the origin of the superior segment bronchus (Figure 3). Narrow band imaging (NBI) bronchoscopy showed dilated and tortuous vessels over the mass (Figure 4). A histopathological examination of the biopsy specimen from the lesion showed rounded cells arranged in a nesting trabecular pattern and exhibited central nuclei and abundant eosinophilic cytoplasm. The nuclei displayed a characteristic salt and pepper chromatin. There was no

Address for Correspondence: Ashok Kuwal, 1007, Gyan Nagar, Near Gyan Mandir School, Sector-4, Hiran Magri, Udaipur, Rajasthan, 313002, India

E-mail: kuwal.dr@gmail.com

©Copyright 2019 by Turkish Thoracic Society - Available online at www.turkthoracj.org

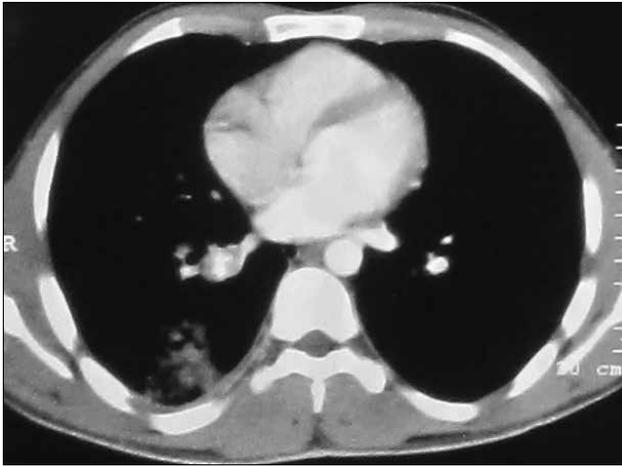


Figure 1. CECT thorax showed 1.7×2.1×2.2 cm well defined, mildly enhancing lesion in the right lower lobe immediately after the division of the superior segment with coarse calcifications
CECT: contrast enhanced computed tomography



Figure 2. CECT thorax (2015) showed a decrease in the size of the lesion (1.5×1.9×1.8 cm)
CECT: contrast enhanced computed tomography



Figure 3. Diagnostic bronchoscopy showed a large, rounded, exophytic mass lesion completely filling the lumen of the right lower lobe bronchus after the take off of the superior segment bronchus
necrosis, hemorrhage, or mitotic activity (Figure 5). Tumor cells were stained positive for chromogranin (Figure 6), synaptophysin, and cytokeratin (Figure 7) and negative for p63. The



Figure 4. Narrow band imaging bronchoscopy revealed prominent dilated and tortuous vessels over the mass lesion

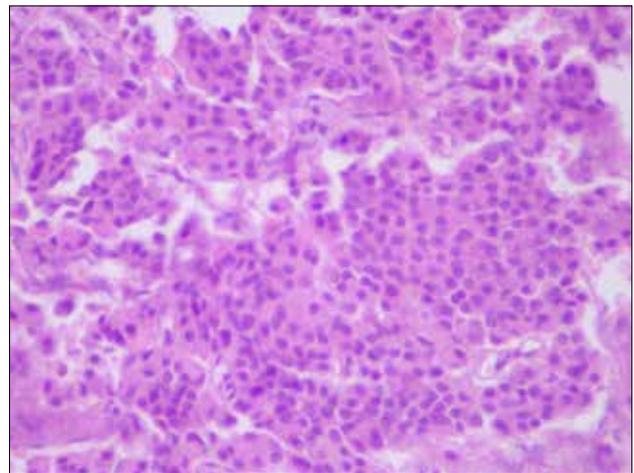


Figure 5. Histopathological examination of the endobronchial biopsy specimen exhibited rounded cells with abundant eosinophilic cytoplasm and central nuclei, which displayed a characteristic salt and pepper chromatin. There was no necrosis, hemorrhage, or mitotic activity

patient was confirmed as a case of endobronchial carcinoid tumor. A further study for the tumor proliferative activity, i.e., Ki-67 proliferation index, was done, which was 50%.

The patient was discussed in the tumor board of our institution, and in view of the increased proliferation index (mitotic activity) and younger age, he was scheduled for right lower lobectomy with mediastinal lymph node dissection. The post-operative period was uneventful, and he became asymptomatic following the surgery. Mediastinal lymph nodes were free from tumor infiltration. The patient did not require any further interventions and was on regular follow up. He provided verbal consent for the publication of the present case report.

DISCUSSION

Spontaneous regression of any cancer, either complete or partial, is an extremely uncommon phenomenon. It is not implicated that SR should progress to complete disappearance of the tumor. SR was first defined by Stewart [3] as “the partial or complete disappearance of the tumor in the

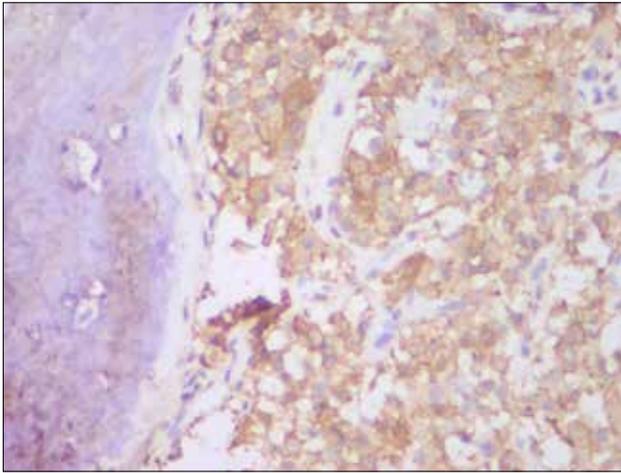


Figure 6. IHC-chromogranin positivity
IHC: immunohistochemistry

absence of all treatment or in the presence of therapy that is considered inadequate to exert a significant influence on neoplastic disease”.

Spontaneous regression has been observed in different cancers, such as renal cell carcinoma, neuroblastoma, hepatocellular carcinoma, and lymphoma. Everson and Cole [7] collected data from 1900 to 1964, and only 130 cases of SR were found. They observed that SR most frequently occurred in neuroblastoma (28 cases), renal cell carcinoma (21 cases), choriocarcinoma (13 cases), malignant melanoma (12 cases), soft tissue sarcoma (9 cases), carcinoma bladder (8 cases), osteogenic sarcoma (6 cases), and breast carcinoma (5 cases).

Spontaneous regression is extremely rare in thoracic malignancies; a review on SR of thoracic malignancies found that out of 782 cases, only 76 thoracic malignancies cases showed SR. A majority of these cases were metastatic thoracic disease (71 cases), and only 5 cases (0.006%) were primary thoracic malignancy [8]. SR of bronchial carcinoid tumor was observed in only few cases. Luosto et al. [4] reported the first case of SR of a bronchial carcinoid tumor following pregnancy. Two cases were recently reported and claimed to be secondary to an injury caused by taking a biopsy of the tumor [7,8].

Various hypotheses have been postulated for SR of tumors, such as immunomodulation, paraneoplastic syndromes, trauma caused by either surgery, biopsy, injection of ethanol, or Neodymium-doped Yttrium Aluminum Garnet (Nd: YAG) laser irradiation [9-12]. In our case, there was partial regression of the tumor based on the thorax CT that was done after an interval of 24 months. It is possible that trauma due to the bronchoscopic biopsy was the inciting event that lead to partial regression of the carcinoid tumor.

The mitotic index (number of mitoses per high power field) is used to differentiate between typical and atypical carcinoids, but because of considerable inter-observer variability, the Ki-67 index is increasingly used to assess the tumor proliferative fraction and is determined as the percentage of Ki-67 positive cells through immunohistochemistry. The

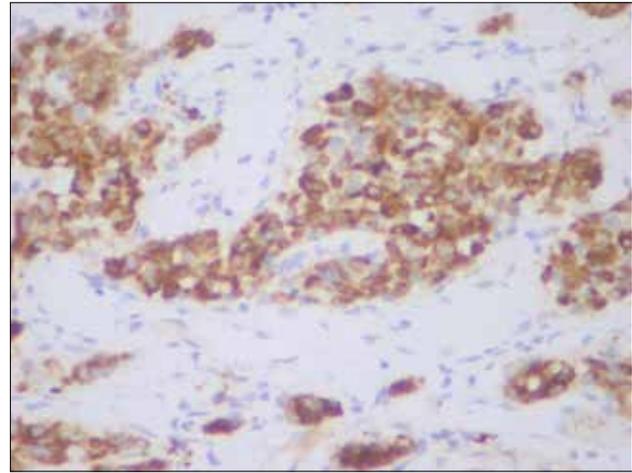


Figure 7. IHC-cytokeratin positivity
IHC: immunohistochemistry

Ki-67 index has a key role in the assessment of non-small cell lung carcinoma prognosis; prediction of brain metastases in patients with lung adenocarcinoma; and in the diagnosis, classification, and prognosis of pulmonary neuroendocrine tumors [13].

A study by Grimaldi et al. [14] analyzed that the cutoff Ki-67 score that discriminates recurrent versus non-recurrent disease was 4%, and they concluded that the Ki-67 score predicts the patient outcome better than the mitotic count, histotype, and tumor stage, and it is therefore helpful in establishing the appropriate follow-up. Another study by Dhall et al. [15] showed that the Ki-67 index greater than 2% at either the primary site or the metastatic site was found to be the only significant predictor of progression-free survival. A study to assess the progression of neuroendocrine tumour also evaluated the utility of the Ki-67 index and found that there was a significant correlation between the expression of Ki-67 and tumor progression [16]. They suggested that Ki-67 is an excellent indicator to assess the progression of neuroendocrine tumors.

Our case demonstrated a Ki-67 score of 50%, which suggests a high proliferative index and a high probability for distant metastasis even in the stage of regression. NBI bronchoscopy also showed numerous dilated blood vessels, which further confirms the tumor’s high potential for proliferation.

CONCLUSION

Surgical resection of the carcinoid tumor is the mainstay of therapy with a good 5-year survival rate. Although our case did not show a complete regression of the tumor, a followup bronchoscopic biopsy with analysis of the Ki-67 score suggested high proliferative potential of the tumor. Hence, for the lung carcinoids showing SR, monitoring only with imaging may be misleading and bronchoscopy with a biopsy of the lesion along with the addition of proliferation indices provides the true picture in such cases. The Ki-67 score owing to its superior inter-observer agreement compared to the mitotic count can serve as an adjunct to serial imaging, bronchoscopy, and biopsy in the evaluation and monitoring of carcinoid tumors.

Informed Consent: The patient gave verbal consent for the publication of the present case report.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - A.K., N.C., N.D.; Design - A.K., N.C., P.E.; Supervision -N.C., N.D., P.E.; Data Collection and/or Processing -A.K., N.C., M.A., S.K.; Analysis and/or Interpretation -N.K.,N.D., A.K.; Literature Search -A.K., N.K., N.D., P.E.; Writing Manuscript -A.K., N.K., N.D.; Critical Review -M.A., S.K., P.E.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Noel-Savina S, Descourt R. Focus on treatment of lung carcinoid tumor. *Onco Targets Ther* 2013;6:1533-7. [\[CrossRef\]](#)
2. Kaifi JT, Kayser G, Ruf J, Passlick B. The diagnosis and treatment of bronchopulmonary carcinoid. *Dtsch Arztebl Int* 2015;112:479-85. [\[CrossRef\]](#)
3. Stewart FW. Experiences in spontaneous regression of neoplastic disease in man. *Tex Rep Biol Med* 1952;10:239-53.
4. Luosto R, Koikkalainen K, Sipponen P. Spontaneous regression of a bronchial carcinoid tumour following pregnancy. *Ann Chir Gynaecol Fenn* 1974;63:342-5.
5. Dao D, Resnikoff J. Spontaneous Regression of a Bronchial Carcinoid Tumor. *Chest* 2015;148:4. [\[CrossRef\]](#)
6. Venkatram S, Sinha N, Hashmi H, et al. Spontaneous Regression of Endobronchial Carcinoid Tumor. *J Bronchology Interv Pulmonol* 2017;24:70-4. [\[CrossRef\]](#)
7. Everson TC, Cole WH. Spontaneous regression of cancer. *Ann Surg* 1956;144:366-80. [\[CrossRef\]](#)
8. Kumar T, Patel N, Talwar A. Spontaneous regression of thoracic malignancies. *Respir Med* 2010;104:1543-50. [\[CrossRef\]](#)
9. Cole WH. Relationship of causative factors in spontaneous regression of cancer to immunologic factors possibly effective in cancer. *J Surg Oncol* 1976;8:391-411. [\[CrossRef\]](#)
10. Papac RJ. Spontaneous regression of cancer. *Cancer Treat Rev* 1996;22:395-423. [\[CrossRef\]](#)
11. Chang WY. Complete spontaneous regression of cancer: four case reports, review of literature, and discussion of possible mechanisms involved. *Hawaii Med J* 2000;59:379-87.
12. Lopez-Pastorini A, Plönes T, Brockmann M, et al. Spontaneous regression of non-small cell lung cancer after biopsy of a mediastinal lymph node metastasis: a case report. *J Med Case Rep* 2015;9:217. [\[CrossRef\]](#)
13. Chirieac LR. Ki-67 expression in pulmonary tumors. *Transl Lung Cancer Res* 2016;5:547-51. [\[CrossRef\]](#)
14. Grimaldi F, Muser D, Beltrami CA, et al. Partitioning of Bronchopulmonary Carcinoids in Two Different Prognostic Categories by Ki-67 Score. *Front Endocrinol* 2011;2:20. [\[CrossRef\]](#)
15. Dhall D, Mertens R, Bresee C, et al. Ki-67 proliferative index predicts progression-free survival of patients with well-differentiated ileal neuroendocrine tumors. *Hum Pathol* 2012;43:489-95. [\[CrossRef\]](#)
16. Kimura N, Miura W, Noshiro T, et al. Ki-67 is an indicator of progression of neuroendocrine tumors. *Endocr Pathol* 1994;5:223-8. [\[CrossRef\]](#)