medicinska revija
medical review

UDK: 616.24-007.63
616.24-006.6
COBISS.SR-ID 23102985

Novković Ostojić S. et al ■ MD-Medical Data 2020;12(3): 161-164

Prikaz slučaja /
Case report

GIANT BULLA AND LUNG CANCER
GIGANTSKA BULA I KARCINOM PLUĆA

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Key words
giant bulla, CT (computerized tomography), lung cancer.

Ključne reči
gigantska bula, CT, karcinom pluća

Abstract

Bullous emphysema is a disease of the lung parenchyma, which causes a parenchimal destruction distally from terminal bronchioles, which is clinically manifested by dispnea. In several studies, the presense of an emphysema, which was detected by a low-grade CT screening for lung examination, was associated with an increased risk of lung cancer. The goal of our work was to describe the case of a patient with surgery of giant bulla. Two years later the patient was diagnosed with lung cancer. For early diagnosis of lung cancer, it's recommended to have an annual low dose CT screening after bullectomy.

INTRODUCTION

In 30% of smokers, computed tomography (CT) detects the presence of emphysema of the lungs[1]. In several studies, the existence of an emphysema detected by low-dose CT screening for lung examination has been associated with an increased risk of lung cancer[2]. Three entities: lung cancer, bullous emphysema and chronic obstructive pulmonary disease (COPD) have intensively been associated with CT screening programs in the last decade[1]. The importance of emphysema for mortality from lung cancer is associated not only in the smoker population. The number of nonsmokers with bulous emphysema is on the rise.[3] Bullous emphysema is a disease of the lung parenchyma, caused by permanent enalargement of air spaces distally from terminal bronchioles, which is clinically manifested by dispnea. COPD is characterized by chronic inflammation of the respiratory tract, resulting in a limited airflow. COPD and emphysema both makes smokers suitable for the development of lung cancer.[4]

In the study by Tores et al., patients who were involved in the screening program for lung cancer, had a higher frequency of diagnosis of lung emphysema. There are data, due to the correlation of worse prognosis lung cancer patients, who also have emphysema diagnosis.[4] The mechanism of the formation of lung cancer is crammed with diseases at which the risk factor is smoking, COPD and emphysema with the co-operation of genetic factors, DNA damage, and chronic inflammation. In smoker patients who have been diagnosed with emphysema, cancer is more commonly occupied by emphysema. In recent years, there has been an increasing research of the role of the immune system and its application in the treatment of lung cancer.[4]

CASE REPORT

A 41 year old male, who has had a 40 pack-year smoking history, was admitted to the hospital due to sudle onset of dispnea. On admission, the patient had a neat cardiac status. After the examination of pulmonary function, normal values of forced expiratory volume and pulmonary capacity (FEV1% 96, FVC 6.36) were obtained. A chest X-ray was performed, which raised suspicion of the presence of pneumothorax (Fig. 1).

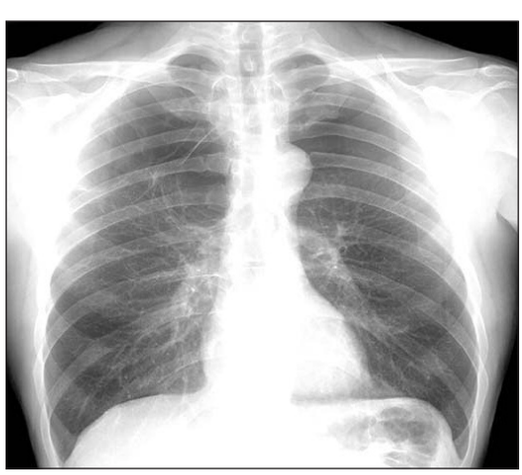

Figure 1. *Chest X ray (PA view)*

A CT scan of the chest was done to see the huge ("giant") bule in the apical segment of the lungs as well as in the lower right side of the lung. The largest measured dimension of the bulla in the right apical segment was 109mm and the left 108mm (Fig. 2).

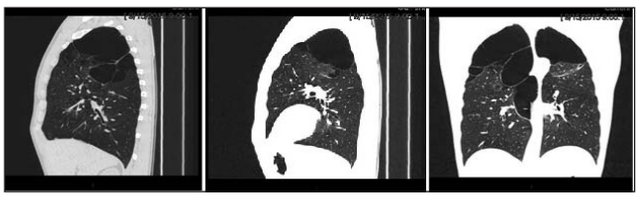

Figure 2. *Chest computed tomography (sagittal and coronal - view, lung soft tissue window) revealed bulla in upper lobe, in right side 10,8cm, and left side 10,9cm diameter*

The cardiological status and pulmonary function parameters allowed the performance of lung volume reduction surgery (LVRS). In the patient, after appropriate preoperative preparation, a video-assisted thoracoscopy and LVRS were performed on two occasions with the removal of the giant bullae. In both resections a pathohistological finding had confirmed the presence of a giant emphysematous bulla. A postoerative chest X-ray was performed and showed no pathological changes (Fig. 3).

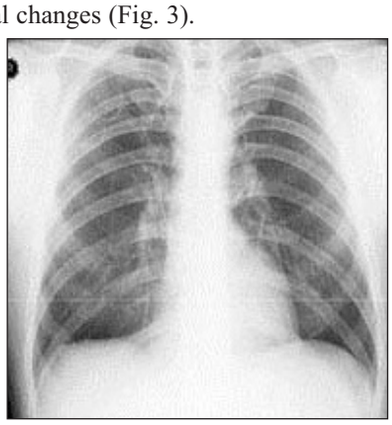

Figure 3*. Normal chest X-ray after LVRS*

Smoking cesattion is required. The patient is advised to quit smoking. Two years after the operative treatment, the patient was admitted to our hospital due to onset of haemoptysis and chest pain. Chest X-ray revealed relatively clear, homogeneous shading in the right upper lung field, along the lateral thoracic wall, as well as the enlargement of the hili. (Fig.4)

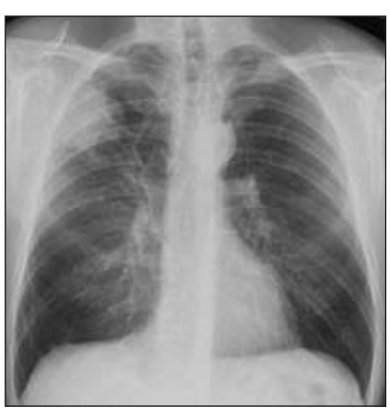

Figure 4. *Chest X-ray revealed ill-defined relatevly clear mass periferal distribution in the right upper lobe with an enlargement of the hili*

Contrast-enhanced CT of the chest confirmed the presence of ill-defined soft tissue masses in right upper lobe (S2 and S3 region) measuring 37x56x55mm. In the right hilar region, an enlarged lymph node was detected. (Fig. 5)

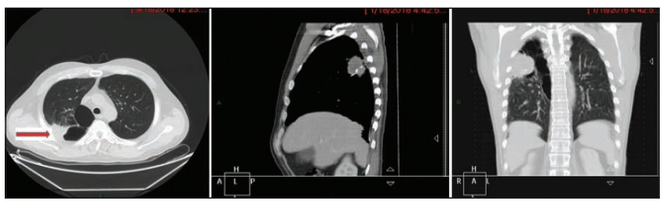

Figure 5. *Chest computed tomography showed ill-defined soft tissue masses in the right upper lobe (S2 and S3 region) 5,7 cm in diameter with enlarged lymph node 1,6cm in diameter*

Fine needle aspiration (FNA) of the lesion was performed and in the obtained material cytological analysis showed tumor cells with moderatly abundant cytoplasm, increased nuclei with prominent nucleoli arranged in small acini and papillas. Based on this finding, the diagnosis of adenocarcinoma was set. (Fig. 6)

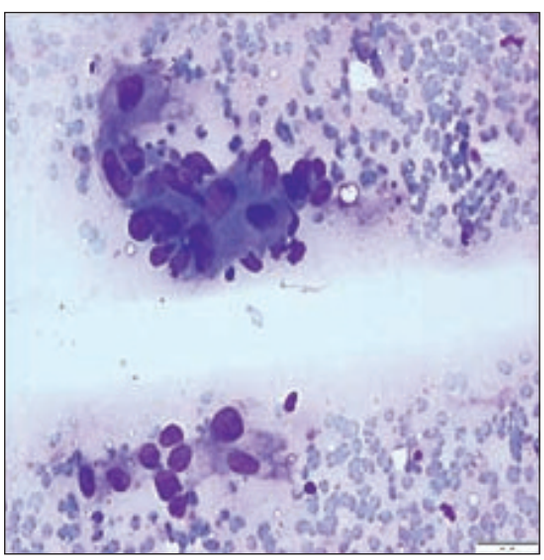

Figure 6. *Fine needle aspiration cytology- adenocarcinoma, MGG x 200*

In addition 18F FDG PET / CT (18 fluorodeoxyglucose positron emission tomography/computer tomography) examination of the whole body was performed. PET/CT discovered more distant lesions than the convencional diagnostic procedure (CT scan). The polygonal focus of the intensive accumulation of radiopharmaceuticals in the S2/ S3 of the right lung (SUV_{max}=26,9), as well as in the lymph node at the 4R position to the right (SUV_{max}=12,88), was detected. Numerous focal points of intense FDG accumulation have also been detected in the liver parenchyma (largest lesion have SUV_{max}=19,77) and bone structures (right humerus and scapula, III, IV rib on the right, VII rib left, ibital bone on both sides and left femur- SUV_{max} value was 16,5) (Figure 7). Molecular testing was conducted on the EGFR receptor status that was negative ("EGFR - wild type"). Further oncological therapy of lung adenocarcinoma was conducted according to the recommendations of the guide of the European Society of Medical Oncology (ESMO - European Society for Medical Oncology).

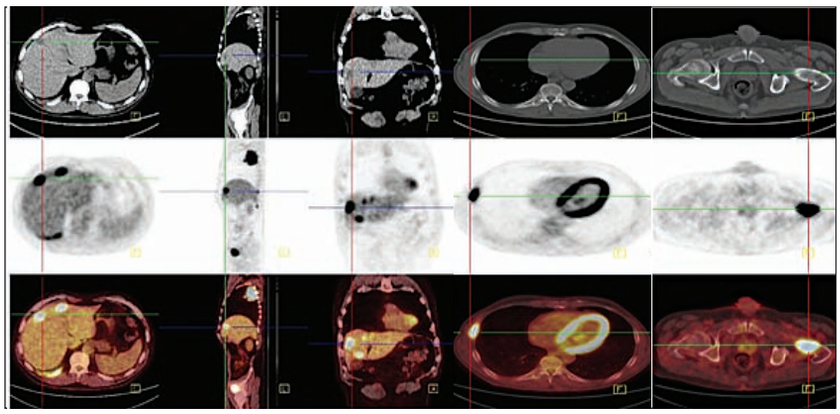

***Figure** 7. A 41 years old man with lungadenocarcinoma, stage T3N2M1c, undervent bullectomy. Coronal, axial and sagital section. This is pretherapeutic PET/CT scan. The MIP image shows multiple hypermetabolic foci in liver and sceleton (located in right scapula, 3th, 4th and 12th rib on the right , 7h rib on the left, both iliac bones, left femoral dyaphisis).*

DISCUSSION

Most research on emphsema was in the late 1990s and early 21st century when the patogenesis of emphysema was identified. The model of emphysema is based on the inflammatory process that occurs in the peripheral tissue of the smokers' lungs. A recent report with serial chest CT examination indicates emphysema progression even after cessation of smoking. There are three types of emphysema: centrilobular, paraseptal and panlobular. The first two are associated with smoking. In the literature, the huge ("giant") bulla was first described in 1937 by Burke in a young male smoker in whom giant bulla were localised in the upper lobes. The giant bulla is usually presented in one or both upper lobes, occupying 1/3 third of the hemitorax with compression of the surrounding lung parenchyma.[5] In the literature the giant bullous emphysema has also been called vanishing syndrome. Araminy et al. showed CT features of giant bullous emphysema and how it differentiates from pneumothorax. Radiologically, the diameter of giant bulla can usually be between 2-8cm, but it can occur in a range from 1 to 20cm. Due to the thin or sometimes invisible wall, it can be misdiagnosed by pneumotorax.[11]

Recent studies showed the role of bronchoscopic bullectomy and implantation of the endobronchial valve, especially in the case when lung function is impaired.[5,6] Surgical treatment in patients with pulmonary emphysema according to GOLD guidelines (Global Initiative for Chronic Obstructive Lung Disease, Inc) involves a reductive type of surgery - LVRS and is applied in the terminal phase of COPD. The exception is an emergency surgical approach for complications such as pneumothorax, dyspnoea, or rarely, infection and bleeding.[4] The criteria for surgical intervention "giant" bulla are often preventive, when the bulla occupies 1/3 of the hemithorax, its surgical resolution is performed in order to prevent complications.[5]

Some authors suggest that patients with this surgical treatment of bulla should have an annual CT screening due to higher incidence of lung cancer.[7] In the case report from literature a large cell carcinoma was detected in an older man after bullectomy who, at first, had a clinically and radiologically confirmed spontaneous pneumothorax. During the surgical intervetion the surgeon didn't have any macroscopical evidence of cancer but after pathological analysis it was confirmed.[10]

Some autors found an association of emphysematous bullae with a 36 times greater risk of developing lung cancer than in patients without emphysematous bulla.[3] According to some studies, in almost 80% of patients who are already diagnosed with lung cancer, patients also show higher incidence of COPD and emphysema.[4] A 1,196 participants with emphysema were included in the study of Torres et al. and who had LD CT performed (Low-dose CT) and had confirmed its presence, that way proving it is an independent risk factor for lung cancer such as smoking history and airflow obstruction.[12] The study of Sancedo et al. demonstrated an important role of emphysema in selection criteria for lung cancer screening. This paper showed the highest lung cancer incidence in individuals with emphysema who were not part of the annual screening.[13] Actually, patients with pulmonary bullous disease and confirmed primary lung cancer have a very poor prognosis. The majority of these patients are in the advanced stage of NSSLC.[14] According to the study by Toyokawe et al., there is a positive correlation between PD-L1 and EGFR wild-type expression in smokers who also have emphysema and lung adenocarcinoma.[3] In another study, Sheard et al. recognised a delayed diagnosis of lung cancer due to cystic airspace (an avascular space with 1mm wall in diameteron chest CT scan). Pulmonary emphysema is often associated with cystic airspaces particularly in the small lesion. Sometimes it can be difficult to mesure the uptake of 18F FDG (Fluorine 18 fluorodeoxyglucose) in the small lesion. The maximum value of radiopharmaceutical uptake in a target tissue is a measure of it metabolic activity, and as such is expressed as SUV_{max}. It is known, if these values after F18 FDG PET/CT acquisition are above 2,5 considerate to originate from malignant tissue. The absence of FDG-avid foci does not exclude potential malignancy.[15] Malignant tumors showed to be highly metabolically active, with increased glucose metabolism and consequently FDG uptake, and can be detected as 'hot spots' with higher standardised uptake values (SUV). The study Ran et al. showed that squamous lung cancer has higher FDG uptake value than lung adenocarcinoma. A meta-analysis concluded that FDG-PET can diagnose malignant pulmonary lesions with an estimated sensitivity of 94.2% and specificity of 83.3%.[17]

In addition to the use of PET CT (positron emission tomography/computed tomography) in assessing the stage of advanced disease, sometimes when the existence of a change associated with cystic air spaces in the lungs or a change resulting from metaplasia of airway cells such as bulla cannot be completely ruled out, therefore requiring further examination. With the introduction of radiopharmaceuticals into the body through increased metabolism and glucose consumption, the place of cancer cells is recognized.

The 18F fluorodeoxyglucose is most commonly used for this purpose. There are other forms of radiopharmaceuticals, so there are radiopharmaceuticals that are used in ischemic heart disease, in neurology due to dementia and epilepsy. However, the most common use of PET/CT belongs to oncology, in assessing the extent of the disease as we had opportunity to see in our case.

Regardless, 18F FDG PET/CT have an irreplaceable role in the staging of lung cancer and also in evaluating treatment response. In the future there is hope of finding radiotracers which may have the ability to assess to receptor expression in occult disease. What remains for us to be able to follow bulectomy patients, with a positive history of smoking according to the indication for the existing screening, is to perform an anual low-dose CT examination of the thorax, in order to detect the lung cancer in the initial stage.

Sažetak

Bulozni emfizem je oboljenje plućnog parenhima kod kojeg dolazi do destrukcije disajnih puteva distalno od terminalnih bronhiola, koja se klinički manifestuje otežanim disanjem. Prisustvo emfizema koje je detektovano niskodoznim CT skriningom je povezano sa povećanim rizikom za razvoj karcinoma pluća. Cilj našeg rada je bio da se opiše jedan slučaj pacijenta, kod koga je dve godine nakon bulektomije otkriven karcinom pluća. Usled povećane koincidence postojanja bula i karcinoma pluća, za ranu dijagnozu karcinoma pluća kod bulektomiranih pacijenata predlaže se godišnje praćenje bolesnika sa niskodoznim CT-om.

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■ The paper was received / Rad primljen: 26.09.2020.
Accepted / Rad prihvaćen: 30.09.2020.