Endobronchial metastasis from extrathoracic malignancies: A clinicopathological study of 11 cases

Monika Breta, Sudheer Arava¹, Karan Madan², Ashok Singh³, Deepali Jain¹, Randeep Guleria²

Department of Pathology, BPS GMC, Sonipat, Haryana, Departments of ¹Pathology and ²Pulmonary Medicine and Sleep Disorders, AIIMS, New Delhi, ³Department of Pathology, AIIMS, Rishikesh, Uttarakhand, India

ABSTRACT

Introduction: Endobronchial metastases are uncommon. It accounts for 2-28%. Most common tumors that metastasize to the endobronchial site are breast, renal, endometrial and colon carcinomas. They have to be identified properly because they present poor prognosis and different treatment modalities when compared to that of primary lung carcinomas. Materials and Methods: We studied a total of 11 retrospective cases of Endobronchial metastasis. Detailed clinical pathological and radiological findings were analyzed along with a detailed Immunohistochemical workup and Endobronchial findings. Results: Mean age of presentation was 55 years with female predominance (Male to female ratio was 1:1.2). Most common tumors encountered were carcinoma breast (3), colorectal carcinomas (2), renal cell carcinoma (2) followed by one each from carcinoma endometrium, cervix and thyroid. Common symptom was cough followed by dyspnea. Exophytic endobronchial growth was common with right main bronchus being the common site. Conclusion: Endobronchial metastasis occurs in various types of malignancies. It should always be differentiated from primary lung carcinomas as they carries poor prognosis and different treatment protocol when compared to that of primary lung tumors.

KEY WORDS: Bronchogenic carcinoma, endobronchial metastasis, flexible bronchoscopy, lung

INTRODUCTION

Endobronchial metastasis (EBM) is defined as documented extrathoracic malignancies metastatic to the endobronchus within a bronchoscopically visible range.¹ Metastases from nonpulmonary malignancies to the lungs are very common and well known, but EBM from extrathoracic malignancies is uncommon ranging from 2% to 28%¹⁻³ according to the various studies. Although many tumors can metastasize to the bronchus, the most common extrathoracic malignancies associated with EBM are colorectal, breast, kidney, stomach, ovarian, thyroid, uterine, testicular, nasopharynx, prostate, and adrenal carcinomas and sarcomas.⁴⁻⁶ The time between the diagnosis of the primary tumor and appearance of EBM is approximately 9 months–5 years.⁷⁻⁸ Most of the times, it is difficult to diagnose EBM from primary bronchogenic carcinoma without the prior history of extrathoracic malignancy, because clinical, radiological, and bronchoscopic findings cannot differentiate these two entities. Diagnosing EBM has clinical importance because of its poor prognosis and different treatment modalities when compared to that of primary bronchogenic carcinoma. In this study, we aimed to investigate the clinical, radiological, endoscopic, and histopathological aspects of EBM in 11 patients.

MATERIALS AND METHODS

This retrospective study includes a total of 11 cases of EBM who underwent bronchoscopic biopsies at All
India Institute of Medical Sciences, New Delhi. Detailed clinical history, radiological, bronchoscopic findings, and the interval between primary tumor and metastasis were retrieved from the medical record section. Histopathology blocks and slides of EBM and the primary tumor were retrieved from the filing room of the histopathology section.

All biopsies were done by a pulmonologist with the help of flexible bronchoscopy under sedation. Final diagnosis of EBM was made by microscopic examination, immunohistochemical characterization, and comparing with that of the primary tumor findings.

RESULTS

A total of 11 patients were diagnosed as having EBM from extrapulmonary malignant tumors. The youngest was 31 years and the oldest was 85 years with a mean age of 55 years. The 11 patients consist of five men and six women with a male-to-female ratio of 1:1.2.

Primary tumors encountered were carcinoma of the breast (3 cases), colorectal (2 cases), renal (2 cases), thyroid (1 case), cervix (1 case), endometrium (1 case), and dedifferentiated liposarcoma of the thigh region (1 case) [Table 1].

Most common clinical symptoms included were cough in seven patients (63.6%), dyspnea in two patients (18.2%), and hemoptysis in two patients (18.2%).

On endobronchial findings [Figure 1], exophytic growth and growth completely occluding the left upper lobe bronchus were found in 4 cases, right intra bronchial growth in 1 case, right upper lobe bronchus growth extending into right main bronchus in 2 cases, multiple nodular outgrowths in right upper and bronchus intermedius in 1 case, exophytic growth in the right upper lobe bronchus in 1 case, infiltrative growth in the right lower lobe bronchus in 1 case, and growth completely occluding the right upper lobe bronchus in 1 case. These lesions were located in the main bronchus in ten patients (six lesions were in the right main bronchus [54.5%] and four in the left main bronchus [36.5%]) and right truncus intermedius in one patient (9.0%).

Chest X-ray and computerized tomography of the thorax showed hilar mass (4 cases), multiple lung nodule (3 cases), lung collapse (2 cases), consolidation (1 case), and mediastinal lymphadenopathy (1 case).

The final diagnosis of EBM includes metastasis from [Figure 2] intraductal carcinoma breast (3 cases), adenocarcinoma colon (2 cases), nonkeratinizing squamous cell carcinoma cervix (1 case), endometrioid carcinoma uterus (1 case), clear cell carcinoma kidney (1 case), papillary carcinoma thyroid (1 case), and dedifferentiated liposarcoma of thigh (1 case).

Immunohistochemical findings include [Figure 2] estrogen receptor and progesterone receptor along with gross cystic disease fluid protein 15 positivity in carcinoma breast. Cytokeratin 7, cytokeratin 20, Carcinoembryonic antigen positivity, and negativity for thyroid transcription factor-1 in adenocarcinoma colon. Pan-cytokeratin and vimentin positivity in endometrioid carcinoma uterus. Pan-cytokeratin and CD10 positivity in clear cell carcinoma kidney. Cytokeratin 19 and thyroglobulin positivity in papillary carcinoma thyroid. Focal S100 positivity in dedifferentiated liposarcoma. Immunohistochemical stains were not useful in nonkeratinizing squamous cell carcinoma cervix; however, it showed positivity for P 40.

The interval from the diagnosis of primary malignancy to EBM was 2–7 years with the mean duration of 36 months, and all of them are still surviving and are under follow-up till date.

DISCUSSION

Metastases from nonpulmonary malignancies to the lungs are very common, but EBM from extrathoracic

---

**Table 1: Summary of the 11 cases of endobronchial metastasis**

| Primary site (number) | Type of malignancy                      | Interval of metastasis (years) | Age (years) | Sex      | Outcome survival |
|-----------------------|----------------------------------------|--------------------------------|-------------|----------|------------------|
| Breast (3)            | Invasive ductal carcinoma (grade II)    | 3, 6, and 8                    | 31, 54, and 64 | Female, female, female | Surviving       |
| Colon (2)             | Adenocarcinoma (WD)                    | 3 and 5                        | 55 and 75   | Male, male | Surviving       |
| Renal (2)             | Clear cell carcinoma (nuclear grade I) | 6 and 2 (months)               | 48 and 63   | Male, male | Surviving       |
| Endometrium (1)       | Endometrioid carcinoma                 | 4                              | 64          | Female    | Surviving       |
| Cervix (1)            | Nonkeratinizing squamous cell carcinoma| 5                              | 54          | Female    | Surviving       |
| Thyroid (1)           | Papillary carcinoma                    | 2                              | 56          | Male      | Surviving       |
| Thigh (1)             | Dedifferentiated liposarcoma thigh     | 7                              | 46          | Female    | Surviving       |

WD: Well-differentiated
malignancies is uncommon constituting about 1.1% of total endobronchial tumors.\textsuperscript{[10]}

According to the literature, EBM is observed in various types of malignancies, including colorectal, breast, kidney, stomach, ovarian, thyroid, uterine, testicular, nasopharynx, prostate, adrenal carcinomas, sarcomas, histiocytoma, and plasmacytomas.\textsuperscript{[10-16]} The most common EBM is from carcinomas of the colorectal region followed by the breast and kidney.\textsuperscript{[13-15]} This was very well correlated with our study as carcinoma breast and colon were the most common. EBM is clinically, radiologically, and bronchoscopically indistinguishable from that of primary bronchogenic carcinoma in most cases. They should be confirmed by histological, immunohistochemical findings along with comparison with that of primary tumor which is important because EBM indicates poor prognosis with different treatment regimen when compared to that of primary bronchogenic carcinoma.

Few studies\textsuperscript{[5-8]} described the histological changes observed in the bronchus at the site of metastatic involvement. They reported the earliest changes to be permeation of the mucosal lymphatic by malignant cells and distension of the lymph channels, subsequently followed by coalescence of the swollen lymphatics to form solid tumor masses under the bronchial epithelium. In the more advanced stages, the tumor tissue ulcerates through the epithelial layer to form a polypoid mass within the bronchial lumen. Eventually, the entire mucosal lining is replaced by malignant tissue resulting in stenosis of the bronchial lumen.

EBM is often a late sign of the primary tumor, but can rarely be detected before the diagnosis of the primary tumor.\textsuperscript{[8-10]} In this study, all patients were presented after the diagnosis of the primary tumor, and EBM was the late sign of systemic metastasis. All of them on follow-up were presented with gradual onset of respiratory symptoms and flexible bronchoscopic examination detected EBM. On histological examination, all the cases were of similar histomorphology with that of the primary tumor and relevant immunohistochemical staining results supported this.

According to the various published literature, the mean time interval between the primary malignancy and EBM may vary from 9 months to 5 years, but in our observation, the longest duration was 7 years.

Common chest radiological findings in EBM depends on the extent and severity of metastasis which includes atelectasis, visible tumors with hilar masses followed by multiple pulmonary nodules, mediastinal or hilar lymphadenopathy, lung mass, collapse, and consolidation. The most common symptoms mentioned are cough and hemoptysis followed by dyspnea and wheezing in patients with EBM.\textsuperscript{[10-16]} In our series, cough was the most frequent symptom followed by chest pain and dyspnea. This indicates that if there is any one of these symptoms in a patient with extrapulmonary malignancy, especially breast, colon or renal tumors, bronchoscopic examination is must to exclude EBM. Few studies also reported that asymptomatic patients might range from 20% to 62.5%. It is still not clear that why EBM is more commonly detected in these tumors. Because flexible bronchoscopy is routinely not performed in all metastatic tumor patients, the exact incidence of these lesions may still be higher.

In most of the cases, EBM is known to manifest late in the course of cancer progression; however, there are cases of lesions being diagnosed at the same time as primary tumors.
The treatment modality of EBM is determined by the histologic features of the primary tumor, biologic behavior and anatomic location, evidence of other metastatic sites, present symptoms, patient performance status, and life expectancy. If the tumor is surgically resectable, resection is the appropriate treatment of choice. Therefore, the accurate diagnosis of EBM is very important for decisions regarding treatment modality. Moreover, regular follow-up is important, even in patients without any respiratory symptoms.

CONCLUSION

As a conclusion, various extrapulmonary tumors can metastasize to the bronchus. Symptoms and radiographic findings are similar to those of primary lung cancer. EBM develops in various types of malignancies at various times with unremarkable manifestations. It should be differentiated from primary lung cancer because of its poor prognosis and different treatment regimen. Although the mean survival time is usually short, long-term survivors were also reported. Consequently, treatment must be planned according to the histology of the primary tumor, evidence of metastasis to other sites, and the medical status of the patient. Therefore, physicians should consider the possibility of EBM in diagnosed cases of extrathoracic malignancies presented with respiratory symptoms during follow-up, and flexible bronchoscopic examination along with histological confirmation should be done to rule out EBM.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Marchioni A, Lasagni A, Busca A, Cavazza A, Agostini I, Migaldi M, et al. Endobronchial metastasis: An epidemiologic and clinicopathologic study of 174 consecutive cases. Lung Cancer 2014;84:222-8.
2. Kho SS, Yong MC, Chan SK, Tie ST, Voon PJ. Colon carcinoma with endobronchial metastasis masquerading as bronchial asthma causing ball valve effect. Med J Malaysia 2018;73:403-4.
3. Shroff GS, Benveniste MF, Carter BW, de Groot PM, Wu CC, Viswanathan C, et al. Imaging of metastases in the chest: Mechanisms of spread and potential pitfalls. Semin Ultrasound CT MR 2017;38:594-603.
4. Schirren M, Bölükbas S, Oguzhan S, Sponholz S, Schirren J. Surgical therapy of lung metastases. Chirurg 2014;85:833-42.
5. Sørensen JB. Endobronchial metastases from extrapulmonary solid tumors. Acta Oncol 2004;43:73-9.
6. Kiyu H, Hoshi H, Matsui E, Iwata H, Kokubo M, Shimokawa K, et al. Endotracheal/endobronchial metastases: Clinicopathologic study with special reference to developmental modes. Chest 2001;119:768-75.
7. Ayub II, Thangaswamy D, Joseph LD, Meenakshisundaram M. Lung parenchymal and endobronchial metastases from ovarian carcinoma. J Bronchology Interv Pulmonol 2018;25:235-8.
8. Katsimbri PP, Bamias AT, Froudarakis ME, Peponis IA, Constantopoulos SH, Pavlidis NA, et al. Endobronchial metastases secondary to solid tumors: Report of eight cases and review of the literature. Lung Cancer 2000;28:163-70.
9. Salud A, Porcel JM, Rovira A, Bellmunt J. Endobronchial metastatic disease: Analysis of 32 cases. J Surg Oncol 1996;62:249-52.
10. Baumgartner WA, Mark JB. Metastatic malignancies from distant sites to the tracheobronchial tree. J Thorac Cardiovasc Surg 1980;79:499-503.
11. Chrysikos S, Karampitasos T, Tzouvelekis A, Dimakou K. Endobronchial metastasis from renal cell carcinoma as a reason for recurrent pulmonary infections. Adv Respir Med 2018;86:245-8.
12. Fournel C, Bertoletti L, Nguyen B, Vergnon JM. Endobronchial metastases from colorectal cancers: Natural history and role of interventional bronchoscopy. Respiration 2009;77:63-9.
13. Çoşğun İG, Kaçan T, Erten G. Late endobronchial pulmonary metastasis in a patient with breast cancer. Turk Thorac J 2018;19:97-9.
14. Hanu T, Kanda T, Matsuji A, Hasegawa G, Yajima K, Tsuichida M, et al. Endobronchial metastasis from adenocarcinoma of gastric cardia 7 years after potentially curable resection. World J Gastrointest Surg 2010;2:270-4.
15. Shen Q, Yao Y, Teng X, Zhou J. Endobronchial metastasis from prostate cancer mimicking primary lung cancer. Intern Med 2010;49:1613-5.
16. Gianella P, Soccal PM, Plojoux J, Frésard I, Pache JC, Permege T, et al. Utility of rapid on-site cytologic evaluation during endobronchial ultrasound-guided transbronchial needle aspiration in malignant and nonmalignant disease. Acta Cytol 2018;62:380-5.