Endotracheal-endobronchial metastases: report of 14 cases

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Abstract

Introduction: Endotracheal-Endobronchial Metastases (EEM) secondary to extrapulmonary neoplasm are rare. Since 1989 we have encountered 14 patients with EEM.

Materials and Methods: EEM were defined as documented extra pulmonary neoplasm metastatic to subsegmental or more proximal central bronchi in a bronchoscopically visible range. The developmental modes were described on the basis of classifying categories of Kiryu.

Results: The primary tumors included breast cancer (4 cases including 3 women,1 man), colorectal carcinoma 1, renal cell carcinoma 1, embryonal cell carcinoma of testis 1,uterine cervix carcinoma 2,melanoma 1,osteogenic sarcoma 2,papillary thyroid carcinoma 1and prostatic sarcoma 1. The chest roentgenographic findings were: collapse 5, parenchyma mass 5, multiple nodule 2 and hilar enlargement 2. Median interval from diagnosis of primary tumor was 39.5 months. Endobronchial lesions were detected by bronchoscopy and their metastatic nature was confirmed histopathologically in all patients. Six patients were treated with external radiotherapy, while 6 patients had chemotherapy and 2 patients underwent surgical resection of metastasis.

Conclusions: The cases we have reported are similar to those found in the literature, regarding their clinical and roentgenographic presentation. Local treatment is effective for palliating symptoms. All patients with extra pulmonary malignant tumor who are suspected to have pulmonary metastasis should undergo bronchoscopy to diagnose end bronchial metastasis and to differentiate it from primary lung cancer.

Keywords: Endotracheal-Endobronchial metastasis, Fiberoptic bronchoscopy, Pulmonary metastasis, Prognosis.

Introduction

The lungs are common site of spread of malignancies so that pulmonary metastases occurring in 20%-50% of all patients who have cancer (1).
A combination of both tumor related factors and pulmonary endothelial factors may determine the predilection of particular cancers to form pulmonary metastases (2,3,4). Tumors more likely to give lung metastases are renal cell, breast, gestational trophoblastic neoplasm, thyroid, gastrointestinal carcinoma, sarcoma of both soft tissue and bony origin, and malignant melanoma (5, 6).

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Endotracheal - endobronchial metastasis (EEM) was defined as documented metastatic non pulmonary neoplasms to sub segmental or more proximal central bronchi in a bronchoscopically visible range (7).

Endoluminal metastasis of the tracheobronchial tree secondary to extra pulmonary solid malignant tumor are rare. The incidence of such metastasis is estimated to be approximately 2% (8).

The most common primary malignancies associated with EEM are renal cell, colorectal, cervical, breast carcinoma and malignant melanoma (9). The clinical and roentgenographic features of EEM and bronchogenic carcinoma were found to be indistinguishable; however in most instances the manifestations of primary tumors are apparent before the endobronchial metastasis is discovered (8,10).

In most cases of EEM histologic appearance of bronchoscopic biopsies suggest the correct diagnosis (8).

In some cases the mean time for the appearance of endoluminal metastasis is long (approximately 5 years) after the diagnosis of the primary tumor (3,8,10,11), therefore a carefully taken history is essential for detection of metastatic diseases (9,10). Clinical and radiological manifestations of metastatic involvement of a major bronchus are indistinguishable from those produced by centrally located bronchogenic carcinoma. Fiberoptic bronchoscopy is a valuable diagnostic tool for all endoluminal lesions including metastases (9,12). The histologic findings of the endobronchial biopsy specimens can be correlated with the previously known primary tumor (12).

If the histological differentiation of the endobronchial tissue from primary bronchogenic carcinoma is still unclear, the demonstration of carcinoma in situ in the adjacent bronchial epithelium strongly suggests the diagnosis of a primary lung tumor (13,14).

Here we report our experience of 14 patients with endobronchial metastasis secondary to solid extrapulmonary malignant tumor who have treated in our department since 1989. We reviewed the literature and compared our patients with other reported series.

Materials and Methods

Since 1989 we have encountered 14 patients with EEM secondary to solid extra pulmonary malignant tumors. We reviewed the records of all patients who underwent fiberoptic bronchoscopy at Ghaem and Imam Reza Hospitals of Mashhad University of Medical Sciences during this period to find all cases of EEM. All patients who had endobronchial lesion in a bronchoscopically visible range and had a history of documented extrapulmonary neoplasm were included in our study.

Slides and reports of biopsy specimens of primary tumor and endobronchial biopsy material were compared to confirm a diagnosis of EEM. Clinical, radiological, bronchoscopic and histologic features of 14 cases were reviewed. Patients with endotracheal-endobronchial lesions as a result of direct invasion by adjacent neoplasm from esophagus and thyroid were excluded from our study.

We used findings from fiberoptic bronchoscopy, chest radiography and computed tomography (CT) and histopathology to classify our patients into four categories on the basis of classification of Kiryu et al (13) for developmental modes of endobronchial metastasis: type 1 direct metastasis to the bronchus (4 cases), type 2 bronchial invasion by a parenchymal metastatic lesion (1 case), type3 bronchial invasion by mediastinal or hilar lymph node metastasis (3 patients), type 4 peripheral lesion extending along the proximal bronchus (6 patients).

Results

The age of the 14 patients at the time of diagnosis of EEM ranged from 22-89 years (mean age 51) male to female ratio was 6/8.

The developmental modes in our patients on the basis classification of Kiryu et al (7) and the source of metastases was shown in (table 1).

Table 1: Developmental modes of EEM in 14 patients

Primary site	Patients, No. (No. of Lesions)	Type I, No. (No. of Lesions)	Type II, No. (No. of Lesions)	Type III, No. (No of Lesions)	Type IV, No. (No. of Lesions)
Breast	4(4)	1(1)	-	2(2)	1(1)
Colorectal	1(2)	-	-	-	1(2)
Melanoma	1(1)	-	-	-	1(1)
Renal	1(1)	1(1)	-	-	-
Osteogenic Sarcoma	2(2)	1(1)	-	-	1(1)
Cervix	2(2)	-	-	1(1)	1(1)
Testis	1(3)	1(3)	-	-	-
Prostatic Sarcoma	1(1)	-	-	-	1(1)
Thyroid	1(1)	-	1(1)	-	-
Total	14(17)	4(6)	1(1)	3(3)	6(7)

The mean interval from diagnosis of primary tumor to the diagnosis of EEM was 39.5 months. The presenting symptoms were cough in all patients (100%), hemoptysis in 6 patients (42.8%), dyspnea in 5 cases (35.7%).

We did not have any aymptomatic patients. Chest radiographic findings included; collapse in 5 cases, single round opacity (nodule) in 5 cases, Hilar enlargement in 3 cases, multiple bilateral pulmonary nodules in 1 case, so the most frequent radiological findings was collapse of the lung and single nodule. Right lung was involved in 7 cases and left lung in 6. Bilateral pulmonary involvement was seen in one case.

Two of 14 patients had multiple endobronchial lesions, the primary sites were colorectal cancer and embryonal cell carcinoma of testis. Interestingly 7 of 18 lesions were recognized in upper lobe bronchi (41.1%); so there was predilection for the airway location in our series. The cause of this predilection is uncertain. Bronchoscopes appearance of EEM in type 1 often presented as a polypoid or nodular lesion covered with necrotic material; and in type 3 and 4, submucosal swelling with irregular margin and narrowing of the bronchial lesions were seen.

Six patients were treated with external radiotherapy while 6 patients had systemic chemotherapy. Two patients underwent surgical resection of metastasis: 1 case of osteogenic sarcoma and another patient with history of prostatic sarcoma.

Discussion

EEM secondary to solid extrapulmonary malignant tumors are rare. The frequencies of endobronchial metastasis are variable by definition ranging from 2% - 50% (8,9).

The inclusion of bronchial involvement by adjacent structures and by parenchyma or lymph node masses instead of development of metastasis in the bronchus itself, will significantly increase the number of endo-bronchial metastasis.

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EEM were defined as documented extra pulmonary tumor metastatic to sub segmental or more proximal central bronchus in a bronchoscopically visible range (7).

In our series we excluded tracheobronchial invasion by malignant tumor of adjacent structures.

In autopsy series only 2% of solid extra pulmonary tumors were found to have EEM, although this frequency is higher in certain reports (8,9). Probably this discrepancy is due to definition differences.

In our series the total number of patients with EEM is probably an under-estimated of true frequency of EEM. Since we do not routinely perform fiberoptic bronchoscopy in all patients presenting with thoracic metastasis, but only when history and physical examination or radiological findings suggest endobronchial involvement. In addition some asymptomatic cases of EEM may have not been diagnosed.

This is probably the reason why we have not had any cases of asymptomatic EEM in our series. In contrast to our series, Kiryu et al, Heitmiller et al, and Wang et al reported that 62.5%, 52.1% and 15% of their patients were asymptomatic respectively (7,13,15).

In our series the most common primary extra thoracic tumors associated with EEM are breast, colorectal, renal cell carcinoma.

It appears to be similar to that reported in the literature (Table 2).

Table 2: Comparison of frequency of four common primary sites of EEM in different reported series.

Author(Ref)	Kiryu (7)	Braman(8)	Katsimbri(16)	Salud(2)	Morgan(11)	Present study
Primary Site						
Breast	3	-	-	20	15	4
Colorectal	6	7	2	3	2	1
Melanoma	-	2	-	2	2	1
Renal	-	15	3	1	2	1
Number of EEM	16	38	8	32	27	14
Duration of Study (years)	11	29.5	10	9	10	15

four of 14 reported patients had breast carcinoma, while both colorectal and renal cell carcinoma were seen in 1 out of 14 patients. We described two patients with EEM associated with osteogenic sarcoma, and one patient with EEM because of melanoma. We had an interesting case of prostatic sarcoma with endobronchial metastasis.

The symptoms and presentation of patients with EEM were similar to those associated with primary bronchogenic carcinoma (7-10). As a result, differentiation between these two diagnoses was difficult on the basis of symptoms and radiographic findings alone (7,10,11). Fiberoptic bronchoscopy is neccesary for establishment a correct diagnosis since treatment strategies differ.

In our series the most common symptoms were cough and hemoptysis followed by dyspnea.

We did not have any asymptomatic EEM patients, perhaps we do not routinely perform bronchoscopy for all patients presenting with thoracic metastasis but only when symptoms and signs or radiographic findings suggest endobronchial disease. Hence some silent or asymptomatic cases of EEM may not have been diagnosed. Similar to other reported series, radiological findings in our patients included atelectasis, single or multiple round pulmonary nodule and hilar enlargement.

Other findings such as signs of pneumonic infiltration, perihilar mass, mediastinal lymphadenopathy and bilateral interstitial-

infiltration and even normal radiographic findings are also encountered (1,7,8,10-12).

Ikezoe et al reported that CT scan was sensitive in detecting endobronchial lesions including metastasis(10). Although CT scan does not always demonstrate intraluminal lesions, it should be performed when an endobronchial metastasis from extra thoracic malignancy is seen by bronchoscopy because it will show hilar or mediastinal lymphadenopathy or single and multiple pulmonary metastasis other than endo-bronchial lesions. Diagnosis of EEM is usually made by fiberoptic bronchoscopy. Bronchoscopy revealed EEM and were diagnostic in all of our patients.

The histologic findings of the endobronchial tissue can be correlated with previously known primary tumor or can serve as a guideline for subsequent investigation in those patients in whom the underlying tumor has not been identified (12).

If the histological differentiation of the endobronchial tumor from the primary bronchogenic carcinoma is still unclear, the demonstration of carcinoma in situ in the adjacent bronchial epithelium strongly suggests the diagnosis of a primary lung tumor (12). It has been stated that EEM tend to occur at a significant interval from the diagnosis of the primary tumor (10).

In our series the mean interval from the diagnosis of primary tumor to the diagnosis of endobronchial metastasis was 39.5 months. The longest recurrence interval was 144 months in a patient with carcinoma of cervix, whereas the shortest was 9 months in a patient with breast adenocarcinoma. Baumgartner and Mark (1), Katsimbri et al (16), Heitmiller et al (13) reported that the mean interval from the diagnosis of the primary tumor to diagnosis of EEM were 5.4 years, 41 months and 59.9 months respectively.

Kiryu (7) reported that the mean recurrence interval for all cases were 65.3 months (ranging from 196 months in renal cell carcinoma to zero month in uterine carcinoma).

In Brahman's series (8) the mean interval of all cases reviewed was 29.5 months. In Shepherd's series (21) the interval between treatment of primary tumor and appearance of endobronchial metastasis, ranged from a few months to 17 years. In Kiryu series there was no predilection for airway involvement, whereas Heitmiller et al (13) reported that the lobar bronchus was the site of involvement in 19 of 23 patients. In our series there was a predilection for upper lobe involvement in 50% of patients.

Two of our 14 patients had multiple lesions, one with embryonal cell carcinoma of testis and another patients with colon cancer. Of 17 endobronchial lesions 10 were located in the right and 7 were in the left lung. The cause of this predilection was uncertain. Kiryu reported that all 3 patients with breast carcinoma had multiple endobronchial lesions; whereas in our series we had 4 cases of breast cancer, and all of them had single endobronchial lesion.

As stated by Baumgartner and Mark (1) EEM can be separated in forms of primary lesions; that is direct bronchial wall metastasis and secondary lesions; that is invasion of tracheobronchial structures by parenchymal or lymph node masses because of differences in pathogenesis and clinical Significance between each of the lesions.

In the 4 types of the developmental modes proposed by Kiryu et al primary lesions correspond to type I and secondary lesions to type II, III and IV(7).

In our series (Table 1) type I accounted for 4 of 14 patients(28.5%), one patient with breast cancer, one with osteogenic sarcoma, one with renal cell carcinoma and one with testicular cancer. Type II accounted for only one patient with papillary thyroid carcinoma. Type III was seen in three patients.

Type IV affected 6 of 14 patients (42.8%) which was the most common type of-

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developmental modes in our series. Treatment of EEM must be individualized (15). It is determined by: the histologic feature of the primary tumor, its biological behavior and anatomic location of the lesion, presence of other metastatic sites and performance status of the patient.

In those patients where EEM represents the only site of metastasis, surgery should be considered if technically feasible, since long term survival is expected after surgical resection in some patients with localized disease. In our series a patient with metastatic osteosarcoma of left main bronchus had sleeve resection and another patient with metastatic prostatic sarcoma had left upper lobectomy. Both patients are alive and good without evidence of recurrence 6 months after surgery. Most patients have extrabronchial metastatic disease at the time of EEM (15,17).

Salud et al reported that 87% had extrabronchial metastasis, Kiryu reported 56.3% and Moragon et al reported 50% had extrathoracic metastasis (2,7,11).

Survival is dependent to a great degree on biologic behavior of the particular tumor and its responsiveness to the treatments and management available. Survival after the diagnosis of EEM is poor. because it is generally a manifestation of far advanced disease stage. Heitmiller et al (13) reported that the mean survival time from the diagnosis of EEM to death was only 12.5 months.

In Kiryu et al series (7), it was 15.5 months. Baumgartner and Mark (1) reported 32 months mean survival in their patients. Therefore treatment must be individualized because some patients can achieve long term survey (10,11).

Wang et al (15) reported that three factors contributed to a poor prognosis including the patient's age, being over 70 years, primary tumors due to head and neck cancer, other than nasopharyngeal cancer and extension of

the endobronchial metastatic lesion to the main bronchus.

Kiryu et al (7) reported that the mean survival time evaluated according to the developmental modes were as follow: Type I, 14 months, type II, 31 months, type III, 2 months (shortest survival time) and type IV, 18 months. Their findings suggest that the developmental modes of EEM may be one of the survival determinant factors.In our series 6 patients were treated by external radiation with symptomatic improvement in all patients and this result sustained for few months. External and intraluminal radiation has long been used for treatment of endobronchial metastasis with success in relieving obstruction or reducing hemoptysis (8,11,16).

Baumgartner and Mark (1), found brachytherapy to be beneficial when the main problem is bronchial obstruction.

Carlin et al (6) employed a combination of external radiation, laser treatment and brachytherapy in EEM secondary to colon cancer. This was safe and resulted in significant symptomatic improvement in 5 out of 9 patients exceeding one year survival after laser treatment.

Shapshy and Strong (18) reported that satisfactory palliation without a significant morbidity was achieved in four out of five patients utilizing a CO_2 surgical laser through a rigid bronchoscope.

Cavaliere(12) reported endoscopic treatment of malignant airway obstruction as rapid, effective, repeatable and complementary to other treatments, although it should be considered that laser resection could be curative in patients with in situ carcinoma and early cancer. The majority of patients with EEM have disease at other sites. Therefore any therapeutic strategy has palliative intent. The efficacy of systemic treatment of EEM is difficult to assess because of the limited number of patients included in the series reported, but it seems-

to offer no significant improvement either in symptoms or survival (10,15,19).

The symptoms and radiographic manifestations of patients with EEM are indistinguishable from those associated with centrally located primary bronchogenic carcinoma (20), especially when there has been a long recurrence interval between the occurrence of the primary tumor and EEM or when the discovery of EEM antedates diagnosis of primary tumor (19).

In conclusion unless careful attention is paid to the clinical, laboratory and pathologic features of each case, a misdiagnosis of primary bronchogenic carcinoma may be made and inappropriate therapy instituted.

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خلاصه

متاستاز داخل برونش و تراشه، گزارش ۱۴ مورد

دکتر محمد توحیدی ، دکتر سید حسین احمدی حسینی، دکتر داوود عطاران، دکتر سید حسین فتاحی

مقدمه: متاستاز داخل برونش و تراشه ثانوی به نئوپلاسم های خارج ریوی نادر است. بیماران با متاستاز داخل بـرونش معمـولا در مراحل پیشرفته بیماری می باشند و پیش آگهی بدی دارند. از سال ۱۳۶۷ با ۱۴ مورد بیمار مبتلا به متاسـتاز داخـل بـرونش ثانویـه بـه تومورهای بدخیم خارج ریوی مواجه شدیم.

روش کار: متاستاز داخل برونش به متاستاز نئوپلاسم خارج ریوی ثابت شده به داخل برونش های ساب سگمانتال و بـرونش هـای مرکزی که در معرض دید برونسکوپ باشند، اطلاق می شود. علائم کلینیکی، رادیولوژیکی و آسیب شناسی این ۱۴ مورد بررسی شده و راه ایجاد و توسعه تومور داخل برونش بر اساس تقسیم بندی Kiryu شرح و توصیف می گردد.

نتایج: محل تومورهای اولیه مشتمل بر موارد زیر مـی باشـد: کانسر پسـتان ۴ مـورد (سـه مـورد زن و یـک مـورد مـرد)، کارسـینوم کولورکتـال ۱ مـورد، کارسـینوم کلیـه ۱ مـورد، کارسـینوم آمبریونـال بیـضه ۱ مـورد، کارسـینوم سـرویکس ۲ مـورد، ملانـوم ۱ مورد، سارکوم استئوژنیک ۲ مورد، کارسینوم پاپیلر تیروئید ۱ مورد، سارکوم پروستات ۱ مورد.

تظاهرات کلینیکی : شامل سرفه، هموپتیزی، تنگی نفس و علائم غیراختصاصی مانند بی اشتهایی و کاهش وزن می باشد.

یافته های رادیولوژیک عبارتند از: کلاپس در ۵ مورد، توده پارانشیم ریه ۵ مورد، ندول های متعـدد ۲ مـورد، برجـستگی هیـل ریـه ۲ مورد. فاصله زمان متوسط تشخیص تومور اولیه تا متاستاز داخل برونش ۳۹/۵ ماه بود. ضایعه آندوبرونکیال به وسـیله برونسکوپی فایبروپتیک تشخیص و ماهیت متاستاتیک آن از نظر هیستوپاتولوژی در همه بیماران اثبات شد. ۶ نفر به وسیله رادیوتراپی اکسترنال درمان شده و بهبودی علامتی پیدا کردند. ۵ نفر شیمی درمانی و ۲ بیمار تحت رزکسیون جراحی متاستاز قرار گرفتند. پـیش آگهی بیماران به طور کلی بد بود و احتمال متاستازهای خارج ریوی در نواحی دیگر وجود داشت.

نتیجه گیری: موارد گزارش شده ما از نظر تظاهرات بالینی و رادیولوژیکی شبیه مـوارد دیگـر گـزارش شـده در مقـالات پزشـکی می باشد درمان موضعی برای تسکین علائم موثر است. ولی پیش آگهی وخیم و اکثر بیماران متاستازهای خارج ریوی مناطق دیگـر دارند. تمام بیمارانی که تومور بدخیم خارج ریوی اولیه دارند و مشکوک به متاستاز ریوی می باشند می بایستی تحت برونسکوپی فایبروپتیک قرار بگیرند تا تشخیص متاستاز داخل برونش داده شود و از سرطان اولیه ریه افتراق گردد.

واژه های کلیدی: متاستاز داخل برونش و تراشه، برونسکوپی فایبروپتیک، متاستاز ریوی، پیش آگهی