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Features of the Clinic, Diagnosis and Methods of Treatment of Complicated Bullous Lung Disease (Literature Review)

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Abstract A review of the literature on video-assisted thoracoscopic treatment of spontaneous pneumothorax as a complication of bullous emphysema is presented. The issues of etiology, diagnostics and therapeutic tactics in video-assisted thoracoscopic treatment of spontaneous pneumothorax in bullous emphysema are considered. An integrated and differential approach to the choice of therapeutic tactics for spontaneous pneumothorax as a result of bullous emphysema of the lung allows us to determine the diagnostic and therapeutic tactics of video-assisted thoracoscopic treatment and the choice of the method of pleurodesis induction, which leads to improved treatment results for this group of patients.

Keywords Pulmonary emphysema, Bullous disease, Bullae, Etiopathogenesis, Clinic, Diagnosis, Treatment

Bullae (false pulmonary cysts) are pathological air cavities in the lungs (from the English blebs - "bubbles") that can occur due to mechanical damage to the parenchyma, an infectious-inflammatory or other disease. Excess air in these sac-like cavities, changes in the structure of the lung matrix, and a reduction in the area of functional areas of the respiratory organ lead to persistent respiratory failure, and the consequences of such pathological changes can be irreversible. The formation and enlargement of bullae in the lungs leads to a decrease in the gas exchange function of the lungs, and in the event of a rupture of a large bulla, it can lead to a life-threatening condition - pneumothorax.

Bullous lung disease (emphysema) is a disease of the respiratory tract, characterized by pathological expansion of the air spaces of the distal bronchioles, which is accompanied by destructive and morphological changes in the alveolar walls; one of the most frequent forms of chronic nonspecific lung diseases.

Epidemiology. Bullous emphysema affects more than 5% of the world's population, with almost 12% among adults over 30 years of age. It also ranks as the third leading cause of death in the US and kills over 120,000 people a year. It is also known that this disease causes spontaneous pneumothorax in 70-80% of cases. In foreign literature, the authors define bullous lung disease as "vanishing lung syndrome" (vanishing lung syndrome) and indicate a trend towards an increase in the incidence and complicated course of this pathology, while noting the absence of a decrease in the rates of unsatisfactory treatment results due to relapse of the disease [1,2,3].

Etiopathogenesis and clinics. Currently, there is no consensus on the etiology, pathogenesis, clinic, diagnosis and treatment of bullous lung disease. The two most common causes of bullous emphysema are smoking and alpha-1 antitrypsin deficiency (A1AD or AATD), an inherited autosomal dominant genetic condition. Less common causes of emphysematous destruction of the lung parenchyma are smoking marijuana, crack cocaine, or intravenous drug use, resulting in inflammatory or destructive damage to the alveoli [4,5].

Bullous emphysema is characterized by the progression of respiratory symptoms and involves a constant expansion of the airspace in the distal terminal bronchioles due to the destruction of the alveolar sacs, loss of elastic tissue, collapse of the airways and impaired gas exchange [6]. The pathophysiology of bullous emphysema involves valvular bronchoblocking, which allows air to enter the cystic space but not exit it.

The morphological basis of this disease is air cavities (bulls) in the lung parenchyma. In foreign literature, it is customary to distinguish between blebs (blebs) - air cavities less than 1 cm in size, located in the interstitium and subpleurally, and bullae - air formations with a diameter of more than 1 cm, which developed due to emphysematous destruction of the lung parenchyma, the walls are lined with alveolar epithelium. Thus, bullae are formed as a result of destruction of the interalveolar walls due to chronic or, more

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rarely, acute stretch injury with increased intraalveolar pressure [4,7].

A giant emphysematous bulla is defined as an air-filled space that occupies more than a third of the hemithorax and develops in a generalized emphysema lung [5,8]. Emphysema is characterized by airflow limitation associated with loss of architecture of the distal lung with constant expansion of the alveolar space, also distal to the terminal bronchiole [9].

Giant bullae usually form slowly with gradual filling with air, but rapid enlargement and spontaneous deflation are also possible. The distribution of giant bullae is usually unilateral and asymmetrical; however, bullous emphysema has bilateral involvement. There are no known factors that determine whether a mass is unilateral or bilateral.

Giant bullae may be asymptomatic, with dyspnea, or rarely with hemoptysis [10]. The diagnosis is made radiologically from an x-ray showing a bulla occupying more than 30% of the hemithorax. Computed tomography of the chest is sometimes required to distinguish giant bullae from pneumothorax.

Unlike bullae, pneumothorax is defined as the presence of air in the pleural space and is clinically classified by whether it develops spontaneously or traumatically. In addition, spontaneous pneumothorax is classified as primary spontaneous pneumothorax if there is no known lung disease, or secondary to chronic lung disease. It is called tension pneumothorax and is associated with varying degrees of hypotension, hypoxia, chest pain, and shortness of breath.

The pathophysiology of bullous emphysema is closely related to chronic inflammation of the distal air spaces, which leads to the destruction of the alveolar walls and, subsequently, the permanent expansion of the air space. Ultimately, this can lead to reduced gas exchange and airflow limitation due to decreased elastic recoil of the chest wall. Often there is an increased number of goblet cells in the airways with hyperplasia of the mucous glands, fibrosis and collapse of the airways due to loss of attachment due to destruction of the alveoli. This decrease in gas exchange and airflow limitation ultimately leads to chronic hypoxia and hypercarbia in these patients.

Classification. An emphysematous lung may show a homogeneous or heterogeneous (regional) pathological lesion, which may affect lung parameters characteristic of bullous emphysema (eg, dynamic lung volume) in different ways [11,12]. Today it is customary, depending on the level of damage to the acinus, to divide bullous emphysema into:

- centrilobular emphysema - the affected areas are localized mainly in the upper parts of the lungs. It is most closely associated with smoking and is the result of the expansion and destruction of the respiratory bronchioles.
- panlobular emphysema - found mainly in the lower lobes and is often associated with a genetic (alpha1-antitrypsin) deficiency.
- paraseptal emphysema - occurs on the periphery of the lobules, especially in the subpleural region.

Constant exposure to harmful particles (cigarette smoke, air pollution) leads to oxidative stress, proteinase-antiproteinase imbalance, increased apoptosis, and chronic inflammation, all of which lead to gradual destruction of lung tissue [13,14].

The progressive destruction of healthy lung tissue leads to the classic physiological characteristics of severe emphysema: lung hyperinflation, loss of elastic recoil, loss of surface area for gas exchange, and flow restriction [15]. Emphysema causes a decrease in elastic recoil pressure and an increase in lung compliance. This, in turn, causes static and dynamic hyperinflation of the lungs, which restricts airflow and leads to clinical outcomes with lower functional capacity, higher levels of dyspnea, and limited exercise capacity.

Bullous disease can lead to complications such as pneumothorax, infection, and bleeding. The most formidable and frequent complication of bullous disease is recurrent pneumothorax, the mechanism of which is due to an exorbitant increase in intrapulmonary pressure in the bullae (due to physical exertion, weight lifting, severe coughing, straining). At the same time, most authors do not consider spontaneous pneumothorax to be an independent disease and consider it a constant companion of a complication of bullous lung disease. Clinical signs of spontaneous pneumothorax are a sharp pain in the chest with irradiation to the neck, collarbone, arm, shortness of breath, inability to take a deep breath, paroxysmal cough, forced position [16,17,18].

Diagnostics. The goals of the examination for bullous disease are as follows:

1) exclusion of other diseases, primarily diffuse cystic ones, such as lymphangioleiomyomatosis, Langerhans cell histiocytosis of the lungs, Burt–Hog–Dube syndrome [19];
2) establishing a possible cause of bullae: smoking, marijuana use, HIV, connective tissue disease;
3) determination of indications and contraindications for surgical treatment, exclusion of complications.

Patients undergo computed tomography (CT) of the chest and functional studies, including body plethysmography and a study of the diffusion capacity of the lungs. For bullous emphysema, an obstructive pattern of impaired respiratory function is characteristic, for bullous disease it is rather restrictive. A pronounced decrease in the diffusion capacity of the lungs indicates the presence of diffuse emphysema, and not just bullae. To assess the severity of respiratory failure and clarify indications for surgery, it is necessary to study blood oxygen saturation (saturation) and arterial blood gas composition. In all patients with giant bullae, the level of α 1-antitrypsin should be measured [20].

Bullae are detected on CT scan of the lungs. This study measures the number of bullae, their size and shape. Also, CT will allow you to assess changes in lung tissue, the presence or absence of emphysema, bronchiectasis or other cavities [26].

CT scan of the lungs can rule out cystic diffuse lung

disease. They may resemble a bullous deformity.

Differential diagnosis. The differential diagnosis of bullous emphysema, which can be mistaken for a disease, includes asthma, which is ruled out by lung function tests, bronchiectasis, which can be seen on imaging, and congestive heart failure [21,26].

Treatment: In the management of patients with bullous lung disease, as a rule, various conservative methods of treatment are used, which do not lead to long-term positive results and are characterized by a large number of complications and relapses (20-50%). In this connection, with the development of complications, surgical intervention is indicated, where specialists have proposed many procedures and in which the choice of the target lung tissue remains a difficult task [4,5,7,22].

The goal of surgery is to remove the giant bullae, allowing the remaining lung to expand and restore respiratory function. An enlarging giant bulla may also be considered for surgical resection, even if it is asymptomatic [23].

Research has shown that removing the most affected and no longer functioning parts of the lung (lung volume reduction surgery) improves the function of the remaining lung by:

- increasing the elastic recoil pressure, thereby increasing the flow of exhaled air,
- reduction in the degree of hyperinflation, which leads to an improvement in the mechanics of the diaphragm and chest wall,
- a decrease in the heterogeneity of regional ventilation and perfusion, which leads to an improvement in alveolar gas exchange and an increase in the efficiency of ventilation while maintaining the level of gases in the blood [24].

Zoumot (2015) adds that surgical lung volume reduction can lead to a decrease in the asynchronous movement of the various compartments of the chest wall, leading to improved ventilation mechanics [25,27].

Group authors from Basil Hetzel Institute for Translational Health Research (Australia), van Agteren et al. (2016) presented an analysis of the results of lung volume reduction surgery (LVRS) operations (1760 patients with bullous lung disease) (1760 patients with bullous lung disease), which leads to an increase in the mechanical efficiency of healthy areas of the lung and, as a result, to more efficient gas exchange [17]. At the same time, several tasks were set: to study the postoperative period in terms of the functioning of the lungs and the quality of life of patients, to determine the rates of morbidity (relapse) and mortality, to study the cost-effectiveness of URL, and to determine which surgical methods lead to the best results in these patients [27]. In particular, the effect of strengthening the suture line on the effectiveness of RULA was considered, the traditional approach to RULA was compared with a surgical approach that did not involve removal of the affected area of the lung (resection).

By the end of the follow-up period, mortality rates were lower in participants who underwent UROL than in those who received standard care. Participants who presented with reduced lung function due to a particular distribution of diseased tissue in the lungs were at higher risk of death at three months and throughout the duration of one large study. One study identified a group of participants who responded better to UROL than other participants, making them particularly suitable for this treatment [17].

A greater percentage of good results was noted in patients with predominant emphysema of the upper lobe and low ability to exercise. The reduction of 13.6-14.7 units on the SGRQ respiratory questionnaire clearly exceeds the minimum clinically important difference (4-point reduction) for this questionnaire [27,30]. More recent studies show that careful patient selection and procedures performed in specialized centers result in a significant reduction in the risk of death over time [31,32].

McNulty and al (2014) noted only palliative effects of OUOL [30]. This fact, among other things, has spurred the development of minimally invasive techniques that can help achieve the benefits of VRLS without the risk of death and associated costs.

The latest British Society of Thoracic Surgeons (2010) guideline for the treatment of primary spontaneous pneumothorax stated that after the first recurrence, treatment should include surgery (bullectomy followed by a pleural adhesion induction procedure). Thus, a surgical approach is considered the best treatment to minimize the risk of recurrence in patients who have experienced primary spontaneous pneumothorax. The video-assisted thoracic surgery approach has been shown to provide significant benefits in terms of pain and patient respiratory function compared to thoracotomy incisions. As an alternative to the standard multiport VATS, a single port, single notch or uniportal approach has been developed. The uniportal technique has proven to be safe and effective not only for lung resection and biopsy, but also for lobectomy. From this perspective, evidence has shown that a minimally invasive approach should be preferred, confirming advantages over traditional methods [29,32].

According to Vanucci et al. (2019) VATS from Uniportal Access (Uniportal video - assisted thoracoscopy) is a feasible and safe method for performing bullectomy, with results that are at least comparable to other methods, resulting in resolution of symptoms, improved lung function, and improved quality of life [8].

Conclusion. Chronic lung diseases, including bullous emphysema, are the third leading cause of death in the world. Representing a heterogeneous group of pathologies, they are characterized by constant airflow restrictions, hyperinflation, a decrease in airway elasticity as a result of structural degradation and inflammation of the lung tissue, and disrupt effective gas exchange between the alveoli and blood.

According to the literature, surgical reduction of lung volume in the development of complications of bullous disease shows a high percentage of good immediate and long-term results by improving the physical capabilities of patients, eliminating shortness of breath, improving the

quality of life and survival. Nevertheless, the search for effective minimally invasive methods of surgical treatment of patients with bullous pulmonary emphysema continues.

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