

ARGON PLASMA COAGULATION USE IN PALLIATIVE TREATMENT OF TYPICAL-ATYPICAL CARCINOID TUMORS

[™]Mustafa Erelel, [™]Ahmet Serhan Dağıstanlı, [™]Fatih Zengin

İstanbul Üniversitesi, İstanbul Tıp Fakültesi, Göğüs Hastalıkları Ana Bilim Dalı, İstanbul

ABSTRACT

Bronchial carcinoid tumors constitute 1-2% of all primary lung tumors. The main treatment for lung carcinoid tumors is surgery but bronchoscopic endobronchial therapy is also a palliative option for poor surgical candidates. This study will discuss the outcomes of bronchoscopic endobronchial treatment for two cases.

Case 1 has a typical carcinoid tumor in right upper lobe and has multiple comorbidities. Case 2 is a patient with metastatic atypical carcinoid tumor who was operated before. We used argon plasma coagulation technique in treatment of both cases.

Keyword: Carcinoid tumor, bronchoscopy, argon plasma coagulation



TİPİK-ATİPİK KARSİNOİD TÜMÖRLERİN PALYATİF TEDAVİSİNDE ARGON PLAZMA KOAGÜLASYON KULLANIMI

ÖZET

Bronşial karsinoid tümörler tüm primer akciğer tümörlerinin %1-2'sini oluşturur. Pulmoner karsinoid tümörler için esas tedavi yöntemi cerrahi olmakla birlikte operasyon için yüksek riskli hastalarda palyatif bronkoskopik endobronşial tedaviler

uygulanabilmektedir. Bu çalışmada bronkoskopik endobronşial tedavi uygulanan 2 vaka tartışılmıştır. Birinci vaka sağ üst lobda tipik karsinoid tümörü mevcut olan ve eşlik eden multipl komorbiditeleri olan hastamız; ikinci vaka ise daha önce opere edilen metastatik atipik karsinoid tümör tanılı hastamızdır. Her iki vakanın tedavisinde de argon plasma koagülasyon tekniği kullanılmıştır.

Anahtar kelimeler: Karsinoid tümör, bronkoskopi, argon plazma koagülasyon

INTRODUCTION

Carcinoid tumor is attributed to neuroendocrine tumors of lung and originates from epithelial cells. Neuroendocrine tumors are classified into 3 main categories according to the degree of differentiation: typical/atypical carcinoid tumors, large cell neuroendocrine tumors and small cell carcinomas.¹

The incidence of carcinoid tumors among all primary lung tumors is 1-2%. The most common primary lung tumors in children and adolescents are carcinoid tumors.² Typical carcinoid tumors occur most frequently in the fourth decade in adults, while atypical carcinoid tumors occur most frequently in the fifth decade in adults. For the typical carcinoid tumors (%90) which are considered as low grade, regional lymph node involvement is 5-15% and distant organ involvement is 3%; despite atypical carcinoid tumors, respectively 40-50% and 20%, therefore they are medium grade. Typical bronchial carcinoids have a good prognosis with a 10-year survival rate of 90% compared with the atypical carcinoids which have 10-year survival below 60%.^{3,4}

75-90% of carcinoid tumors are central; 10-25% is peripheral. Central localized tumors may show complete or partial bronchial obstruction. Cough, hemoptysis and recurrent infections are classical symptoms. Approximately 40% of carcinoid tumors are detected incidentally on radiological examinations without clinical evidence. Computed tomography can be seen as radiologically well defined, round / ovoid, as well as nodular nodules or as polypoid nodules with stalk only in airways.

Assessment of the presence of non-airway involvement of masses, especially within airways, is crucial in determining the treatment plan. Atypical carcinoid tumors have more involvement and SUV degree than typical carcinoid tumors.¹¹ Gallium 68 is

a radioisotope agent commonly used in PET imaging with somatostatin analogues in carcinoid tumors.¹²

In bronchopulmonary carcinoid tumors, complete resection of the tumor is the main treatment method by preserving as much lung tissue as possible. Resection of lung tissue with non-reversible changes due to obstruction at the distal end of the tumor may also be necessary in some cases.¹³

Bronchoscopic endobronchial therapy is a good palliative option in cases where surgical treatment is required but cannot be performed due to comorbid conditions. In superficial tumors, techniques may be chosen to provide tissue penetration of a depth of several millimeters. Techniques used for this purpose are argon plasma coagulation (APC), cryotherapy, electrocautery or laser.¹⁴

In this study, we present palliative treatment by using APC for two carcinoid tumor cases (a typical carcinoid tumour case and a recurrent atypical carcinoid tumour case) for an alternative treatment option.

CASE 1

Total thyroidectomy due to thyroid papillary ca, cholecystectomy due to cholelithiasis and gastric resection due to stomach gastrointestinal stromal tumor and diagnosis of chronic hepatitis C infection were known in a 77-year-old male patient; and presented with complaints of cough, sputum and shortness of breath to our hospital. Findings compatible with atelectasis were seen in chest XR. The patient underwent a bronchoscopy in December 2013 and a biopsy+cytology sample was taken. Atypical cells were not seen in the bronchial lavage of the patient and the pathology was compatible with the neuroendocrine tumor. On PET CT examination performed in December, 2013, on the right lung hilar region, there was increased Ga-68 DOTA-NOC



Figure 1.

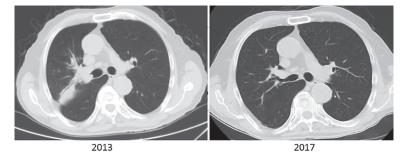


Figure 2.



Figure 3. Right main bronchus entry nearly totally blocked



Figure 4. Right main bronchus airway clearance provided



involvement due to intense somatostatin receptor content in a mass lesion area of approximately 29x18 mm, forming pressure on the right lung upper lobe segment bronchus and atelectasis was detected near to the fissure and upper lobe posterior segment. The bronchoscopy was reperformed in December 2013. The bronchus of the upper lobe of the right lung nearly totally occluded and the main bronchus protruded but not infiltrated with a flat bright mass lesion. Occlusion was cleaned by using cryotherapy, using argon and mechanically. The patient's pathology was reported as typical carcinoid tumor. In April 2014, the patient was re-bronchoscopied due to airway obstruction and obstruction was removed. Bronchoscopy was performed 6 times in total between 2013 and 2017 to clear the obstruction (Figure 1). In the last CT scan done in 2017 the tumor was lost which was seen in CT scan in 2013 (Figure 2).

PET CT which was performed in August 2017, did not select the lesion in the right upper lobe which was seen on previous PET CT.

CASE 2

A 66-year-old man with a diagnosis of atypical carcinoid tumor presented with cough, sputum, shortness of breath and with a mass of 14 * 9 mm at right main bronchus in the chest CT scan. Left upper lobectomy was performed in July,2006 and pathology was reported as atypical carcinoid tumor. The patient didn't have chemotherapy or radiotherapy postoperatively. Metastasis was detected in the right lobe of the liver and right hepatectomy was performed in September, 2007. The post-operative pathologic result was reported as well differentiated endocrine carcinoma metastasis. After right hepatectomy, 4 cycles cisplatin + etoposide treatment were performed in 2007 and 15 sessions of 30 Gy dose of cranial RT in 2008. Patient follow-ups showed left lobe of the liver and vertebrae metastatic lesions in 2010 and 6 more cisplatin + etoposide treatments were applied in 2010. In the GA68 DOTA TATE PET / CT study performed in March, 2015, the lesion was seen in the right bronchus of the right main bronchus with recurrence in the lesion (Figure 5), in the residual liver parenchyma, in the bilateral surrenal gland and in the colonic cecum, 177 DOTATATE treatment for somatostatin receptor-positive lesions was performed in 4 courses because of the presence of intramuscular mass lesions consistent with implantation in the peritoneal areas and in the lesions observed in the skeletal system showing intense somatostatin receptor

positivity. A bronchoscopy performed in November, 2017 revealed a mass lesion obstructing the right main bronchus (Figure 3). Coagulated with argon, cleared by forceps. Airway clearance was provided (Figure 4). No complications occurred during and after the procedure. After the procedure, the breathe sounds in the lower and middle zones of the right lung increased. The patient's pathology was reported as atypical carcinoid tumor. Chromogranin +, synaptophysin +, CD 56 + and Ki67 index were seen as 5%. In the Gallium 68 DOTA TATE PET / CT study performed in December, 2017, the patient's polypoid lesion detected on the right main bronchus in the PET / CT examination of 2016 was detected as millimetric and no significant involvement was detected in the lesion (Figure 6).

DISCUSSION

Oncologically, surgical treatment is considered the gold standard treatment for bronchial carcinoid tumors but bronchoscopic excision techniques applied in selected cases-especially surgically inoperable- may be beneficial because they are tissue protective and increase the quality of life of the patient by removing surgical stress. Various bronchoscopic resection techniques can be applied for curative purposes, especially for typical carcinoid cases with central localization, intraluminal and stemmed. But the studies done in this subject is limited.

In most of these studies, neodymium-doped yttrium aluminium garnet (Nd: YAG) laser was used as bronchoscopic treatment. In 19 patients with intraluminal typical bronchial carcinoid resected by Van Boxem et al, 14 cases (73%) of 19 patients were totally eradicated according to a study using Nd: YAG laser under photodynamic or brachytherapy under general anesthesia; in the remaining 5 patients, radical surgical procedure was performed due to residual atypical carcinoid tumor. ¹⁵ In another study by Cavaliere *et al.*, Nd: YAG laser methods were used in selected 38 of 150 typical carcinoid tumors with no lymph node metastasis and the tumor was confined to the intraluminal region and the success rate in the 24-month follow-up period was 92%. ¹⁶

In the article published by Brokx *et al.* in 2015, %42 of 112 cases of central pulmonary carcinomas with bronchoscopic treatment were reported to have no need for surgical treatment in at least five years follow-up period.¹⁷ However, six weeks later than initial bronchoscopic treatment, after high resolution

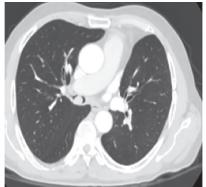




Figure 5. Endobronchial lesion in the right main bronchus





Figure 6. Right main bronchus was cleaned from the lesion after the endobronchial procedure

tomography and bronchoscopy; surgical treatment were performed in patients with recurrence and atypical carcinoid histology despite endobronchial treatments, which had extraluminal component. They reported a 5-year and 10-year survival rate of 97% and 80%, respectively. These results indicate that endobronchial treatment at the initial stage of central pulmonary carcinoid disease and completion of the treatment with surgical resection in patients with extraluminal component is a suitable approach.

In conclusion, this article describes a case of bronchoscopic endobronchial therapy applied to a recurrent endobronchial atypical carcinoid tumor patient with a history of surgical trauma and a typical carcinoid tumor case due to accompanying comorbid conditions. Bronchoscopic endobronchial therapy is a powerful alternative to bronchial carcinoid tumors because of the protection of lung tissue and removal of surgical stress and surgical complications from the patient. Bronchoscopic endobronchial intervention may be performed in central bronchial carcinoid cases without extraluminal involvement. In addition, atypical carcinoid cases that are bronchoscopically resected require long term follow-up because of the recurrence risk.

*The authors declare that there are no conflicts of interest.



REFERENCES

- **1.** Travis W, Brambilia E, Andrew G, et al. The 2015 World Health Organization Classification of Lung Tumors. J Thorac Oncol 2015; 10: 1243-1260.
- 2. Dishop MK, Kuruvilla S. Primary and metastatic lung tumors in the pediatric population: a review and 25-year experience at a large children's hospital. Arch Pathol Lab Med 2008; 132: 1079-1103.
- Mezzetti M, Raveglia F, Panigalli T, et al. Assessment of outcomes in typical and atypical carcinoids according to latest WHO classification. Ann Thorac Surg 2003; 76: 1838-1842.
- 4. Travis WD, Rush W, Flieder DB, et al. Survival analysis of 200 pulmonary neuroendocrine tumors with clarification of criteria for atypical carcinoid and its separation from typical carcinoid. Am J Surg Pathol 1998; 22: 934-944.
- **5.** Wirtschafter E, Walts AE, Liu,ST, and Marchevsky AM. Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia of the lung (DIPNECH): Current Best Evidence. Lung 2015; 193: 659-667.
- **6.** Lim E, Goldstraw P, Nicholson AG et al. Proceedings of the IASLC international workshop on advances in pulmonary neuroendocrine tumors 2007. J Thorac Oncol 2008; 3: 1194-1201.
- Öberg K, Hellman P, Ferolla P, Papotti M, ESMO Guidelines Working Group. Neuroendocrine bronchial and thymic tumors: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann-Oncol 2012; 23: 120-123
- 8. Katsas G, Androukalis II, de Herder WW, Grossman AB. Paraneoplastic syndromes secondary to neuroendocrine tumors. Endocr Relat Cancer 2010; 17: R173-R193.
- **9.** Jeung MY, Gasser B, Gangi A, et al. Bronchial carcinoid tumors of the thorax: spectrum of radiologic findings. Radiographics 2002; 22: 351-365.
- **10.** Detterbeck, F. C. Clinical Presentation and Evaluation of Neuroendocrine Tumors of the Lung. Thorac Surg Clin 2014; 24: 267-276.
- Lococo F, Cesario A, Paci M, et al. PET/CT assessment of neuroendocrine tumors of the lung with special emphasis on bronchial carcinoids. Tumour Biol 2014; 35: 8369-8377.
- **12.** Özkan EÇ. Nöroendokrin Tümörlerde Teranostikler. Nucl Med Semin 2015; 1: 103-110
- **13.** Caplin ME, Baudin E, Ferolla P, et al. Pulmonary neuroendocrine (carcinoid) tumors: European Neuroendocrine Tumor Society expert consensus and recommendations for best practice for typical and atypical pulmonary carcinoids. Ann Oncol 2015; 26: 1604-1620.
- **14.** Karasulu L, Altın S, Dalar L, ve ark. Endobronşiyal yolla tedavi edilen iki tipik karsinoid tümör olgusu. Tüberküloz ve Toraks Derqisi 2009; 57: 212-217.
- **15.** Van Boxem TJ, Venmans BJ, van Mourik JC, Postmus PE, Sutedja TG. Bronchoscopic treatment of intraluminal typical carcinoid: a pilot study. J Thorac Cardiovasc Surg 1998; 116: 402-406.
- **16.** Cavaliere S, Foccoli P, Toninelli C. Curative bronchoscopic laser therapy for surgically resectable tracheobronchial tumors: personal experience. J Bronchol Intervent Pulmonol 2002; 9: 90-95.
- 17. Brokx HAP, Paul MA, Postmus PE, et al. Long-term follow-up after first-line bronchoscopic therapy in patients with bronchial carcinoids. Thorax 2015; 70: 468-472.

