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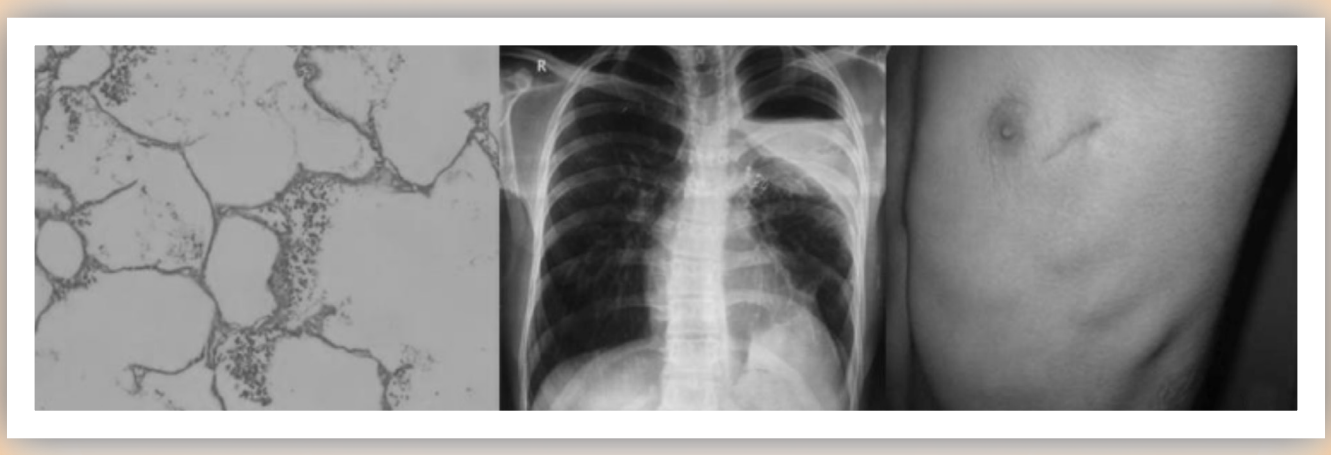

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Original Article

The differential diagnostic role of PET-CT in sarcoidosis and lymphoma

Ahmet Bülent Kargi[1*], Harun Süslü[2], Çağatay Ünsal[3], Osman Fatih Boztepe[4], Yener Koç[3]

[1]Department of Thoracic Surgery, Medicalpark Hospital Antalya, Turkey
[2] Department of Nuclear Medicine, Medicalpark Hospital Antalya, Turkey
[3]Department of Hematology and Stem Cell Transplantation Unit, Medicalpark Hospital Antalya, Turkey
[4]Department of Otolaryngology, Istinye University Health Sciences Faculty, Istanbul, Turkey

ABSTRACT

Background: Mediastinal lymphadenopathy (MLAP) is observed in various conditions of malignant or benign diseases. The two common diseases leading to MLAP are mediastinal lymphomas and sarcoidosis. The aim of study is to describe distinctive lymph node involvement patterns with sarcoidosis and lymphoma defined by PET-CT.

Materials and Methods: 82 patients (45 women and 37 men) with a median age of 53.5 (21-88) years who had PET-CT for differential diagnose for MLAP were evaluated retrospectively. 31 (37.8%) patients diagnosed sarcoidosis, and 51 (62.2%) lymphoma that had histologically proven by various surgical procedures.

Results: There were no statistical difference between gender, age and average SUV max of groups ($p = 0.068$, $p = 0.846$, $p = 0.338$). 26 of 31 patient (83.9%) of sarcoidosis group had abnormal findings compared the lymphoma group (51.0%) which showed statistically significant difference ($p = 0.003$). Meanwhile there were no statistical difference between hilar lymph nodes and liver involvement among the groups ($p = 0.239$ and $p = 0.917$), cervical, axillary, abdominal lymph nodes and spleen involvement was significantly higher in the lymphoma group ($p = 0.008$, $p < 0.001$, $p < 0.001$ and $p = 0.001$). Bone marrow (BM) involvement were also significantly higher in lymphoma group ($p < 0.001$).

Conclusions: There are no specific MLAP findings to differentiate sarcoidosis from lymphomas by PET-CT. It is more likely that the pathological conclusion will be consistent with lymphoma rather than sarcoidosis, in case of involvement of cervical, abdominal and axillary lymph nodes, spleen and BM involvement; however abnormal pulmonary parenchymal findings are in the favor of the diagnosis of sarcoidosis.

Key Words: mediastinal lymphadenopathy, sarcoidosis, lymphoma, PET-CT

Corresponding Author*: Ahmet Bülent Kargı, MD. Department of Thoracic Surgery, Medicalpark Hospital, Fener Mah. Tekelioglu Cad. No: 7, 07200 Antalya, Turkey
E-mail: abkargi@hotmail.com
Phone : +90 532 4337377
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Introduction

Mediastinal lymphadenopathy (MLAP) is observed in various conditions during evolution of malignant or benign diseases. The two common diseases leading to MLAP are mediastinal lymphomas and sarcoidosis [1]. Radiologic evaluation is the first step for diagnosis. Plain chest X-ray and computerized tomography (CT) findings are well described in the medical literature for decades [2]. Sarcoidosis preferentially involves bilateral and symmetrical hilar and mediastinal lymph nodes [2,3]. In the advanced stages of the disease, sarcoidosis may also involve pulmonary parenchyma, other lymph nodes or other organs as well [4].

Lymphoma is a malignant disorder of lymphatic system, mostly originating from lymph nodes. Hodgkin lymphoma (HL) and Non-Hodgkin lymphoma (NHL) may both involve mediastinal lymph nodes [1,5]. Positron emission tomography with 18-fluorodeoxyglucose (PET-CT) is widely used in differential diagnosis of MLAPs [6]. High FDG uptake levels may be present in both disease, but additional findings are thought to be helpful in differential diagnosis.

The aim of this study is to describe distinctive lymph node involvement patterns among patients with sarcoidosis and lymphoma involving the mediastinum defined by PET-CT.

Materials and Methods

Between September 2008 and September 2017, totally 82 patients (45 women and 37 men; median age of 53.5, range 21-88 years) were retrospectively evaluated by PET CT for differential diagnosis of MLAP greater than 1 cm in contrast-enhanced CT, at a single center.

The PET-CT was obtained using Discovery ST4 PET-CT fusion system (General Electric Medical Systems, Milwaukee, WI, USA). Following 6 hours of fasting, patients were administered intravenous 18F-FDG (5.2 MBq/kg body weight) and scanning was done 60 minutes later. Three-dimensional PET acquisition and attenuation corrections for CT attenuation maps were carried out. Using the lean body mass-based maximum standardized uptake value (SUV), the SUV max was calculated. PET/CT images were retrospectively interpreted by the same experienced nuclear medicine physician. The SUV max values of above 2.5 were considered as positive for lymph nodes, liver, spleen, and bone marrow involvement. Nodules, infiltration and mass in the lung were considered as parenchyma involvement.

Patients were included into the study who had histologically proven by mediastinoscopy, mediastinotomy, peripheral lymph node biopsy, open surgical procedures, Ultrasound (US) or CT guided core needle biopsy. The biopsy localization was determined according to accessibility with the physical examination and visibility on PET-CT. Lymphoma diagnosed by peripheral lymph node biopsy was 68.6% of all lymphomas, whereas sarcoidosis diagnosed prominently with mediastinoscopy or mediastinotomy (77.45%). Open surgical procedures with general anesthesia such as thoracotomy or laparotomy were performed in 7 (8.5%) patients, and 7 (8.5%) patients were diagnosed via interventional radiologic approach using US or CT guided biopsies (Table 1).

Table 1. Diagnostic procedures according to groups.

	Diagnosis			
Operation	Sarcoidosis (%)	Lymphoma (%)	Total (%)	P value
Peripheral lymph node biopsy	4 (12.9)	35 (68.6)	40 (47.6)	<0.001**
Mediastinoscopy or mediastinotomy	24 (77.4)	5 (9.8)	29 (35.4)	<0.001**
Open surgical biopsy	2 (6.5)	5 (9.8)	7 (8.5)	>0.05
Interventional biopsy	1 (3.2)	6 (11.8)	7 (8.5)	>0.05
Total	31 (100)	51 (100)	82 (100)	

***Significant*

Except age and gender, clinical physical examination findings or laboratory data were not analyzed. Mediastinal masses caused other than sarcoidosis or lymphoma, tuberculosis, sarcoid reactions, and metastasis of solid tumors were excluded in this study.

Statistical Analysis

Results were evaluated with SPSS20tm statistical software (SPSS Inc., Chicago, IL, USA). Categorical values were compared with non-parametric Independent Sample t test, and non-categorical values were tested with Pearson chi-square and Fisher exact test. Statistical significance was accepted for the p-value was <0.05.

Results

There was no statistical difference between gender and disease groups (p = 0.068). Mean age of sarcoidosis group was 51.54 (± 13.54) and lymphoma group was 50.54 (± 19.71) without statistical difference (p = 0.846). Average SUV max was 10.14 (± 6.11) in the sarcoidosis group and 8.85(± 5.73) in the lymphoma group without a statistically significant difference (p = 0.338) (Table 2).

Table 2. Demographic features.

	Diagnosis				
	Sarcoidosis	Lymphoma	Total	Average	P value
n	31	51	82		
F/M	21/10	24/27	45/37		0.068
Mean age	51.54 (±13.54)	50.54 (±19.71)		51.06 (±17.60)	0.846
SUVmax	10.14 (±6.11)	8.85 (±5.73)		9.34 (±5.87)	0.338

F: *female*, M: *male*

Analysis of PET-CT findings apart from the mediastinal region is summarized in Table 3. When pulmonary parenchymal findings evaluated, 26 of 31 patients (83.9%) of sarcoidosis group had abnormal findings compared the lymphoma group (51.0%) which showed statistically significant difference (p = 0.003). (Figure 1a).

Table 3. Additional PET-CT findings according to diagnosis.

	Diagnosis			
PET-CT Findings	Sarcoidosis (% in sarcoidosis)	Lymphoma (% in lymphomas)	Total (Average %)	P value
	26 (83.9)	26 (51.0)	52 (63.4)	0.003**
Cervical LAP	12 (38.7)	35 (68.6)	47 (57.3)	0.008**
Hilar LAP	27 (87.1)	39 (76.5)	66 (80.5)	0.239
Axillary LAP	0 (0.0)	17 (33.3)	17 (20.7)	<0.001**
Abdominal LAP	5 (16.1)	33 (64.7)	38 (46.3)	<0.001**
Hepatic involvement	2 (6.5)	3 (5.9)	5(6.1)	0.917
Splenic involvement	2 (6.5)	21 (41.2)	23 (28.0)	0.001**
Bone marrow involvement	0 (0.0)	19 (37.3)	19 (23.2)	<0.001**

***Significant*

When hilar lymph nodes were evaluated, there were no statistical difference in involvement among the patient groups (p = 0.239). When cervical, axillary and abdominal lymph nodes were compared, it was commonly observed in the lymphoma group with statistically significance (p < 0.008, p < 0.001, and p < 0.001 respectively) (Figure 1b).

When liver and spleen involvement were evaluated, although there was no difference was observed in terms of hepatic involvement (p = 0.917), spleen involvement was significantly higher in the lymphoma group (p = 0.001) (Figue 1c).

BM involvement determined by PET-CT were also significantly different between the two groups favoring the patients with lymphoma (p < 0.001) (Table 3).

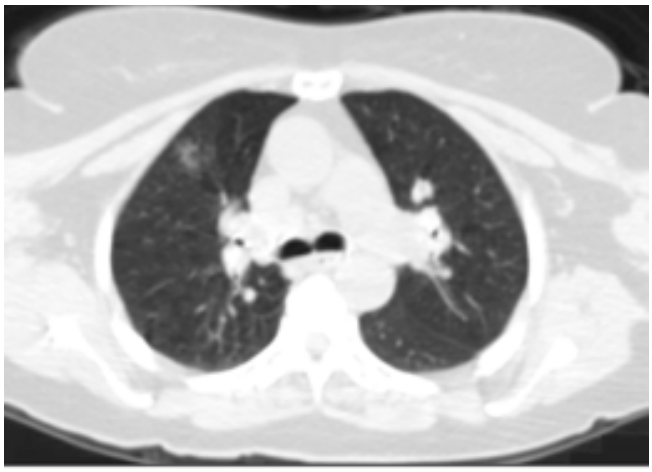

Figure 1a. Parenchymal nodules, sequels and atelectasis of a sarcoidosis patient on CT parenchyma window imaging.

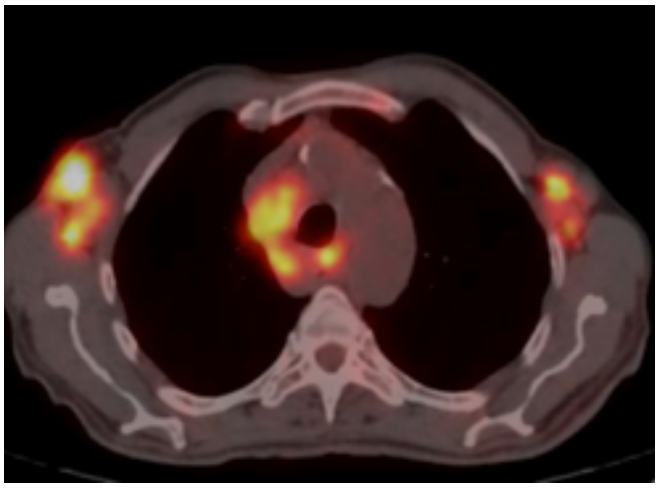

Figure 1b. PET-CT image of MLAP patient (Symmetrical axillary involvement in a NHL patient on PET-CT fusion imaging).

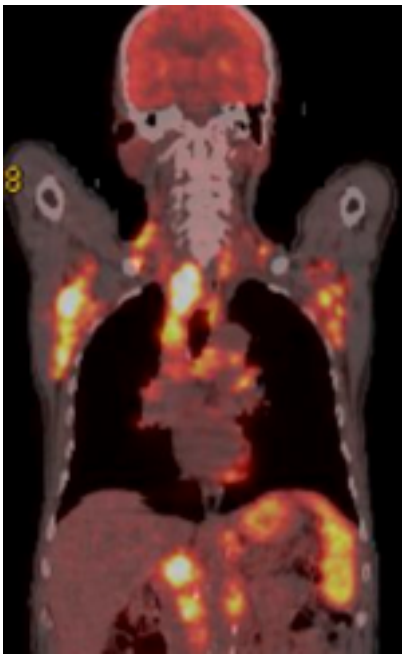

Figure 1c. Cervical, axillary lymph nodes and splenic involvement in a NHL patient on PET-CT.

Discussion

MLAP is observed in several inflammatory, infectious or malignant diseases. It is important to diagnosis and differentiate benign from malignant conditions. Most common malignant etiology is mediastinal lymphoma, whereas common benign disease is sarcoidosis [1].

Sarcoidosis is a multisystem granulomatous disorder of unknown etiology, characterized by noncaseating granulomas in preferentially involves bilateral and symmetrical hilar and mediastinal lymph nodes [3,7]. Duration of disease, sarcoidosis may also involve less commonly cervical lymph nodes, lung parenchyma, liver, spleen, eyes, kidneys and heart as well as thyroid glands [4,8].

Lymphoma is a malignant disorder of lymphatic system, mostly originating from lymph nodes. Hodgkin lymphoma (HL) and Non-Hodgkin lymphoma (NHL) may both involve mediastinal lymph nodes. In our series 12 (23.5%) of the patients were HL, and 39 (76.5%) of them were NHL similar to the rates reported in the literature [1,2,5].

Although tuberculosis-associated MLAP is usually seen in the primary infection complex in childhood, it can be seen in adults in endemic region and immunocompromised or HIV patients. Pulmonary findings are predominantly found in adult tuberculosis patients and diagnosed with microbiologic methods regardless of biopsy in general [9,10]. In our 9-years' experience, we only encountered 9 adult patients with tuberculosis depended MLAP.

Thoracic radiologic examination is the first step in differential diagnosis. Chest X-ray and CT findings are well described in both conditions. CT has low sensitivity (64%) and specificity (62%) in detecting malignant lymph nodes [2]. PET-CT is widely used in differential diagnosis of MLAP increasingly for last two decades [2,5,11].

The SUV max levels cannot differentiate sarcoidosis from malignancy, as PET-CT may be positive in both [6,11-13]. In our study, sarcoidosis patients' average level of SUV max was 10.14 (± 6.11), meanwhile lymphoma was 8.85 (± 5.73) with no statistical difference ($p = 0.338$).

In patients with sarcoidosis, parenchymal findings in the lungs are variable and pulmonary manifestations may occur in up to 90% of cases. Chest radiographic findings may be observed in advanced stages. Stage IV disease is characterized by reticular opacities with evidence of volume loss predominant in the upper zones of the lungs [2,3,7]. In our study, 83.9% of sarcoidosis patient had parenchymal findings versus 51.0% in the lymphoma group which showed statistically significant difference ($p = 0.003$) (Figure 1c).

Bilateral hilar symmetrical lymphadenopathy is a classic radiologic finding in sarcoidosis [2,3,7]. Hilar lymph node involvement is also common in the lymphoma and more frequent in HL (85%) and in about half of NHL. HL most commonly involves anterior and superior mediastinal nodes, pre-vascular and para-tracheal lymph nodes are also affected [5,13]. In our study, hilar lymph nodes were involved 87.1% in sarcoidosis and 76.5% lymphoma group, without statistically significant difference between groups ($p = 0.239$).

In HL, mediastinal involvement is present in 60% of patients at the time of diagnosis whereas the disease is limited to mediastinum only in 3% of cases. In patients with NHL a higher percentage of mediastinal involvement is observed compared to (10-20%) HL, which may be present either as the sole involvement (e.g., primary mediastinal large B cell lymphoma) or as part of systemic disease [3,5,14]. PET-CT is highly sensitive and specific for detecting NHL in nodal and extra nodal sites

[14]. Additional LN involvement patterns in areas other than mediastinal region may help differential diagnosis among lymphoma and sarcoidosis [6,8,14] (Figure 1a,b).

Even though peripheral lymph node involvement determined by PET-CT is not common and specific for sarcoidosis, it may be helpful for identify occult or coincidental sites and diagnostic accessibility when observed [6,12,15]. In our study, 4 (12.9%) of sarcoidosis patients had undergone peripheral lymph node biopsy to avoid invasive surgery requiring general anesthesia.

Spleen involvement by lymphoma generally presents either diffuse involvement with higher uptake compared to liver or solitary / multiple nodules in splenic parenchyma determined by PET-CT. Besides of the size which does not correlate with involvement, spleen is affected in one third of all lymphomas [16,17]. In this study, splenic involvement was found to be significantly higher in the lymphoma group compared to the sarcoidosis group (41.2% vs 6.5%, $p = 0.001$).

Bone marrow involvement is found in approximately 50% to 80% of patients with low grade NHL, 25% to 40% of high-grade NHL, and 5% to 14% of HL during the time of diagnosis [18,19]. In a meta-analysis that included data from seven studies with 654 patients with newly diagnosed NHL, PET had moderate sensitivity (88.7 %) and high specificity (99.8 %) for the detection of BM involvement [19]. Thus, for patients with NHL, normal BM on PET scan does not rule out presence involvement, but, FDG uptake in BM is highly specific for involvement with lymphoma [18,19]. As PET-CT is not routinely used for the diagnosis of sarcoidosis, there is no correct data about BM involvement rates yet. Yanardag and de Prost reported that, BM involvement must be suspected in case of anemia in a sarcoidosis patient [20,21]. In our study, BM involvement determined by PET-CT was significantly different between the two groups favoring the patients with lymphoma ($p < 0.001$).

In the literature, although PET-CT findings of MLAP due to lung cancer, metastatic diseases, sarcoidosis, tuberculosis, and lymphoma was separately investigated, a study comparing sarcoidosis and lymphoma findings has not published yet before this study to our knowledge.

Our study has a limitation; none of the diagnoses was made with endobronchial ultrasound guided transbronchial biopsy.

In conclusion, sarcoidosis and lymphoma are the common causes of MLAPs that may both involve hilar and mediastinal lymph nodes. There are no specific findings to differentiate sarcoidosis from lymphomas by PET-CT. However, lymph node involvement patterns, spleen and BM invasion may help for differential diagnosis and define biopsy procedure. It is more likely that the pathological conclusion will be consistent with lymphoma rather than sarcoidosis in case of involvement of cervical, axillary and abdominal lymph nodes, spleen, and BM by PET-CT, however, abnormal pulmonary parenchymal findings are in favor of diagnosis of sarcoidosis.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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Case Report

Completion middle lobectomy by VATS after thoracotomy

Cagatay Tezel, Ilker Kolbas*, Talha Dogruyol, Serkan Bayram, Volkan Baysungur

Department of Thoracic Surgery, Sureyyapasa Chest Diseases and Thoracic Surgery Teaching Hospital, Istanbul, Turkey

ABSTRACT

Completion lobectomy is a complex procedure performed mostly in tumor recurrences or after the presence of complications like lobar torsion or bronchopleural fistula. This operation is generally done via re-thoracotomy. Here, we present a case of completion middle lobectomy via videothoracoscopy after an upper lobectomy by thoracotomy.

Key Words: minimally invasive surgery, pulmonary resection, completion lobectomy

Corresponding Author*: Ilker Kolbas, MD. Department of Thoracic Surgery, Süreyyapaşa Göğüs Hasrtalıkları ve Göğüs Cerrahisi Eğitim ve Araştırma Hastanesi D Blok Başıbüyük, Maltepe, İstanbul, Turkey
E-mail: dr_ilkerkolbas@hotmail.com Phone: +90 216 421 42 00
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Introduction

Lobectomy via video-assisted thoracoscopic surgery (VATS) is widely performed all around the world with growing experience and better technique. Open surgery is more preferable in completion lobectomy because of adhesions. It is clear that there is a learning curve and VATS lobectomy ratio can be increased with experience [1]. We here in report a case of completion middle lobectomy via (VATS) after an upper lobectomy by thoracotomy in Turkey.

Case Report

A 50 year-old man presented to our clinic with blood tinged sputum. Thorax computed tomography (CT) showed an 8x7 cm mass in the right upper lobe. The maximum standard uptake value (SUVmax) was 43.5 in positron emission tomography (PET/CT) with no uptake elsewhere (Figure 1).

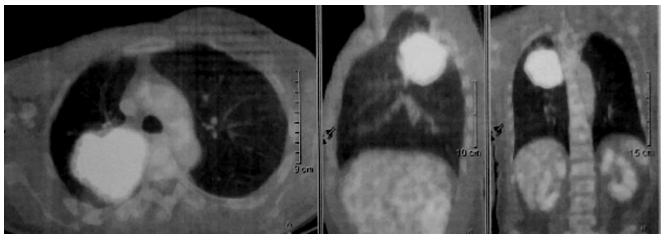

Figure 1. Positron emission tomography (PET/CT) of patient

Fiberoptic bronchoscopy revealed an obstruction at the right upper lobe posterior segment ostium with an endobronchial lesion, which was confirmed as an adenocarcinoma. Brain metastasis was excluded with cranial MRI. The patient had no comorbidity and his forced expiratory volume in one second (FEV1) was 2.1 L (89%). Due to the endobronchial localization of the tumor we preferred thoracotomy and a right upper lobectomy was performed after standard cervical mediastinoscopy. At the end of the operation right middle and lower lobes showed full expansion and filled the thoracic cavity. We sutured the middle lobe to the lower lobe because of complete oblique fissure as usual.

On the postoperative day 1, his breath sounds were diminished in the right upper zone. His condition deteriorated, with vital measurement of sinus tachycardia (120 beat/min) and tachypnea (30 breaths/min). Body temperature was 37.8 0C, white blood count was 18,300/mm3 and CRP (C reactive protein) was 12 mg/dL. Blood gas analyses showed; PO2 131 mm/hg, PCO2 47.2 mm/Hg, and pH 7.373 on supplemental oxygen. Upon suspicion of a lobar torsion on postoperative chest X-ray and CT (Figure 2) besides clinical findings, rigid bronchoscopy and VATS exploration was planned on the second postoperative day. Rigid bronchoscopic examination showed that right middle lobe bronchus was occluded showing a “fish mouth” appearance.

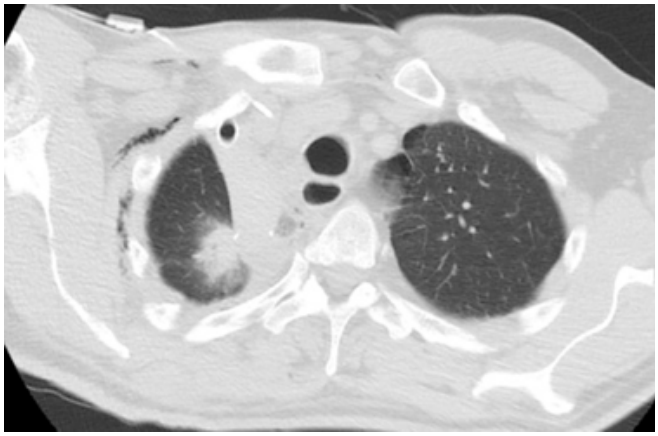

Figure 2. Postoperative thorax computed tomography of patient

Under general anesthesia and double lumen endotracheal intubation, he was placed in left lateral decubitus position and VATS exploration using a 10 mm 30 degree rigid endoscope through the former drain incision was performed. As the right middle lobe was congested than, we decided to perform a middle lobectomy. A 4 cm utility incision was made at the fifth intercostal space (Figure 3), the middle lobe vein, artery, bronchus was divided respectively with endostaplers, and the specimen was removed inside an endobag. The patient was discharged on the 4th postoperative day after the second operation uneventfully.

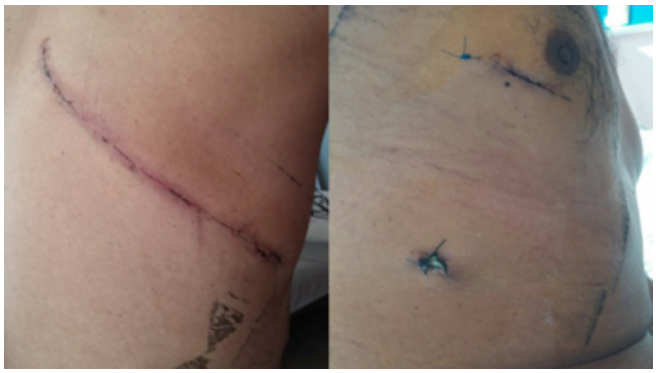

Figure 3. The appearance of the incision after the surgery

Discussion

Numerous VATS lobectomies have been completed thenceforward the first VATS lobectomy, only now most

lobectomies are still completed with thoracotomy. While most lobectomies could be performed with VATS, the lower part is done with this method. Compared with a thoracotomy, VATS offers patients a shorter hospitalization, less pain, and a came around, not to compromise on operational adequacy [1,2]. VATS lobectomy is performed increasingly for early-stage lung cancer. Several published reports thoracoscopic lobectomy can be performed safely and has satisfactory oncologic results [3].

Lobar torsion may occur spontaneously, due to blunt trauma or as a postoperative complication of thoracotomy with or without lung resection [4]. Physical findings consist of fever, tachycardia, sudden termination of air leak and reduction of breath sounds at the affected lung field. The radiologic finding is rapid opacification of the affected lobe [4,5].

Postoperative lobar torsion is an infrequent, however it is a life-threatening complication. Several previous cases have been treated with completion lobectomy. When preserving a twisted lobe, it is important to consider the damage to the twisted lung, risk of thrombosis, and residual pulmonary function [6].

In the literature, right upper lobe resections is reported as the most common cause of the lobar torsion, whereas the second most common cause is resection of the left upper lobe [5]. Middle lobe torsion rate is reported as 0.089-0.3%. The management is generally done via exploration on thoracotomy with the resection of the affected lobe [7]. Lobar torsion after pulmonary resection has a low incidence and a nonspecific presentation. When lobe torsion is suspected reoperation and pulmonary resection should be performed to minimize mortality, similar to the management we performed in this case [5].

Completion lobectomy is speculated that it requires dissection of dense adhesions and thus results in prolonged operative time, excusive blood loss, and increased morbidity [8]. However, in such cases requiring prompt surgical intervention for postoperative complication, VATS may be feasible, and can be the first option of choice. The most common cause of conversion to open thoracotomy in VATS lobectomy is adhesions, which is reduced with increasing experience. In the early post-operative period we can use thoracoscopic surgery owing to less adhesions.

As a conclusion, we suggest that in similar cases, VATS must be tried or even forced to be completed if a complication due to the first resection is faced.

Declaration of conflicting interests

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Case Report

Adult congenital lobar emphysema treated with video-assisted thoracoscopic lobectomy

Serkan Bayram[1*], Ilker Kolbas[1], Mustafa Vayvada[2], Serdar Evman[1], Cagatay Tezel[1]

[1]Department of Thoracic Surgery, Sureyyapasa Chest Diseases and Thoracic Surgery Teaching Hospital, Istanbul, Turkey
[2]Kartal Kosuyolu Heart & Research Hospital, Thoracic Surgery, Istanbul, Turkey

ABSTRACT

Congenital lobar emphysema (CLE) is a rare developmental anomaly of the lower respiratory tract, which generally presents during the neonatal/pediatric period. Lobectomy is the only curative treatment for CLE. An 18-year-old male with enlarging left anterior chest wall deformity and progressive breathlessness for the last 2 years admitted to our clinic.

Physical examination revealed asymmetrical expansion of left hemithorax. Chest radiography and thoracic computed tomography demonstrated hyperinflation of the left upper lobe and a mediastinal shift to the right side. FEV1 was 1.70 L (50%). Ventilation-perfusion scintigraphy showed reduced perfusion and ventilation in the right lung to 33.4% (upper zone, 1.9%; middle zone, 10.0%; lower zone, 22.5%). Patient underwent a successful video-assisted thoracoscopic surgery (VATS) left upper lobectomy, and was discharged on postoperative day 5. He is still being followed-up on fifth year, asymptomatically, with normalized chest wall appearance. VATS lobectomy is a feasible, safe and effective treatment for congenital pulmonary disorders, even for delayed cases.

Key Words: video-assisted thoracic surgery, lobectomy, congenital lobar emphysema

Corresponding Author*: Serkan Bayram, MD. Department of Thoracic Surgery, Süreyyapaşa Göğüs Hastalıkları ve Göğüs Cerrahisi Eğitim ve Araştırma Hastanesi D Blok Başıbüyük, Maltepe, İstanbul, Turkey
E-mail: dr.serkan@hotmail.com Phone: +90 216 421 42 00
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Introduction

Congenital lobar emphysema (CLE) is a rare developmental anomaly of the lower respiratory tract characterized by over-inflation of one or more pulmonary lobes [1]. Its etiology is unknown. CLE is usually diagnosed in the neonatal period and early childhood. It is almost always unilateral with a male dominance [1,2]. Its curative management has traditionally been surgical.

Interestingly, the present report describes an adult with symptomatic CLE diagnosed at the age of 18 years, and treated with a minimally invasive surgical approach.

Case Report

An 18-year-old man with gradual onset of mild breathlessness and expansion of left anterior chest wall, for the last 2 years, admitted to our clinic. There was no history of cyanosis, jaundice, convulsion, or heart failure. Physical inspection showed an expanded left hemithorax. On cardiovascular system examination, the heart sounds were shifted to the opposite side. No gross cardiac anomaly was found. Chest radiography and thoracic computed tomography (CT) demonstrated hyperinflation of the left upper lobe and a mediastinal shift to the right side (Figure 1). Pulmonary function tests revealed restriction by forced vital capacity 2.18 L (51%) and forced expiratory volume in first second 1.70 L (50%). Ventilation-perfusion scintigraphy showed reduced perfusion and ventilation in the right lung to 33.4% (upper zone, 1.9%; middle zone, 10%; lower zone, 22.5%). Fiberoptic bronchoscopic examination confirmed the absence of an endobronchial lesion.

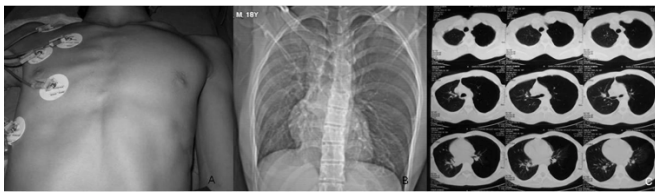

Figure 1. (a) Physical inspection showing enlarged left hemithorax, (b) Preoperative chest x-ray, (c) Computed tomography scan revealing hyper-inflated left upper lobe and mediastinal shift.

After receiving an informed consent from the patient, VATS lobectomy was planned. The patient was placed in a lateral decubitus position and single lung ventilation was achieved. A tree-port thoracoscopic lobectomy was performed through a 4cm utility incision without using a rib retractor. Space restrictions added difficulty to the procedure, as the distended nondeflated lung lobe left too little room for the surgeon to achieve adequate manoeuvres, the resection was successfully completed without conversion to thoracotomy.

Histopathological examination revealed distended alveoli and elongated cystic spaces, consistent with CLE (Figure 2a). Postoperative chest X-ray showed inadequate expansion of the remaining lobe due to prolonged compression (Figure 2b). However, no clinical signs or symptoms were occurred and he was discharged on postoperative day 5. He is still being followed-up on fifth year, asymptomatically, with a small utility incision (Figure 2c).

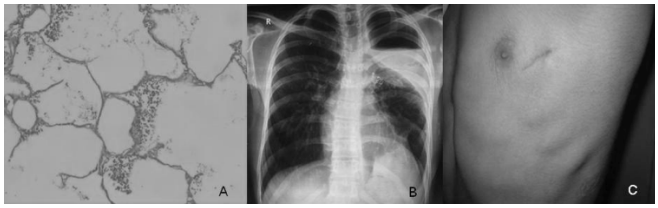

Figure 2. (a) Histopathology of the distended alveoli x100 HE, (b) Postoperative chest x-ray showed expansion failure after upper lobectomy with normalization of the mediastinal shift, (c) Skin incisions of the patient.

Discussion

CLE has a prevalence of approximately 1:20,000 to 1:30,000 and was first identified in 1932 by Nelson [1-5]. Gross and Lewis declared the first successful surgical repair [6]. Typically, a single lobe on one side is affected but multi-lobar involvement may occasionally occur. Most frequently affected sites are the left upper, right middle and upper lobes, respectively [2]. Our case was 18- year old male and he had left upper lobe CLE.

Clinical presentation varies from acute neonatal respiratory failure to chronic recurrent episodes of tachypnea or infections [3]. Late manifestation is unusual; adults often present with dyspnea, infection or cough. In infancy, it usually arises as respiratory distress. Progressive hyperinflation of a lobe or lobes results in compression atelectasis, mediastinum shift, impaired venous cardiac return, secondary hypoxia, and hypotension. In our case the patient had mild shortness of breath.

The etiology of CLE is unknown, and in 50% of cases no specific cause was found [7]. It is likely that abnormal interactions between embryonic endodermal and mesodermal components of the lung during bronchopulmonary development lead to progressive lobar hyperinflation [5]. The current theory, which suggests

inadequate cartilaginous support of the bronchus, was first proposed by Gross and Lewis [8]. However, a preferred theory is based on a recently described pathological entity called the polyalveolar lobe, caused by a 3 to 5 fold increase in the number of alveoli in the whole lobe [9]. More commonly, in 25% of cases, a congenital defect of cartilage and bronchial obstructions are encountered. In another 25%, the development of CLE is caused by bronchial obstruction. Reports showed an association of CLE with other congenital diseases as heart failure and various cardiac defects [7].

Clinical diagnosis of congenital lobar emphysema is difficult and requires perception. Anterior-posterior and a lateral chest radiograph view provides vital information, but not definitive. The characteristic appearance is a hyper-inflated lobe with compression to adjacent lobes. The vascular supply to the emphysematous lobe is poor and vascular markings in the affected lobe are vanished, but maintained on the periphery of the lung [1]. In contrast to pneumothorax, there is no line of pleural demarcation. Widening of the rib spaces and depression of the diaphragm on the affected side is as seen in Figure 1. The mediastinum may be displaced away from the emphysematous side. In severe cases, the over-expanded lung may herniate into the contralateral hemithorax [1,6]. A scintigraphic scan depicts ventilation defects and decreased perfusion in the hyper-expanded lobe due to decreased vascularity [9]. Computed tomography scan of our patient revealed hyper-inflated left upper lobe and mediastinal shift.

The curative treatment of CLE in symptomatic patients is surgical resection by either thoracotomy or using a thoracoscopic approach. Greatest risk of surgery is on induction of anaesthesia i.e. if positive pressure ventilation is applied before opening of the chest, it may cause rapid inflation of the emphysematous lobe or cyst, resulting in a sudden mediastinal shift and cardiac arrest. Therefore, induction of anaesthesia should provide adequate spontaneous ventilation with minimal airway pressure and intermittent manual assistance is essential. Three-portal VATS using single-lung ventilation was performed in the present case. The anterior port was enlarged to 4 cm and instruments were used through this site without a rib retractor. The major difficulty of performing thoracoscopic resection on an emphysematous lobe is the huge intrathoracic area occupied by the nondeflated lobe, while vascular structures are easy to manage with endoclips.

As a conclusion, even though CLE is rare, clinical awareness of this condition is important for early diagnosis and effective surgical treatment. For a certain subgroup of patients, VATS lobectomy can be a safe and effective treatment for congenital pulmonary disorders, despite late diagnosis or physical complication occurrence.

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Case Report

Lung cancer and Warthin's tumor: a case report and review of the literature

Ekin Zorlu[1*], Pınar Atasoy[2], Nesimi Günal[1], Koray Dural[1], Berkant Özpolat[1]

[1]Department of Thoracic Surgery, Kırıkkale University Faculty of Medicine, Kırıkkale, Turkey
[2]Department of Pathology, Kırıkkale University Faculty of Medicine, Kırıkkale, Turkey

ABSTRACT

Warthin's tumor (WT) is a salivary gland neoplasm, which is also called as papillary cyst adenoma lymphomatosis. Herein, we present an uncommon coexistence of WT in an 80-year-old patient with PET/CT positive cervical lymph nodes, during the diagnostic workup of a pulmonary mass lesion. Histopathologic diagnosis of the lymph node was reported as Warthin tumor and transthoracic biopsy of the mass as non-small cell lung carcinoma. We want to emphasize that it would be essential to identify patients with WT as an association with lung cancer was suggested in the recent literature.

Key Words: lung cancer, Warthin's tumor, positron emission tomography, lymphatic metastasis, smoking

Corresponding Author*: Ekin Zorlu, MD. Department of Thoracic Surgery, Kırıkkale University Faculty of Medicine, Yenişehir, Yahşihan, Kırıkkale, Turkey
E-Mail: ekinzorlu@hotmail.com
Phone: +90 312 3051774
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Introduction

Warthin's tumor (WT) is the second most common salivary gland neoplasm after pleomorphic adenomas [1]. It constitutes about 6-10% of all salivary gland tumors. 8% of WT is at extraparotid localization, periparotid and upper cervical lymph nodes that are known to be the regions where it is most commonly detected [2].

Patients with lung cancer have been incidentally found to have WT and were misdiagnosed as metastatic disease based on radiologic imaging alone [3]. Here we present an 80-year-old man where PET/CT demonstrated positive cervical lymph nodes for a preliminary diagnosis of a lung tumor. The histopathologic examination of the excised lymph node is reported as a WT.

Case Report

An 80-year-old man presented with complaints of cough and shortness of breath started one month previously. He also defined pain at right leg, lumbar region and iliac bone. He had 40 packets/year of smoking history. The physical examination revealed enlarged lymph nodes in the right submandibular and right cervical region on palpation. Routine biochemistry and hemogram results were in normal ranges except, erythrocyte sedimentation rate 65 mm/h and CRP 10 mg/L. The FEV1 was 0.7 L and FVC was 1 L.

Thorax computerized tomography (CT) showed a 44.5x36.6 mm mass lesion with spicular margins in the posterobasal segment of the left lower lobe close to thoracic aorta at 9th thoracic vertebra level (Figure 1). PET/CT examination demonstrated pathologic 18F-FDG uptake in the defined lesion and bilateral cervical, left hilar and mediastinal lymph nodes. Pathologic uptake was also reported at right iliac bone totally and sacroiliac joint showing sclerotic and lytic changes.

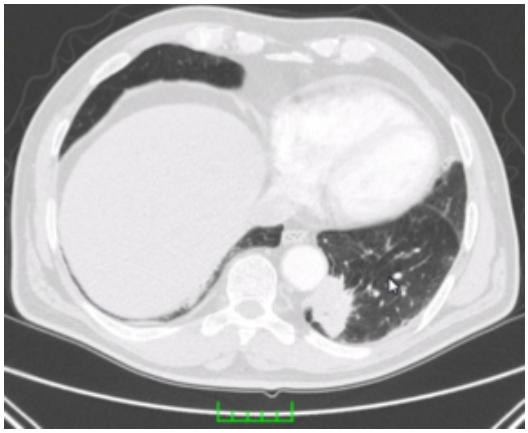

Figure 1. Thorax CT showing mass localized at left lower lobe.

An excisional biopsy of palpable right upper cervical lymph node was performed for tissue diagnosis. Histopathological examination of the lymph node revealed a different tumor growth from lung carcinoma, which contained double row epithelial papillae structures and cystic areas, and central germinal marked lymphoid tissue under the oncocytic epithelium and the pathologic findings were compatible with the WT (Figure 2).

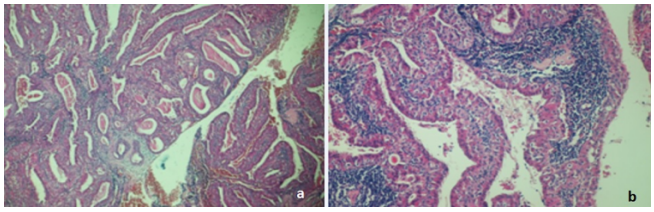

Figure 2. Histopathological examination of WT showing: a. Papillary cystic growth pattern, b. lenphoid stroma and papillary structures originating from two layered eosinophilic epithelial cells.

The patient underwent a transthoracic percutaneous fine needle aspiration biopsy for the left lung mass after a nondiagnostic fiberoptic bronchoscopy, which was reported as non-small cell lung carcinoma (NSCLC) resembling a poorly differentiated adenocarcinoma. Considering PET/CT examination data and comorbidities, histopathologic confirmation of mediastinal lymph nodes were not performed. He was deemed inoperable and directed to the department of medical oncology. The patient died approximately 4 months later after a cerebrovascular accident.

Discussion

Warthin tumor is frequently originated from parotid gland and constitutes 5-10% of benign parotid neoplasms [4]. Oral cavity (palate and lips) and larynx localization have been reported. It is also noted that it may be bilateral in 3-10% of the cases and it may be in multiple localizations in 12% [5]. Histologically it contains a stroma consisting of dense, lymphoid tissue that fills between two-layered long columnar and oncocytic epithelial cells forming papillary structures. Cystic structures are present in the stroma [6]. WT can be seen at any age, with a peak incidence at 6th and 7th decades. In males like in this case, it is seen 10 times more frequently than females. However, in recent years, the rate of incidence in females has increased which is associated with the increase in the number of women who are smokers [7]. Although it has been a century since its definition, the etiopathogenesis of the tumor is still unknown. It is believed that genetic and/or environ-

mental factors, nutritional and metabolic deficiencies, chronic infections play a role in the development of WT by these inclusions [8].

The majority of WTs are localized in the parotid gland and in 4-10% of patients, they are multicentric and/or bilateral. It grows very slow and it is painless. The current size doubles approximately in 20 years [9]. Pain and fast growth is very rare and suggests a malign transformation, which was reported as 0.06-3% [10]. 8% of WT is at extraparotid localization, periparotid and upper cervical lymph nodes that are known to be the regions where it is most commonly detected [2]. Rapid growth and/or painful lesions especially in the extraparotid localization, creates serious diagnostic difficulties like in this case.

Routine MR imaging protocol at diagnosis is often insufficient [9]. 18F- FDG PET-CT should be used to show the high glucose metabolism in WT [11]. WTs with serious FED involvement is reported as 6-24% [5]. In this case the SUV max value of lung mass was 10.2, mediastinal lymph nodes were between 3.2 to 4.4 and cervical lymph nodes was between 8.5 to 14, where the later was the value of the excised one (WT). Although this SUV max value was considered to be high for a metastatic lymph node, it is compatible with the serious FED involvement of WT as reported in the literature.

Smoking is accepted as the primary etiologic factor and frequently reported in the literature similar to our patient, who was a heavy smoker. Kotwall et al reported that WT is seen eight times more in smokers compared with non-smokers [12]. As smokers have an increased risk for lung cancer, it is not surprising that those with WT are also have a risk of lung cancer.

In the English literature WT and lung cancer coexistence is very rarely reported. Dua et al [13] reported a case with bilateral synchronous and multifocal WT mimicking metastasis from lung cancer, Arora et al [14] reported 3 cases, and Thomas et al [15] reported 2 cases. Although there has been no proven association, a retrospective study by White et al [3] reported that, among 144 patients with WT, 24 (19%) had a concomitant lung cancer, the most common being NSCLC. They suggested that given the association between WT and lung cancer, earlier recognition of these benign lesions might potentially facilitate earlier diagnosis of lung malignancies [3].

As a conclusion, Warthin's tumors that are found at an extraparotid localization might cause a diagnostic dilemma, when they show intense FGD uptake. An appropriate tissue diagnosis should be performed for the misinterpretation of a metastatic disease. Foremost, it would be essential to identify patients with WT, as an association with lung cancer was suggested.

Declaration of conflicting interests

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Case Report

Application of tracheal stomal stent for upper airway obstructions: report of four cases

Necdet Öz[1*], Metin Çevener[2], Tülay Dikencik[3], Murat Yılmaz[3], Mustafa Özdoğan[4]

[1]Department of Thoracic Surgery, Private Medstar Antalya Hospital, Antalya, Turkey
[2]Department of Radiology, Private Medstar Antalya Hospital, Antalya, Turkey
[3]Department of Anesthesiology and Reanimation, Private Medstar Antalya Hospital, Antalya, Turkey
[4]Department of Medical Oncology, Private Medstar Antalya Hospital and Memorial Antalya Hospital, Antalya Turkey

ABSTRACT

Upper airway obstructions with malignant or benign causes have high mortality and morbidity rates and may lead to sudden respiratory distress. Head-neck tumors, cervical esophagus tumors, long-term intubation, and tracheostomies can lead to airway obstruction. Four cases (one with a long-term intubation tracheomalacia and three with malignant upper airway obstructions) that tracheostomy had been inadequate and performed tracheal stomal stent application were presented with literature. These cases show that tracheal stoma stents are an effective method for providing airway palliation and increasing quality of life.

Key Words: upper airway obstruction, tracheostomy, tracheal stomal stent.

Corresponding Author*: Necdet Öz, MD. Medstar Antalya Hospital, Department of Thoracic Surgery, 07020, Antalya, Turkey
E-Mail: drnecdetoz@gmail.com
Phone: +90 532 5638073
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Introduction

Upper airway obstructions with malignant or benign causes have high mortality and morbidity rates and may lead to sudden respiratory distress [1]. Surgery is the primary treatment for airway obstructions and fistulas for head-neck tumors and cervical esophagus tumors [1-5]. When surgery is not possible, airway continuity is provided by tracheostomy; however, in some cases tracheostomies are inadequate for keeping the airway open due to involvement of the distal part of the trachea. Here we present case studies of 4 patients in whom tracheal stomal stents (TSS) were placed.

Case Report

Case 1

A 40-year-old female patient underwent a tracheostomy due to cervical esophagus carcinoma. The patient was undergoing radiochemotherapy and was evaluated for a complaint of respiratory distress. In the computed tomography (CT) examination, progressing tumor tissue was observed in the cervical region and a stenosis that had progressed until the end of the tracheostomy canula was observed in the trachea. Bronchoscopy revealed the presence of a tumor leading to airway obstruction, therefore, a TSS (80 mm partial-coated, 20 mm diameter) was placed under sedation over the carina to the tracheostomy stoma. The start of the stent was fixed to the stoma via polypropylene suture (Figure 1). The patient died on the 45th day with disease progression

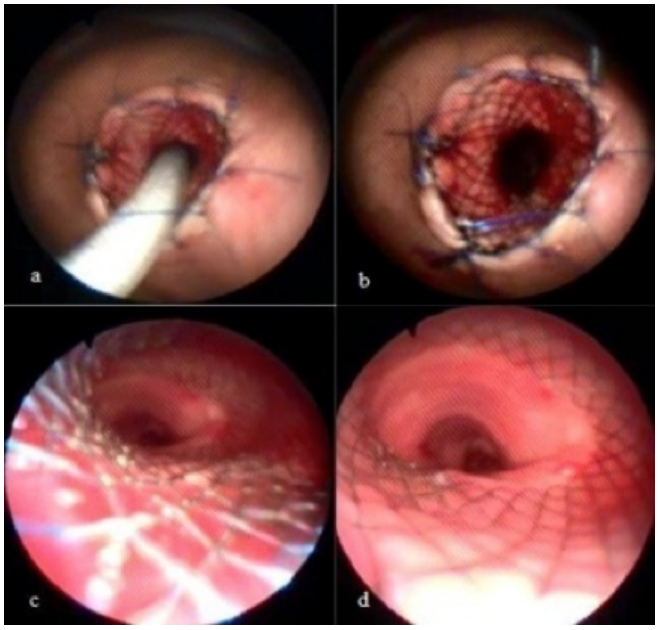

Figure 1a-d. Bronchoscopic images of case 1.

Case 2

A 62-year-old male patient undergoing radiochemotherapy for a head-neck tumor complained of respiratory distress and underwent a tracheostomy. Upper gastrointestinal endoscopy revealed a tracheo-esophageal fistula (TOF). A stent had been previously placed in the esophagus. Progressing tumor tissue was observed in the cervical region and stenosis, which had progressed to the end of the tracheostomy, was observed in the trachea. The bronchoscopy revealed a stenosis in the trachea and a 3-cm sized TOF at the back wall of the trachea. A TSS (80 mm partial coated stent with a 20 mm diameter) was placed under sedation to the tracheostomy stoma over the carina (Figure 2). The procedure resulted in mitigation of respiratory distress and provided a clear airway during 175 days.

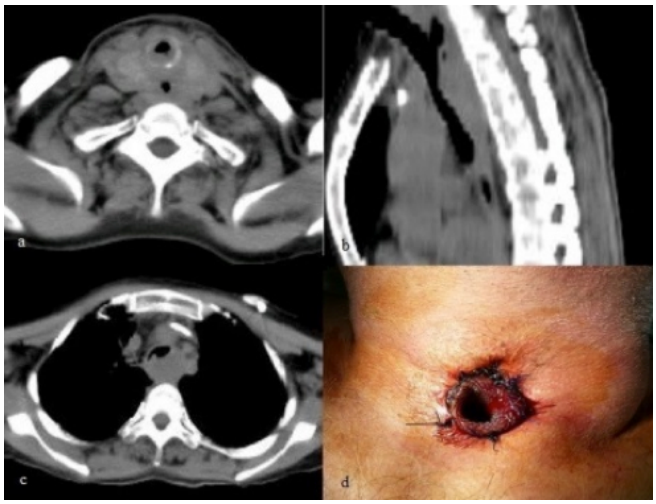

Figure 2a-c. Thorax CT images of case 2, d. stoma image of same case.

Case 3

A 72-year-old male patient receiving radiochemotherapy for larynx carcinoma was evaluated for respiratory distress and subsequently underwent a tracheostomy. Progressing tumor tissue was observed in the cervical region with CT, as well as a stenosis in the trachea that had progressed 3 cm over the carina. Bronchoscopy revealed tumor invasion and a stenosis starting in the stoma and progressing until the mid-trachea following a tracheostomy. Under sedation, a TSS (80 mm partial coated stent with a 20 mm diameter) was placed until the tracheostomy stoma was over the carina. There was a significant reduction in respiratory distress and no problems during 33 days.

Case 4

A 60-year-old male patient who received a tracheostomy 19 years ago due to a vehicle accident, followed by home-care services on a ventilator, and was evaluated for respiratory distress. The patient had a restricted airway despite an adjustable special tracheostomy cannula, and thorax CT imaging revealed that the diameter of the trachea was as large as 6 cm. Approximately 4 cm TOF was detected via upper gastrointestinal endoscopy. Bronchoscopy revealed reduced vocal cord movements and significant tracheomalacia starting at the tracheostomy cannula. The 2 cm of the trachea exceeding the carina was healthy. A 120x22 mm partially coated esophagus stent was placed under sedation, followed by placement of a TSS (140 mm partial coated stent with a 22 mm diameter) over the carina, reaching the tracheostomy stoma under the guidance of a fiberoptic bronchoscope. To avoid any shifts, the stent was fixed to the stoma with polypropylene sutures and fixed with a tracheostomy cannula (Figure 3). During 105 days, the patient was then connected to a ventilator without any issues.

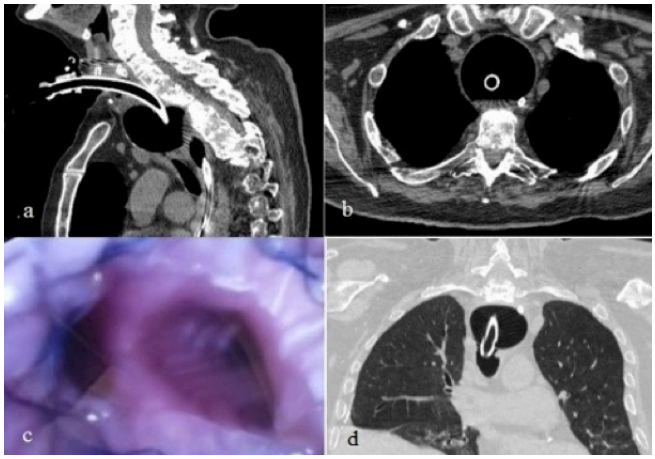

Figure 3a,b,d. Thorax CT images of case 4, c. bronchoscopic image of the distal trachea.

Surgical Technique

The patients were evaluated via head-neck tomography and thorax CT. The localization of the stenosis and normal sizes of the trachea were noted, and the localization of the stenosis and TOF and status of the left and right bronchial systems were determined by a fiberoptic bronchoscope prior to the procedure. Finally, the proper stent was selected (Metallic, partially coated, "self-expandable" stents (M.I.Tech Co. Ltd, Gyunggi -do, Korea). The procedure was performed in an operating room under sedation and local anesthesia. The stent system was placed compromising the 2 cm healthy part of the distal trachea under the guidance of fiberoptic bronchoscopy, the cover on the stent system was pulled back, and the TSS was placed at the proximal part touching the stoma. The stoma was fixed by prolene surrounding sutures to avoid displacement (Figures 1, 2).

Discussion

In upper airway pathologies, symptoms depend on the additional pulmonary pathologies that accompany the localized obstruction of the airway. Initially, coughing and exertion increase respiratory effort, and subsequently respiratory distress is observed while resting. Sudden respiratory failure may be observed with secretions and accompanying infections [3]. A history of aspiration, severe cough, and unmanageable pneumonia may suggest TOF [6]. Physical exams reveal the presence of stridor, low oxygenation, wheezing sounds, and noisy respiratory sounds. Test results indicating impaired respiratory function and blood gases aid in diagnosis. Cervical and thorax CT determine the localization and length of the pathologies, as well as any pressure from the external regions or intraluminal pathology. Gafaar et al. [7] reported using "multi-slice" tomography, 3-dimensional reconstruction, and virtual bronchoscopy of the neck and thorax in pre-operative evaluation. Bronchoscopy is a standard diagnostic and treatment method using invasive procedures. All of our cases had previous tracheostomies, cervical CT, thorax CT and fiber optic bronchoscopy were performed to clarify the underlying cause(s) of respiratory distress.

Tracheal stents are indicated for stenosis or obstructions caused by external pressures; in the presence of greater than 50% stenosis after laser or brachytherapy, TOF, primary or post-operational tracheomalacia, and in patients not suitable for surgery [1,2,8-10]. Tracheostomy is another method for providing an open airway in cases not suitable for tracheal stents. TSS is another method used to provide an open airway when a standard tracheal stent is not appropriate and tracheostomy is inadequate [11]. The objectives here were to correct the airway obstruction related to progressing local tumor

tissue via a stent, increase the quality of life, and avoid airway obstruction [10]. For 3 of the 4 cases considered here, the Montgomery T tube was not an alternative since there was no proximal airway; in the remaining case, TSS was preferred based on accompanying TOF, long-segment tracheomalacia secondary to tracheostomy, and the need for ventilator support.

TSS is preferred in cases not suited for a standard tracheal stent, such as trachea stenosis, TOF, and tracheomalacia [11]. Only Spelsberg et al. [11] has reported an application of TSS for TOF in 6 laryngectomized cases, which is the same type of case as ours. The TSS applications defined by Samuel Garcia et al. [12] and Hall et al. [13] are not exact matches to our application.

Consecutive or concomitant stent placement into the trachea or esophagus is particularly recommended in the presence of TOF [6]. However, this method has the disadvantage of fistula widening due to necrosis in healthy tissue that is exposed to pressure [1]. For our two TOF cases, the esophagus was stented first followed by the application of a TSS. This provides back-support for the stent placed into the trachea within the mediastinum, prevents displacement, and avoids closing of the fistula. In this case, stenting of the esophagus or trachea should be planned based on the location of the fistula.

Tracheomalacia is another indication for TSS [3, 9]. Stent placement is indicated in multiple long-segment malacias, although there are no constant areas of stenosis [1]. The most important issue in cases with tracheomalacia is the prevention of stent displacement [3, 9, 15]. Patient selection must include screening for limited malacia and the presence of healthy tissue in the distal regions [3]. In one of our cases, TSS was performed due to post-tracheostomy tracheomalacia. Here, a long-term tracheostomy with cuff led to tracheomalacia. The most important problems were displacement of the silicone or metal stent and fixation to prevent leakage from its surroundings and some methods were reported for fixation [3,14,15]. Our case did not require additional fixation since we believed that the stent placed in the distal trachea was fixed in the environment and covered with 2 cm of healthy tracheal tissue. However, air leakage was observed through the TOF area after the procedure, but ventilation of the patient was not impaired. Here, the fixation of TSS at the tracheal end via thoracotomy is preferred due to the decreased risk of morbidity.

Metal and silicone stents are the most commonly used tracheal stents. Metals stents are preferred to silicone stents since they are more effective at opening the areas of stenosis, more compatible with the anatomy, provide better mucociliar cleaning, and lead to less bacterial colonization and migration [1,7,8]. Partial coated, "self-expandable" metallic stents were used as TSS in our 4 cases based on the considerations mentioned above.

The complications of stents are migration, spitting out of the stent while coughing, erosion to the surrounding tissues, bleeding, difficulty swallowing, chest pain, secretion accumulation, granulated tissue development, obstructions, bad breath, infection, and stent breakage [2,3,7-9].Intermittent bleeding was observed in one of our cases, but was not life-threatening. In another case, air leakage to the gastrointestinal system was observed through TOF from the distal part of the TSS under ventilator support.

In conclusion, in presence of tracheomalacia, TOF and tracheal obstructions related to head-neck tumors or cervical esophagus tumors, placing a metallic coated stent in the healthy distal part of the trachea in contact with the stoma (TSS) is an effective method for providing a clear airway. This method may be preferred for providing an open airway.

Declaration of conflicting interests

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Case Report

Penetrating chest trauma with a dagger: an appalling case at the emergency department

Demet Yaldız[1*], Yunus Türk[2]

[1]Department of Thoracic Surgery, Celal Bayar University, Faculty of Medicine, Manisa, Turkey
[2]Department of Thoracic Surgery, Dr. Suat Seren Chest Diseases and Thoracic Surgery Training Hospital, İzmir, Turkey

ABSTRACT

Penetrating chest traumas constitute nearly one third of all chest traumas with a high high mortality and morbidity. Herein we present a 29-year-old male patient presented at the emergency department with a the penetrating thoracic trauma with a dagger. The management was reported in the light of relevant literatüre.

Key Words: penetrating chest trauma, stab wound, hemothorax.

Corresponding Author*: Demet Yaldız, MD. Dr. Suat Seren Göğüs Hastalıkları ve Cerrahisi Eğitim ve Araştırma Hastanesi, Gaziler Caddesi, Yenişehir, İzmir, Turkey
E-mail: demetyaldiz@gmail.com Phone: +90 532 3376834
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Introduction

Penetrating chest traumas constitute 30% of all chest traumas and they have high mortality and morbidity hence the organs in thorax are vitally important [1,2]. Therefore, the hemodynamics of the cardiorespiratory system should rapidly be corrected and treated.

Herein we present a penetrating thoracic trauma due to a dagger wound.

Case Report

A 29-year-old male patient was admitted to the emergency department due to a stab wound to his chest. He was drunk, wandering around despite the security guards with a dagger on his chest, and refused to lay down at the beginning. He was calmed down and persuaded for examination. On inspection, it was observed that the dagger was on the third anterior intercostal space of the left hemithorax (Figure1). Vital signs were stable at the moment.

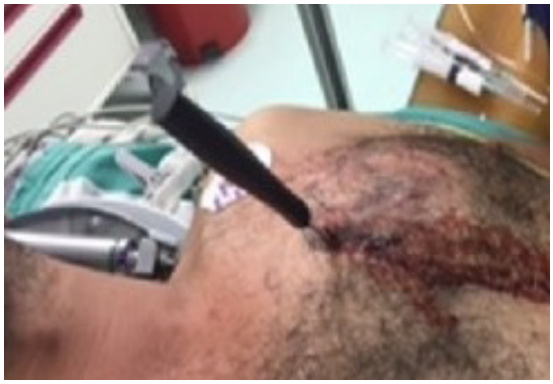

Figure 1. Dagger is seen in the chest wall (emergency department)

Computed tomography (CT) revealed that the half of the dagger was in the thoracic cavity and in the pulmonary parenchyma (Figure 2).

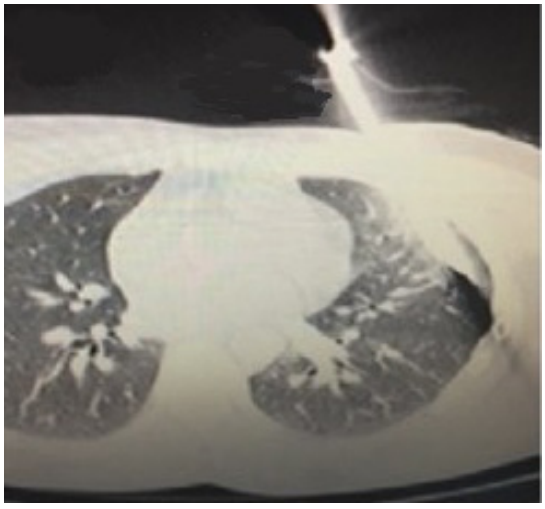

Figure 2. Thorax CT showing the trace of the dagger in the left hemithorax

Laboratory results were stable, and he underwent surgery under urgent conditions. A mini posterolateral thoracotomy, preserving the serratus anterior muscle was performed. The dagger was removed from the lung parenchyma in a controlled manner (Figure 3).

Figure 3. The appearance of dagger after removal

The laceration at the lung parenchyma was repaired primarily. There was no vascular and cardiac injuries. Post operative follow-up was uneventful and he was discharged on the 3rd day of hospitalization.

Discussion

Penetrating trauma to the chest usually causes pneumothorax, hemothorax, hemopneumothorax and diaphragmatic injury. Widened mediastinum indicates injury to the vascular structures and hemopericardium. It is mostly seen in young adult group than children and the elderly. Since young people represent the active and productive age, these injuries causes significant economic and social loss [3-6]. In addition, penetrating chest traumas are most commonly seen in the male population as weapons and sharpening tools can be used and supplied more easily by men then women [5]. Robison et al [7] reported 32.8% gunshot injuries and 67.2% penetrating injuries in a series of 1168 cases. A normal sized knife caused most of the penetrating wounds. In our case it was a dagger and appalling. Although there is a consensus on when and where foreign body should be removed, we think that this issue should be discussed. Many handbooks properly warn against the removal of these sharp tools during the transfer of the patient. Molnar [8] emphasizes that patients are transferred from long distances with a strange foreign body in their chest, and the sharp edges of indwelling objects inevitably rub and cut the surrounding parenchyma. In our patient the dagger was moving synchronously with the heart beat and respiratory movements. Molnar [8] also says that extraction of knives after insertion of a chest drain may be evaluated as alternative to the present protocol.

The most common intrathoracic pathologies in penetrating chest trauma are hemothorax, pneumothorax and hemopneumothorax. Two different studies conducted in our country supported this finding [3,4]. Pulmonary parenchymal laceration is also common in penetrating chest trauma. In patients requiring a surgical treatment, laceration is usually repaired with primary sutures. However, resection varies from wedge resection to pneumonectomy in cases of major vessel injury, bronchial injury, or large lacerations that cannot be repaired [9,10]. In our case, primary repair of parenchymal laceration was sufficient although the view was terrifying no major vessel injury or bronchial injury was noted.

As a conclusion, penetrating chest injuries generally look smaller in the first sight but majority of them are fatal due to vital organ and major blood vessel injuries. Patients with penetrating chest trauma should be treated promptly under monitorization, and an urgent operation should be performed warrantably.

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Review Article

Current surgical management of extrapulmonary oligometastatic non-small cell lung carcinoma

Alkin Yazicioglu*

Thoracic Surgery and Lung Transplantation Clinic, Turkiye Yuksek Ihtisas Training and Research Hospital, Ankara, Turkey

ABSTRACT

Lung cancer is one of the leading cause of mortality around the world, and it is widely known that survival is limited in metastatic lung carcinoma cases. However, in oligometastatic, non-small cell lung carcinoma cases, surgical excision of both the primary tumor and the metastatic site may yield a survival advantage in selected cases. In non-small cell lung carcinoma cases, especially after metastasectomy of brain and adrenal gland metastasis, studies in which survival advantage is reported are common in the literature, and metastasectomy is the treatment method applied to selected patient groups in brain and adrenal gland metastases. In surgical treatment of extra-cranial and extra-adrenal oligometastasis, on the other hand, there are several cases in which morbidity-free survival rates were reported after successful management. In this report, the surgical treatment results were evaluated, and the contribution of treatment methods to survival rates were investigated in extrapulmonary oligometastatic non-small cell lung carcinoma cases receiving surgical excision.

Key Words: extrapulmonary, oligometastasis, lung cancer, brain, adrenal gland, non-small cell

Corresponding Author*: Alkin Yazicioglu M.D. Yasamkent mah. 3272. Cad. Sonmez Residence 4/11 Yasamkent, Cankaya, Ankara, Turkey.
E-mail: yazicioglu.md@gmail.com
Phone: +90 533 4177985
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Introduction

Lung cancer is a worldwide problem and the leading cause of cancer-related mortality around the world [1]. It is also the leading cause of death from cancer in both genders, accounting for approximately 26% of all cancer deaths in the United States [2]. Similarly, in Turkey, the most frequently diagnosed carcinoma is lung cancer, as well as the leading cause of cancer-related mortality [3]. Smoking is the leading prognostic factor of lung cancer; however, genetics also plays a key role [1,4].

Lung cancer consists of two main subtypes, including small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC), and the latter accounts for approximately 85% of the diagnosed lung malignancies [2,5]. Non-small cell lung cancer has several subtypes such as adenocarcinoma, squamous-cell carcinoma, and large-cell carcinoma. In addition, adenocarcinoma is the most common subtype accounting for about 40% of all NSCLC cases, followed by squamous-cell carcinoma, which accounts for about 25-30%. The gold standard treatment for NSCLC is anatomic pulmonary resection with mediastinal lymph node dissection; and complete surgical resection with en-block excision is the goal of the surgery [6].

Although the gold standard for NSCLC is en-block surgical excision, unfortunately not every patient is detected in the appropriate stage for surgery. Most of the cases are diagnosed at advanced stages, and the number of those diagnosed with metastasis is not few. At diagnosis, approximately 70% of NSCLC cases present at a locally invasive or metastatic stage [7]. The metastasis of NSCLC generally diagnosed in the brain, followed by liver, adrenal glands, and bones; however, it is also possible to observe its metastasis in almost all of the tissues of the body aside from the organs.

Metastasis is the secondary implant of a malign tumor in tissues that are distant from the primary tumor [8]. Metastasis includes several biochemical events in which biology and mechanisms are complex. Metastasis consists of steps like angiogenesis, invasion stages consisting four different phases (detachment, attachment, proteolysis, and cell migration), intra vascular phase, and extravasation [9]. In addition, metastatic pathways are classified as lymphatic metastasis, hematologic metastasis, and dropped metastasis [8]. At every stage of metastasis, several numbers of cytokines, chemokines, proteolytic enzymes, metalloproteinases and free radicals play roles [10-13]. In general, it is known that as the tumor diameter and lymphatic invasion increases, the possibility of metastasis increases. However, it was reported in some previous studies that even the tumors with low T and N status caused distant metastasis in series in which metastasectomy was applied. In the series of Mordant et al., it was reported that the diameter of the tumor was below 3 cm in 40% of the NSCLC cases that had distant metastasis and to which metastasectomy was applied; whereas only in 6% of cases, the diameter of the tumor was greater than 7 cm [14]. Similarly, it is also known that the tumors which N status is low may be metastatic. In the study by Plönes et al., 56 patients with distant metastasis were evaluated; 30 patients (53.6%) had N0 disease, 18 (32.1%) patients had N2, and one patient (1.8%) had N3 disease [15]. In another study by Mordant et al., 49% of metastatic NSCLC patients had N0 disease, and 33% of the patients had N2 disease [14].

In diagnosing metastasis, the contribution of radiodiagnostic methods is significant, and the definite diagnosis is established in a pathologic examination. According to the doubted metastasis site, one or more of the radiologic tools such as ultrasonography, computed tomography (CT), magnetic resonance imaging (MRI), various scintigraphy and positron emission tomography (PET/CT) contribute to the diagnosis. Especially, a high maximum standard uptake value (SUVmax) in the doubted area in PET/CT contributes to the metastasis in cancer patients [16-18]. In detecting brain metastasis, MRI is the first radiodiagnostic tool, and must definitely be performed in routine metastasis screening of the patients with lung cancer [19]. In evaluating the bone metastasis, the superiority of whole body bone scintigraphy to PET/CT is on debate [20-22]. Although radiodiagnostic methods are guiding, the definite diagnosis of extrapulmonary metastasis is made with pathological examination. In this review, the purpose is to evaluate the contribution of the treatment of metastasis according to the implanted organ in extrapulmonary, oligometastatic NSCLC cases to overall survival, local disease-free and distant disease-free survival rates.

For this purpose, brain, adrenal gland, skeleton system (bone, muscle), and other organ involvements are examined under separate headings.

The management of extrapulmonary oligometastatic NSCLC

a. General consideration

According to the TNM International Staging System for NSCLC, 8th classification, M1b represents a single extrathoracic metastasis in a single organ, M1c represents multiple extrathoracic metastasis in one or several organs [23]. The principle treatment strategy for NSCLC patients with distant metastasis is chemotherapy as a systemic treatment [24]. Local treatment strategies, such as radiotherapy, are generally used for palliative purpose to relief cancer-related symptoms. Surgical excision of metastatic site is rarely indicated. However, survival benefit of surgical excision is controversial. In a study by Mordant et al., 94 patients with distant metastasis were enrolled between 1983-2006; brain metastasis was the most common (n = 57; 60.6%), followed by bone (n = 14, 14.9%), adrenal gland (n = 12, 12.8%), skin (n = 6, 6.4%), and liver (n = 5, 5.3%) metastasis [14]. The site of the bone metastasis was rib in seven patients, femur in two patients, vertebra in two patients, and scapula, skull, foot big toe in one each [14]. All patients underwent surgical excision for the primary tumor site, lobectomy was the common preferred type of surgery (n = 65, 69.2%) [14]. Sixty-nine (73%) metastasis was excised surgically, and in-hospital mortality reported as 7% [14]. When in-hospital mortality was excluded, 5-year survival rate was calculated as 16% with a median of 13 months [14]. According to Mordant et al., the resection of hepatic or bone metastasis was never associated with long-term survival, even when the bone metastasis was on the rib [14]. The resection of solitary cutaneous metastasis was associated with long-term survival; solitary synchronous brain and adrenal metastasis were associated with 5-year survival rates of 12 and 22%, respectively [14]. In another study by Plönes et al, 46 patients (82.1%) suffered from brain metastasis, four patients (7.1%) had adrenal gland metastasis, four patients had soft tissue metastasis (7.1%), and two patients (3.7%) had bone metastasis [15]. All patients underwent anatomical surgical excision for the primary tumor site; and for the metastasis, the resection was macroscopically and microscopically completed in all cases [15]. Analyzing the influence of metastatic site, authors found a median overall survival of 23 months for patients with soft tissue metastasis, 16 months for patients with brain metastasis, nine months for patients with adrenal gland metastasis, and only four months for patients with bone metastasis [15]. The multivariate analysis revealed that bone metastasis was the only significant parameter influencing median overall survival ($p \square 0.001$) [15]. In another study by Congedo et al., 53 patients with oligometastatic NSCLC were examined, and the most commonly involved organ was brain (n = 39, 73.6%), followed by adrenal gland (n = 7, 13.2%), bone (n = 3, 5.7%) and vertebrae (n = 3, 5.7%) metastasis [25]. Distant disease was completely resected in 42 (79.2%) of patients, and other patients were treated with chemotherapy and/or radiotherapy [25]. In this study, median follow-up was 28 months and 1- and 5-year survivals were 73.1% and 24%, respectively [25]. Median overall survival, local disease-free survival, and distant disease-free survival was calculated as 19 months, 72 months, and 12 months; respectively by using the Kaplan-Meier method [25].

In other series in which less number of cases included, similar survival rates were reported. In a study by Yamaguchi et al, 23 consecutive synchronous, M1b-c, NSCLC patients were enrolled; all patients underwent curative anatomical pulmonary resection [24]. Brain metastasis was the most common (n = 13, 56.5%) followed by bone (n = 3, 13.0%). For the treatment of extrapulmonary metastasis, surgical resection was commonly preferred management method (n = 13, 56.5%) [24]. Seven patients with brain metastasis were managed without surgical interventions (whole brain radiotherapy (WBRT) and stereotactic radio-surgery (SRS)), two patients with bone metastasis were managed with radiotherapy, and one liver metastasis was managed with chemotherapy [24]. During follow-up, 17 patients experienced recurrence; three patients (17.6%) had local recurrence, 13 patients (76.5%) had distant recurrence, and one patient (5.9%) had both [24]. The median progression-free survival and 3- and 5-year progression-free survival rates in the 23 patients were 11.8 months, 21.7%, and 14.5%, respectively [24]. The

median progression-free survival for patients with brain metastasis was 12.5 months and for those patients with metastasis outside the brain was 9.2 months, without statistical significance [24].

Finally, Karagkiouzis et al examined 12 extrapulmonary oligometastatic patients with NSCLC; adrenal metastasis was common (n = 6, 50%) followed by brain metastasis (n = 3, 25%), thoracic wall metastasis (n = 2, 16.7%), and diaphragm (n = 1, 8.3%) [26]. All patients underwent combined resections of the primary lung tumor and solitary hematogenous metastasis; subsequently all patients received adjuvant chemotherapy, and the median follow-up period was 13.5 months [26]. The median survival was 24.1 months, survival rates at 1- and 5-years were 73%, and 39%, respectively [26].

Although we review the literature data on extrapulmonary oligometastatic NSCLC cases we wish to include the survival study results of ipsilateral or contralateral lung oligometastasis. Tönnies et al. compared the survival rates in NSCLC cases with ipsilateral or contralateral lung oligometastasis to extrapulmonary oligometastasis [27]. It was reported that all of the 99 patients whom were included in the study received surgery both for primer lung cancer and for solitary metastasis [27]. The organ in which solitary metastasis was most commonly detected in ipsilateral or contralateral lung (n = 57, 57.6%), followed by brain (n = 21, 21.2%), adrenal gland (n = 10, 10.1%), bone (n =4, 4.0%), liver (n = 2, 2.0%), and other organs (n = 5, 5.0%) [27]. Ipsilobar metastasis was excluded from the study; and anatomical lung resection with mediastinal lymph node dissection was the common surgical procedure for the primary tumor site [27]. As the survival results, Tönnies et al. reported a 5-year survival rate of 48.5% in the patients with a solitary metastasis in the ipsilateral or contralateral lung; whereas the rate was 23.6% in patients with extrapulmonary metastasis [27].

So far, the studies in which primary lung cancer and related oligometastasis were treated with surgical procedures have been mentioned. However, it was reported in the study by Griffioen et al, surgery for lung cancer was applied only in nine of 61 lung cancer patients, and none of the 39 patients in the series of Ruysscher et al. received surgical procedures for lung cancer [28,29]. In these series, although different protocols were applied for the treatment of metastasis, the overall survival, disease-free survival, 1- and 5-year survival rates were reported to be more limited [28,29].

b. The management of brain oligometastasis of NSCLC

The most frequent organ metastasis of lung cancer is in the brain; and in most of the series, brain metastasis ranks the first among extrapulmonary metastasis [14,15,24-30]. For this reason, every patient with pathologically proven lung carcinoma and for whom a pulmonary resection is planned should be examined in terms of a possible brain metastasis .At present, the best tool for the diagnosis of brain lesions is Magnetic Resonance Imaging (MRI) [19,31]. Computed Tomography of the brain underestimates the magnitude of intracranial metastases, and accuracy is poorer than MRI [19]. The treatment modality is on debate in NSCLC cases with brain oligometastasis, and the clinical reports published in this field may be guiding for us in the efficiency of the treatment methods and their effectiveness. The review of literature is demonstrated that different treatment approaches were applied for different case groups by several authors. Whole brain radiotherapy (WBRT), cranial metastasectomy, and stereotactic radio-surgery (SRS) or combinations of these modalities are the treatment options for brain metastasis. In addition, there are different groups of patients with brain metastasis like those with a brain metastasis synchronous with the primary tumor or those with brain metastasis that develops months or years after successful management of the primary tumor.

In a study by Antuna et al., 71 patients with brain metastasis from NSCLC underwent surgical metastasectomy, and 80.3% of cases had solitary brain metastasis [32]. Complete resection was achieved in 90.1% of cases; however, 15.4% of the cases had complications such as intracranial hematoma, neurologic deficits, hydrocephalus, and pneumothorax [32]. The average survival after brain surgery was 20.4 months; the survival rate was 45.1% in one year, 22.5% in two years, 14.1% in three years, and 8.5% in four years [32]. Antuna et al. did not find any significant difference to affect survival rates such as size or number of the metastases [32]. In

another study by Yuksel et al., 28 patients with solitary brain metastasis at the time of diagnosis underwent surgical resection to sites, brain metastasectomy and primary lung tumor [33]. Yuksel et al. followed-up the patients for 23.6 months and reported the overall survival rates were 79% in one year, 42% in two years, and 8% in five years; these survival rates were better than those reported by Antuna et al. [33]. Yuksel et al concluded NSCLC with resectable solitary cranial metastasis, low locoregional stage, without mediastinal lymph node involvement, without any extrathoracic spread would mostly benefit from consecutive complete resection of both tumors, and were supposed to have a better survival [33].

Brain metastasectomy is also an efficient method in the treatment of recurrent metastases for NSCLC. In a study by Bae et al., 86 patients had post-operative brain metastasis as the initial recurrence after complete pulmonary resection [34]. The median follow-up time after the initial lung resection was 24.0 months (range: 2-126 months); median overall post-recurrence survival was 11 months [34]. Seventy-nine of the patients (91.9%) were symptomatic at the time of recurrence, 50 patients (58.1%) had multiple metastases, and 62 (72.1%) patients received systemic chemotherapy for brain metastasis [34]. Surgical metastasectomy was preformed to 17 of the patients (19.8%); however, the rest of the patients were treated with either SRS or WBRT or combination of treatment modalities [34]. An initial lung lesion of adenocarcinoma, non-pneumonectomy patients, a disease-free interval of longer than 10 months from the initial lung resection, solitary brain metastasis, and a size of less than 3 cm for the brain lesion, were reported as positive factors for post-recurrence survive [34].

With the increasing experience in Stereotactic Radio-Surgery applications, it was reported with increasing frequency and success rates in brain metastasis [35-38]. In a study by Harris et al., 126 patients with cranial metastasis due to several tumors were treated with SRS and the most common (50%) tumor histology was NSCLC, followed by breast cancer (12.7%) [36]. However, patients with breast cancer had the longest median survival time of 9.2 months; the median overall survival time for all patients was 5.8 months [36]. Similarly, Abacioglu et al. reported series of 100 patients with brain metastasis from NSCLC; 78 of the patients were received WBRT prior to or after gamma knife radio-surgery, 26 patients had surgical removal of metastasis [35]. Local tumor control was achieved in 95% of the lesions and median overall survival for all patients was 9 months from the date of radio-surgery and 14 months from the diagnosis of brain metastasis [35]. Bai et al. compared the survival times between the patients underwent brain surgery as primary treatment and the patients received SRS [38]. Of 76 patients, 54 patients (71.1%) received SRS, 22 patients (28.9%) underwent brain surgery [38]. The overall survival for patients treated with SRS and brain surgery were 12.6 months and 16.4 months, respectively (p=0.08) [38]. In this series, 21 patients (27.7%) underwent primary tumor resection; however, they did not experience a significantly improved overall survival compared to those who did not undergo lung resection. The overall survive of the patients who underwent lung resection was 16.4 months compared to those who did not undergo lung resection was 11.9 months (p=0.46) [38].

On the other hand, Patchell et al. recommended whole brain radiotherapy after a complete metastasis surgery to avoid recurrences [39]. In a study by Patchell et al., 95 patients who had single metastasis to the brain that were treated with complete surgical resection were enrolled; and the patients were randomly assigned to treatment with post-operative WBRT (n = 49) or no further treatment group (n = 46) with median follow-up of 48 and 43 weeks, respectively [39]. The recurrence of tumor anywhere in the brain was less frequent in the radiotherapy group than in the observation group [39]. Only 9 patients (18%) of 49 patients in the radiotherapy group had recurrence compared to 32 patients (70%) of 46 patients in the observation group (p □ 0.001) [39]. Postoperative radiotherapy prevented brain recurrence at the site of the original metastasis and at other sites in the brain (p □ 0.001) [39]. Similarly, Chung et al. also advised WBRT after resection of brain oligometastasis due to NSCLC [40]. According to Chung et al. WBRT seems to enhance intracranial control [40]. However, according to the series of Abacioglu et al., opposite to this option, an addition of WBRT did not have any effect on overall survival [35].

c. The management of adrenal gland oligometastasis of NSCLC

The adrenal gland is a common site of metastasis due to the presence of multiple pathways of blood supply. Adrenal metastasis is often confined with the adrenal capsule, offering more opportunities to obtain en-block adrenalectomy. The histories, symptoms, and diagnostic methods of the NSCLC patients with brain oligometastasis may be different from the NSCLC patients with adrenal oligometastasis. A significant rate of the metastatic NSCLC cases may be diagnosed with brain metastasis, and these cases are directed to Thoracic Surgery Clinics after brain metastasectomy [8]. However, adrenal metastasis is generally detected accidentally during distant metastasis screening, and the cases diagnosed NSCLC after pathological examination of the adrenalectomy material is uncommon [8]. The value of adrenal metastasectomy for oligometastatic NSCLC cases; which patient group will benefit from metastasectomy; the contribution of the surgery to survive are still on debate in the literature.

In a study by Raz et al., 37 patients with isolated adrenal metastasis from NSCLC were identified; and 20 patients (54.1%) underwent complete adrenalectomy and lung resection compared with non-surgical group [41]. None of the non-surgical group patients had resection of their primary lung cancer. Raz et al. tried to determine the reason why adrenal resection was not part of the treatment for the group of patients managed non-operatively [41]. Patients did not undergo adrenalectomy owing to suspicion of N2 disease, medical comorbidities, or patient preference [41]. The five-year overall survival was 34% for patients treated operatively and 0% for patients treated non-operatively (p □ 0.05) [41]. Among patients treated with adrenalectomy, patients with ipsilateral metastasis had a 5-year survival of 83% compared with 0% for patients with contralateral metastasis (p □ 0.05) [41]. Patients without mediastinal nodal disease had a 5-year survival of 52% compared with 0% for patients with mediastinal nodal disease (p □ 0.05) [41]. Raz et al. concluded surgical resection of isolated adrenal metastasis from NSCLC provides a survival benefit in selected cases compared with non-operative management [41].

In a study by Ma et al., 75 patients with adrenal metastasis underwent adrenalectomy, the most common primary tumor was renal cell carcinoma (n = 26), followed by NSCLC (n = 23), and hepatocellular carcinoma (n = 12) [42]. The 5-year survival rate was 6.1%, the local recurrence rate was 5.3%, and the median survival was 24 months [42]. Ma et al. compared the median estimated survival of patients who underwent adrenalectomy to those who did not undergo any operations for adrenal metastasis and to whom adjuvant therapies were carried out [42]. The median estimated survival of the non-operation group and open operation group were nine months and 22 months, respectively [42]. Patients who suffered metastasis from renal cell carcinoma had the most favorable outcome (median survival was 36 months), whereas, patients with NSCLC was the worst group (median survival was 13 months) [42]. Although the contribution of adrenalectomy to survive was demonstrated in various studies, there are some studies claiming this process does not have any contribution to survive in oligometastatic NSCLC cases. According to Huang et al. adrenalectomy does not improve survival rates of patients with solitary adrenal metastasis in NSCLC [43]. Huang et al. identified 22 NSCLC patients with solitary adrenal metastasis; 10 of these patients had adrenalectomy, and 12 were treated by non-surgically [43]. The median survival was 11 months and 1-year survival rate was 51.4% for all 22 patients [43]. There was no significant survival difference between patients who underwent primary and metastasis resection and those treated conservatively [43]. Moreno et al. reported adrenal metastasectomy for oligometastatic NSCLC had lower survive rates when compared to the metastasectomy applied to other tumors, especially for renal cell carcinoma [44]. Moreno et al. studied adrenalectomy for solid tumor metastasis of several tumors; NSCLC was the most frequent tumor type (n = 148, 46.7%), followed by colorectal carcinoma (n = 43, 13.6%), renal cell carcinoma (n = 37, 11.7%), breast cancer (n = 11, 3.5%), and melanoma (n = 11, 3.5%) [44]. Adrenal metastasis were synchronous in 73 patients (23.0%), isolated adrenal metastasis occurred in 234 patients (73.9%) [44]. Patients with renal cell carcinoma showed a median survival of 84 months, patients with colorectal carcinoma showed a median survival of 29 months, and patients

with NSCLC showed a median survival of 26 months ($p \square 0.05$) [44]. Also, patients with metachronous adrenal metastatic disease showed a median survival of 30 months compared with 23 months in patients with synchronous adrenal metastatic disease ($p \square 0.05$) [44]. Howell et al., on the other hand, reported shorter median survival rates for the NSCLC cases to whom adrenalectomy was performed [45]. In the series of Howell et al., the median survival rate was 17 months in NSCLC cases with adrenal metastasectomy (n = 31, 50%), and the median survival rate was 47 months in the group which received adrenalectomy for other carcinomas (n= 31, 50%) ($p \square 0.05$) [45]. However, there are some other studies reporting longer median survival rates when compared with these series. Solaini et al. demonstrated the results of 37 adrenalectomies in 34 patients, patients with NSCLC (n = 15) had a median survival of 63 months and disease-free survival of 35 months [46]. According to Solaini et al., the concurrent resection of the adrenal metastasis with the primary tumor was the only factor influencing disease-free survive [46].

Laparoscopic adrenalectomy surgery is one of the methods performed frequently in the surgical excision of adrenal metastases. Tonyali et al. examined survival analyses following laparoscopic adrenalectomy for solitary metastasis of lung cancer [47]. In this series, 13 patients underwent 15 laparoscopic adrenalectomy, and the mean estimated survival in the patients with metachronous adrenal metastasis was lower than in those with synchronous adrenal metastasis (33.1 ± 5.4 vs. 33.2 ± 7.5 months, respectively) [47]. The estimated survival in the patients with contralateral metastasis was higher than those with ipsilateral metastasis (43.7 ± 7.6 vs. 24.1 ± 4.8 months, respectively) [47]. In total, ten patients had NSCLC and three had SCLC; and the estimated survival in the patients with NSCLC was higher than in those with SCLC (33.9 ± 5.7 vs. 24 ± 4.2 moths, respectively) [47]. None of the differences were significant; and the estimated overall survival was 33.4 ± 5.2 months [47]. Beside those studies, some other series in which small groups of patients were evaluated, also offers adrenalectomy in selected NSCLC patients who have good performance status and with minimal local nodal involvement from primary tumor [48,49]. Adrenalectomy for metastatic NSCLC patients is associated with low morbidity and may offer a chance for long-term disease-free survival.

d. The management of skeletal system oligometastasis of NSCLC

The metastasis of NSCLC could be detected in many bone tissues in the body. Vertebrae, ribs, and iliac wings come to the forefront in which metastasis detected in the first order [50]. In a study by Tsuya et al., the most common site of skeletal metastasis due to NSCLC was the vertebrae in 50% of patients, followed by the ribs (27.1%), ilium (10%), sacrum (7.1%), and femur (5.7%) [51]. As mentioned in the "general considerations" section, excision of the bone metastasis in oligometastatic NSCLC cases have limited contribution to survival rates. The resection of bone metastasis was generally not associated with long-term survival, even when the bone metastasis was on the rib [14,15]. Additionally, the prognosis was worse in patients with metastasis to the appendicular bone than in patients with metastasis only on an axial bone [52]. In a study by Plönes et al., the worst median overall survive was detected in patients with bone metastasis and the multivariate analysis revealed bone metastasis was the only significant parameter influencing median overall survival ($p \square 0.001$) [15]. In the series of Yano et al., three of the four cases with diagnosed bone metastasis and metastasectomy was performed did not survive, the patients were deceased in the 8th, 32nd, and 58th months, and the survivor case was in the 95th month without disease [53]. However, there are several studies reporting satisfactory survival rates after metastasectomy of bone oligometastasis [54-56]. In a study by Murakami et al., six cases had total en-block spondylectomy due to spinal canal and vertebral metastasis, and four cases were still alive for more than three years [54]. In another report by Hirano et al., two NSCLC cases had bone oligometastasis in the fibula and femur, surgical excision was performed both for the primary tumor site and bone metastasis, and the patients were still alive for more than five years [55]. In another case series by Zhao et al., five patients underwent synchronous lung cancer resections and solitary bone metastasectomies, the progression-free survive of the patients was 13.2 ± 7.7 months [57]. Zhao et al. concluded lung tumor resection with bone metastasectomy is a safe method in selected cases [57].

Aside from the bony counterpart of the skeletal system, NSCLC metastasis may be diagnosed in the muscles [58-61]. In the literature, these patients were mostly reported as case reports, and some reports declared long-term survive rates after metastasectomy from muscles. In a case report by Santini et al., a solitary muscle metastasis after resection of lung cancer was presented, and 24 months after surgical excision and chemotherapy, the patient was alive without disease [61]. Hence, the authors concluded more aggressive treatment modalities might be considered for selected patients with solitary muscle metastasis [61].

e. The management of extra-cranial, extra-adrenal, and extra-skeletal system oligometastasis of NSCLC

Aside from the brain, adrenal glands, muscle and bone tissues, NSCLC may cause metastasis in any organs or tissues in the body. The detected metastatic organs and tissues of NSCLC were reported as abdominal organs such as spleen, stomach, small intestine, colon, rectum, pancreas, omentum; and retroperitoneal organs such as kidneys and ureters; the breast, thyroid gland, internal ear, spinal channel, and skin [56,62-75]. In a case report, Tomita et al. presented two cases of isolated renal metastasis for NSCLC [62]. Both cases had anatomical pulmonary resection for primary lung tumor [62]. Subsequently, case one had a mass in the right kidney, was diagnosed as metastasis of NSCLC, and underwent right nephrectomy. Six months after nephrectomy, the patient reported as doing well without sign of recurrence [62]. A hypodense mass was detected in the right kidney in the second case, and this case also underwent a radical nephrectomy. One year after surgery, this patient was also disease-free without recurrence [62]. In oligometastatic NSCLC, there were some other reports in which better survival rates than previously mentioned cases were reported for kidney oligometastasis. In a report by Adamy et al., five patients underwent nephrectomy due to lung carcinoma metastasis [63]. One of the patients was deceased at 19 months after metastasectomy, and the other four patients had survival rates between 5-39 months [63].

There are several studies reporting successful survival rates for metastasis in other abdominal organs aside from the kidneys [70,76]. In a study by Fujiwara et al., nine patients with gastrointestinal metastasis due to NSCLC underwent surgical excision. After pulmonary resections of the patients, gastrointestinal metastasis was observed in the small intestine (n = 4), colon/rectum (n = 4), and stomach (n = 1) [76]. Gastrointestinal surgery was performed in five patients; the median survival after the diagnosis of gastrointestinal recurrence was 10.8 months [76]. Three patients who underwent surgery for gastrointestinal metastasis survived for more than 2 years without recurrence [76]. However, there are also some other studies reporting limited survival rates with the surgical management for solitary abdominal metastasis after anatomic resection and/or chemotherapy for NSCLC treatment. Matsuda et al. described three NSCLC cases, first one received anatomical pulmonary resection for treatment of NSCLC, and four months later she was diagnosed to have a metastasis around the stomach [70]. She underwent a laparotomy with surgical excision of the metastatic site. However, she succumbed to recurrent disease eight months after the resection for metastasis [70]. The other two cases received chemotherapy and radiotherapy for NSCLC; and several months later, both were diagnosed with omental metastasis, and surgical excision of metastasis was performed to both cases [70]. Subsequently, both cases received chemotherapy and were reported without recurrence eighth and 20th months after surgical excision for metastasis [70]. The pancreatic metastasis of NSCLC was also reported in the literature, and it was discussed in some case reports that metastasectomy could contribute to survival. In a case report by Wilson et al., surgical resection of pancreas for NSCLC metastasis improves survival of patient [68].

Aside from the abdominal organs, the other organ metastases treated surgically are uncommon and reported as case reports. In these case reports, the management strategy of the primary lung tumor and metastatic site show differences. For this reason, there is no consensus on the management protocols of these cases. As case reports and series are presented, the missing points in this field will be covered, and management protocols will be clarified in the treatment of oligometastasis of several organs in NSCLC cases.

As a conclusion, patients with M1b-c Stage IV meta-

static NSCLC are generally believed to have an incurable disease. However, some M1b-c Stage IV NSCLC patients who have extrapulmonary oligometastatic disease are able to achieve longer survival by receiving curative intent pulmonary resection with mediastinal lymph node dissection and surgical treatment of distal metastasis. In many of the series, it is observed that different treatment modalities applied for the treatment of oligometastatic NSCLC cases. For example, some authors chose the management strategy of firstly neoadjuvant treatment is applied, then lung surgery is performed, and subsequently metastasis surgery may be applied. However, some other authors designed the treatment protocol as firstly performing metastasis surgery and later lung surgery. In addition, in many of the series, chemotherapy, radiotherapy, and radio-surgery might be applied as the treatment for metastasis in addition to surgical procedures, and all of the cases evaluated in the same series. A consensus has not been made on oligometastatic NSCLC patients in the literature due to reasons such as the scarcity of the cases, the differences in the patient selection criteria between the studies, and non-homogeneity of the study groups. It is documented that the survival advantage of metastasectomy surgery in the brain and adrenal gland oligometastasis is better than that in the metastasis in other organs. Additionally, the importance of selection of patients, and the essentiality of performing metastasectomy surgery to the selected patient groups are important points which emphasized in almost all of the studies. Among the criteria that must be considered in selecting patients, the most important ones are the good performance status of patients, the primary tumor being controlled or controllable, metastatic lesion that may be resected, and long survival expectations. In the treatment of oligometastatic NSCLC patients, multidisciplinary approach and coordination between teams are of great importance, and there must be a consensus in selecting proper patients that might benefit from surgical treatment.

In extrapulmonary oligometastatic NSCLC patients, aggressive surgical treatment of the metastatic lesion and primary tumor allows acceptable long-term survival advantages in selected patient groups when a successful local control is ensured.

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