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КТ-ПРИЗНАКИ ИНФЕКЦИОННОГО БРОНХИОЛИТА. РУКОВОДСТВО ПОЛЬЗОВАТЕЛЯ ДЛЯ КЛИНИЦИСТА

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Characteristics Radiologic Signs of Infectious Bronchiolitis. A Practical Approach for the General Doctors

Резюме

Термин «бронхиолит» объединяет гетерогенную группу заболеваний воспалительной природы, анатомическим субстратом которых являются воздухопроводящие пути без хрящевой стенки — бронхиолы. Несмотря на этиологическое разнообразие бронхиолитов, патоморфологически они проявляются определенным набором изменений в легочной ткани. Это определяет сходство визуализации различных типов бронхиолитов при проведении компьютерной томографии органов грудной клетки (КТ). Залогом успешной диагностики бронхиолита является четкое понимание определения данной патологии и комплексный анализ врачом-клиницистом анамнестических, клинико-лабораторных и рентгенологических данных. В данной статье рассматриваются три типа клеточного бронхиолита, которые объединены визуализацией паттерна «дерево в почках» при проведении КТ органов клетки: инфекционный, аспирационный бронхиолиты и диффузный панбронхиолит.

Ключевые слова: компьютерная томография, инфекционный бронхиолит, аспирационный бронхиолит, центрилобулярные узелки, «дерево в почках»

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Abstract

The «bronchiolitis» unites a heterogeneous group of diseases of inflammatory nature, the anatomical substrate of which are Airways without cartilage wall-bronchioles. Despite the etiological diversity of bronchiolitis, pathomorphological they manifest a certain set of changes in the lung tissue. This determines the similarity of visualization of different types of bronchiolitis during computed tomography of the chest. The key to successful diagnosis of bronchiolitis is a clear understanding of the definition of this pathology and a comprehensive analysis by a Clinician of anamnestic, clinical, laboratory and radiological data. In this article, we will consider three types of cellular bronchiolitis, which are combined by imaging on computed tomography of the chest pattern «tree in the kidneys»: infectious, aspiration bronchiolitis and diffuse panbronchiolitis.

Key words: *computed tomography, infectious bronchiolitis, aspiration bronchiolitis, centrilobular micronodules, tree-in-bud opacities*

Conflict of interests

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Introduction

Bronchiolitis refers to a heterogeneous group of inflammatory diseases whose anatomical substrate is airways without a cartilage wall with a diameter less than 2 mm, i.e., bronchioles [1, 2].

Despite the etiological diversity of bronchiolitis, morphologically, it is manifested by a certain set of changes in lung tissue. That is why various types of bronchiolitis are visualized similarly on CT.

For diagnosis and effective differential diagnostic search, it is important for clinicians, radiologists, and pathologists to use this term consistently. For example, hypersensitive pneumonitis, which, from a morphological and pathophysiological point of view, is bronchiolitis, is not always regarded as bronchiolitis by pulmonologists and therapists.

As for the clinical presentation of bronchiolitis, this diagnosis can be hardly suspected during the initial visit of the patient with complaints of cough and shortness of breath. These signs are non-specific and appear with a wide range of both lung and extrapulmonary diseases (for example, collagenoses and other autoimmune diseases) [3, 4]. CT of thoracic organs (CT-Th), the most affordable method of indirect assessment of morphological changes in the lung parenchyma, is an important step in establishing the right diagnosis.

Therefore, the key to the successful diagnosis of bronchiolitis is a clear understanding of the definition of this disease and a comprehensive analysis of medical history, clinical, laboratory and radiological data by the clinician.

Classification of Bronchiolitis

Various classifications of bronchiolitis in literature sources are based on etiological, morphological, clinical or radiological criteria. The most rational and often

used classification is dividing bronchiolitis according to histological patterns. This enables dividing all diseases of small airways into strictly defined groups, each with a distinguished set of morphological and radiological signs, and outline a range of etiological factors and clinical symptoms. This strategy allows creating a diagnostic search model [2, 4].

According to histological classification, bronchiolitis is divided into cellular (proliferative) and constrictive (obliterating).

Cellular (inflammatory or proliferative) bronchiolitis is characterized by the accumulation of inflammatory cells in the bronchiole wall and filling their lumen with mucus or exudate [2, 4]. Cellular bronchiolitis includes infectious, respiratory, aspiration and follicular bronchiolitis, hypersensitive pneumonitis and diffuse panbronchiolitis.

Constrictive (obliterating) bronchiolitis is the result of impaired processes of regeneration of the epithelium and submucosal part of bronchioles with an underlying chronic pathological process. It leads to fibrosis and narrowing of the lumen of small airways [3, 4]. Obliterating bronchiolitis can be an independent disease (idiopathic constrictive bronchiolitis) or can develop with other conditions (autoimmune diseases, as a manifestation of chronic rejection after transplantation, due to some viral infections, most often in childhood) (Table 1) [5].

Computed Tomography

Radiographical options for visualizing the structure of small airways are very limited. This is due to both the resolution of radiography and the overall effect that does not allow to clearly differentiate structures that are involved in the pathological process of bronchiolitis. Sometimes X-ray images can show a local increase in the

Table 1. Classification of bronchiolitis

Pathologic types	Clinical and morphologic types	Causes
Cellular bronchiolitis	Infectious bronchiolitis	Bacterial, mycobacterial, fungal, and viral
	Aspiration bronchiolitis	Aspiration
	Respiratory bronchiolitis	Smoking
	Hypersensitivity pneumonitis	Allergic
	Follicular bronchiolitis	Autoimmunity states
	Panbronchiolitis	Unknown
Constrictive bronchiolitis	Constrictive bronchiolitis	Idiopathic
		Posttransplantation
		Autoimmunity

transparency of lung tissue with a pronounced obstructive disease component, increased pulmonary vascularity due to interstitial component, and the appearance of its grid pattern [2, 6].

CT is the method of choice for confirming bronchiolitis in a patient since its resolution is enough to assess the state of the structures of secondary lobules that play a key role in the diagnosis. A secondary lobule is a minimal structural unit of the lung surrounded by connective tissue, with borders that can be visualized on CT (Fig. 1). A terminal bronchiole passes through the center of a secondary lobule (in axial interstitium), dividing distally into respiratory bronchioles and even smaller airways. These particular structures are primarily involved in the pathological process during bronchiolitis.

Pathologically altered bronchioles are displayed on CT in a different manner depending on the slice. They may look like centrilobular (intralobular) nodules when located perpendicular to the scanning plane, or like centrilobular branching Y-structures with small nodules at the ends if the course of bronchioles is parallel — it looks like a twig of a flowering tree. That is why this sign is referred to as «tree in buds» [1, 4].

Since intralobular nodules, based on the name, are located in the center of a secondary lobule, they are absent in the pulmonary parenchyma at the border with pleura (including pleural fissures), which is an important differential sign [4, 6–8]. Centrilobular nodules can be different in size and density: from micronodules (up to 3 mm in size, according to the classification of Fleischner community, [1]) to nodules up to 1 cm in diameter; from nodules with ground glass density to the foci of consolidation [9, 10].

Such centrilobular nodules, thickened walls of bronchioles, filling their lumen with exudate or mucus, and the formation of bronchiectases and «air traps» are typical for cellular bronchiolitis (Fig. 2). The latter arise due to the narrowed lumen of small airways [10].

However, centrilobular nodules can also appear along with peribronchiolar inflammation due to increased density of lung tissue in the center of the secondary lobule. In this case, there will be no “tree in buds” on any slice. Such presentation can be observed for constrictive bronchiolitis; its X-ray picture is defined by irreversible fibrotic changes and concentric narrowing of bronchioles [9, 11, 12].

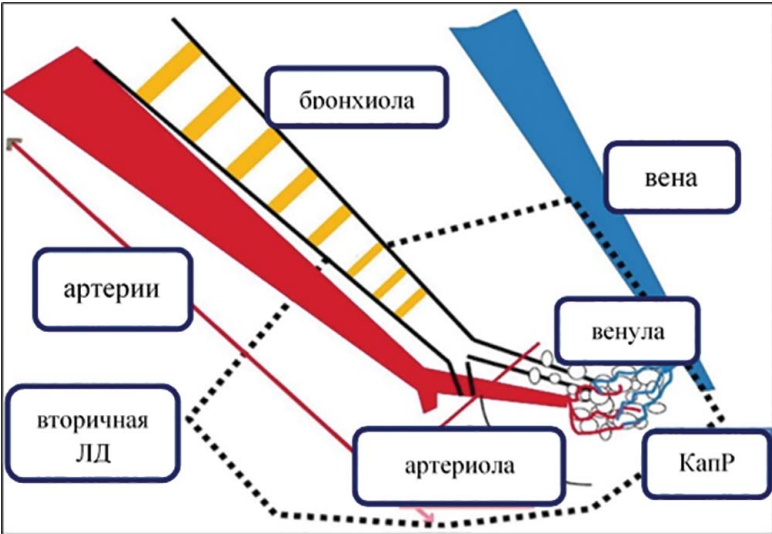


Figure 1. Diagram of the structure of the secondary pulmonary lobule
Notes: LD-pulmonary lobule; CapR-capillaries

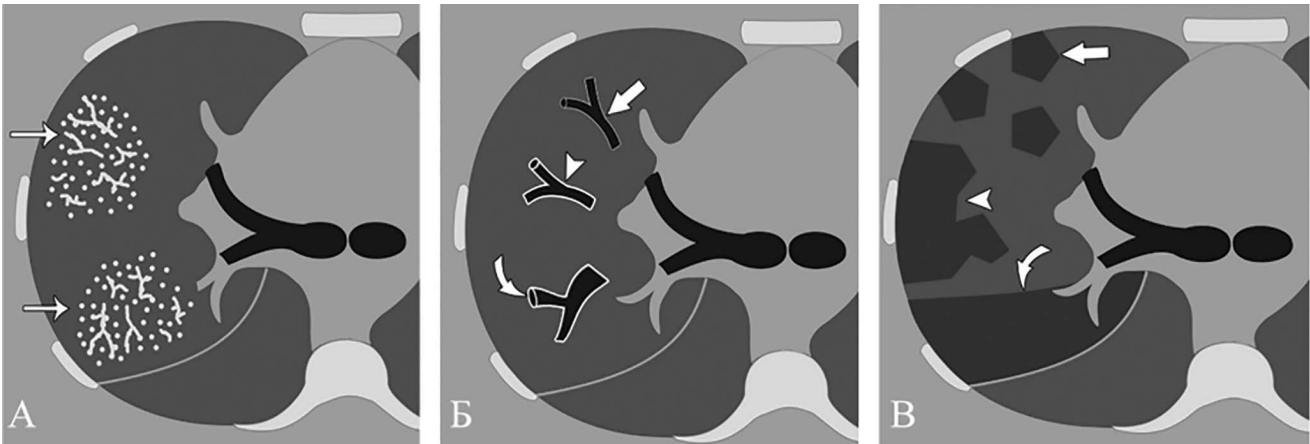


Figure 2. Diagram of the main CT patterns in cellular bronchiolitis [2]
A. Centrilobular nodules combined with Y-structures — the «tree-in-bud» pattern. Note the typical feature of centrilobular nodules — that subpleural zones are free.
B. Different patterns of visualization of the bronchi: normal bronchus (arrow), bronchus with a thickened wall (arrow head), bronchiectasia with the absence of normal bronchial narrowing towards the periphery (curved arrow)
C. Mosaic attenuation: uneven ventilation of the lung parenchyma due to narrowing of the of bronchioles

Table 2. Systematic approach to the diagnosis of bronchiolitis

Тип бронхиолита Types of bronchiolitis	КТ-признаки CT signs	Клинические особенности Clinical features
Aspiration bronchiolitis	Tree-in-bud, progresses to bronchiectasis and fibrosis	Risk of aspiration
Infectious bronchiolitis	Tree-in-bud opacities, bronchiectasis and bronchial wall thickening	Non-specific signs of ARI: dry cough + shortness of breath
Hypersensitivity pneumonitis	Diffuse ground-glass centrilobular micronodules with superimposed mosaic attenuation, air trapping	Allergic +temperature ± bronchial obstruction
Respiratory bronchiolitis	Diffuse nodules, predominantly in the upper lobes	Smoking
Follicular bronchiolitis	Centrilobular nodules, which may have solid or ground-glass attenuation	Can be seen in the setting of autoimmune disease (rheumatoid arthritis and Sjögren syndrome)
Panbronchiolitis	Centrilobular nodules, tree-in-bud opacities, bronchiolectasis, and mosaic attenuation and/or air trapping that characteristically involve all pulmonary lobes	There is an association with chronic sinusitis and P. aeruginosa, H. influenzae

Note: ARI — acute respiratory disease

Table 2 presents the differential diagnosis of three types of cellular bronchiolitis that are combined by a visible “tree-in-buds” pattern. When conducting CT of thoracic organs: infectious and aspiration bronchiolitis, diffuse panbronchiolitis (Table 2).

In order to achieve better visualization of bronchi and blood vessels and to distinguish foci of various etiologies, such methods of CT image postprocessing as maximum (MIP) and minimum intensity (MinIP) projection are used [13].

Infectious Bronchiolitis

Acute infectious bronchiolitis is most common among children in the first years of life and is most often caused by respiratory syncytial virus [5]. However, infectious bronchiolitis can be a manifestation of respiratory viral infection in adults that develops when infected with various viruses (respiratory syncytial, influenza viruses, parainfluenza, adenovirus), bacterial infection

(e.g. *S. pneumoniae*, *H. influenzae*, *M. pneumoniae*) and infection with mycoplasmas or chlamydiae [12, 14].

Infectious bronchiolitis in children usually manifests with low fever, rhinitis and mild dry cough, then progressing to tachypnea, diffuse dry and small bubbling rales, inspiratory crackles [5]. It is important to remember that severe adenovirus bronchiolitis, and, in rare cases, bronchiolitis caused by *M. pneumoniae* in children during the first two years of life can cause serious complications, such as constrictive bronchiolitis, localized or bilateral panlobular emphysema, lobular hypoplasia, including possible bronchiectasis that can form in the structure of Swyer — James — MacLeod syndrome [16].

Adults usually have a more inapparent clinical picture. At the beginning, the disease manifests as symptoms of acute respiratory infection, later complaints of shortness of breath and dry, often paroxysmal cough appears. Auscultatory presentation is characterized by weakened vesicular breathing with dry wheezing on exhalation and inspiratory crackles [3].

In addition to the above pathogens, bronchiolitis can be a sign of the bronchogenic spread of tuberculosis. When mycobacteria are destroyed, oxygenated mycolic acids are secreted, inducing the accumulation of lipids in macrophages [17]. *M. tuberculosis* also inhibits surfactant synthesis [18]. Both these pathological effects lead to the blockage of bronchioles with a viscous secretion. This condition will inevitably lead to inflammation around such small foci. Inflammatory reaction will also be facilitated by the gradual accumulation of mycobacterial antigens in clogged alveoli. It is this local inflammatory process that determines the CT presentation of bronchiolitis, including the “tree in buds” pattern [19]. Further progression is due to the spread of mycobacteria and inflammation along the collateral ventilation pathways, pores of Kohn and canals of Lambert. This bronchiolitis often progresses to caseous pneumonia with subsequent formation of caverns. In this case, pathologists note that the formation of cavities also starts centrilobularly, that is, from the site of primary localization of *M. tuberculosis* [19].

Chronic Bronchiolitis

Chronic infectious bronchiolitis is a term used more often by pathologists to describe changes in the small airways at the microscopic level. There are no specific clinical criteria for this diagnosis. Chronic inflammation of small airways is often of mycobacterial origin (tuberculosis or non-tuberculous mycobacteriosis), but it can be caused by *P.aeruginosa* or can have a fungal etiology, for example, of invasive aspergillosis. In such cases, the disease usually has an inapparent clinical picture with shortness of breath of varying severity as a predominant symptom, sometimes combined with cough. Spirometry often reveals obstructive changes [20].

CT picture of infectious bronchiolitis does not allow establishing its etiology. Inflammation of small airways leads to the filling of bronchioles with pathological secretion and, consequently, to the appearance of centrilobular nodules of various densities, the “tree in buds” pattern, and thickening of bronchial walls. The prevalence of pathological changes can be different, often asymmetric, and includes one or more pulmonary lobes (Fig. 3).

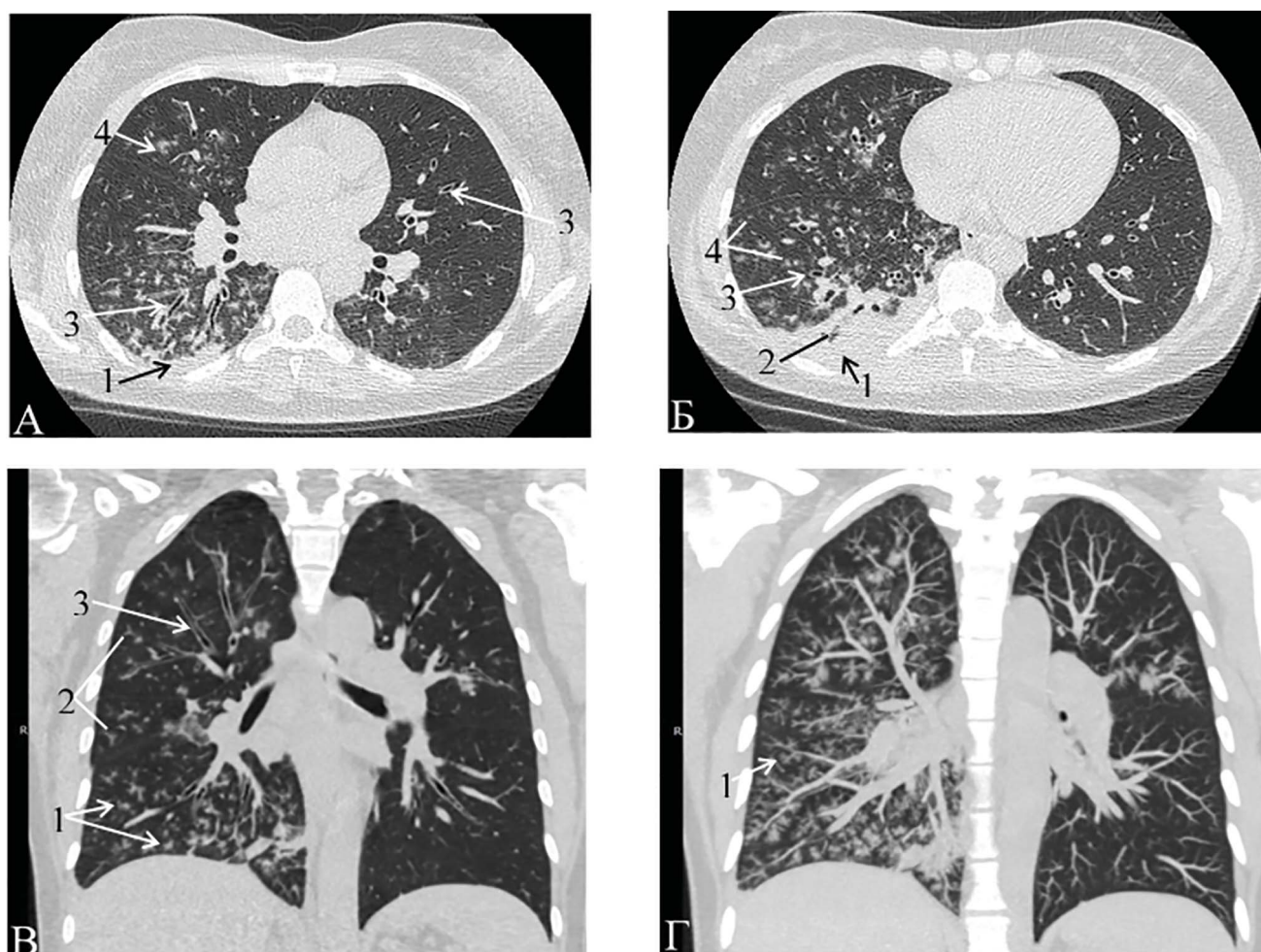


Figure 3. 43-year-old woman with community-acquired right-sided polysegmental pneumonia of moderate severity

A, B. Area of consolidation in S6,9,10 of the right lung (1) with a air bronchogram (2). The walls of the bronchi of both lungs are thickened, hardened (3). In both lungs there are centrilobular nodules of ground-glass (4)
C. Reconstruction in the coronal plane. There are multiple centrilobular nodules of ground-glass (1), more in the right lung, a «tree-in-bud» pattern (2). The walls of the bronchi are thickened (3)
D. Maximum Intensity Projection (MIP) reconstruction allows for better visualization of compressed and exudated small airways (1), more on the right

Bronchiolitis of mycobacterial etiology (tuberculous and non-tuberculous) can be hard to differentiate from a disease caused by another pathogen. Other changes may lead to the right diagnostic path — consolidation focus (often in the upper lobe of the lung), sometimes combined with a decay cavity, bronchial and bronchioectasia in the long course of the inflammatory process, with calcified intrathoracic lymph nodes [2]. It should be borne

in mind that signs of bronchiolitis can be visualized in the areas of lungs that are remote from the site of consolidation, prevailing in the lower lobes [21].

In cases of chronic infectious bronchiolitis, in addition to the immediate signs of inflammation of the small airways, symptoms of a long-term inflammatory process in the lungs can be detected: bronchiectases and bronchioectases, areas of fibrosis, fibroatelectasis (Fig. 4, 5) [2, 7, 13, 14].

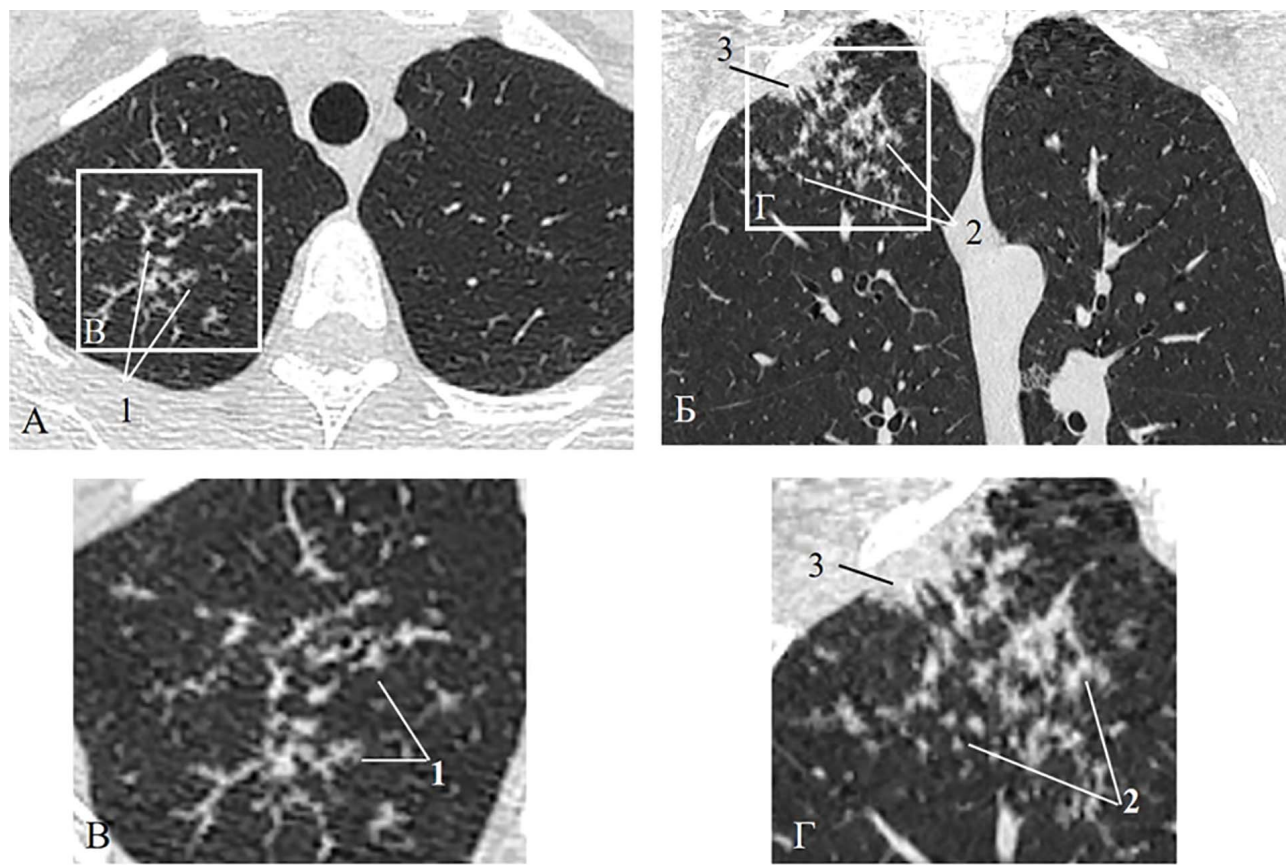


Figure 4. 32-year-old woman with pulmonary tuberculosis (MBT +)
In S1,2 of the right lung, there is a tree-in-bud pattern (1) and small centrilobular nodules (2). Subpleurally, a small area of consolidation is localized in S1 of the right lung (3)

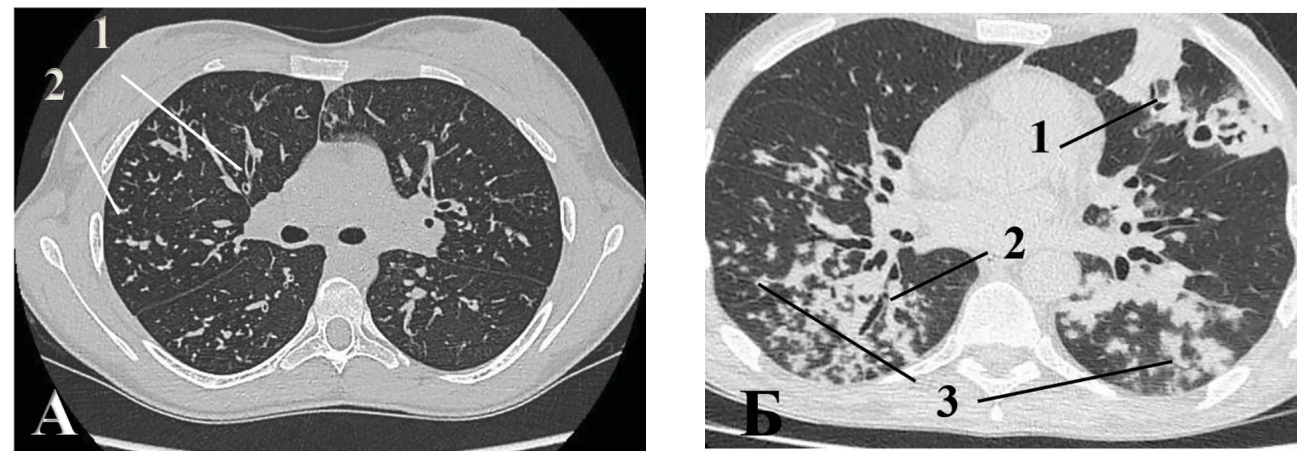


Figure 5. CT picture of chronic infectious bronchiolitis
A. 17-year-old girl with pulmonary-intestinal cystic fibrosis (homozygous for delta F-508). In both lungs, the walls of the bronchi are compacted, thickened, and cylindrical bronchiectasis are visualized (1). Diffusely in both lungs there is a «tree in the kidney» pattern (2), combined with centrilobular nodules
B. 58-year-old man with pulmonary tuberculosis (MBT +). In both lungs, areas of consolidation with expanded deformed lumens of the bronchi (1) in their structure are visualized. For the rest of the length, the bronchial tree is also deformed like cylindrical bronchiectasis (2). Mainly in the lower lobes of the lungs — multiple small centrilobular nodules (3)

Aspiration Bronchiolitis

Aspiration bronchiolitis is one of the manifestations of lung tissue lesion during aspiration. Despite its prevalence, this type of bronchiolitis is rarely diagnosed due to non-specific clinical signs. The course of aspiration bronchiolitis, as well as infectious bronchiolitis, can be acute or, with constant microaspiration, chronic. Histologically, aspiration bronchiolitis is an aseptic inflammation of bronchioles and peribronchiolar tissue, with the formation of granulomas with frequently found aspirated material [15, 16].

There is a higher likelihood of aspiration in bedridden patients, as well as in patients with dysphagia [16]. Therefore, patients in severe conditions should be suspected for the possibility of developing aspiration bronchiolitis: in cases of neurological diseases (stroke, traumatic brain injury, multiple sclerosis), laryngeal cancer, diseases of esophagus (tumor, achalasia, esophagitis with the formation of strictures, esophageal diverticulum,

tracheoesophageal fistula and large diaphragmatic hernia) [15, 16].

Aspiration bronchiolitis usually manifests as a long-lasting cough with clear sputum discharge, bronchospasm and shortness of breath. These symptoms are often regarded as the course of bronchial asthma or chronic obstructive pulmonary disease that are refractory to steroid therapy and bronchodilators. Therefore, the diagnosis should be made only at the stage of the chronic pathological process in lungs when bronchiectasis and fibrotic changes in lung tissue are formed, and respiratory failure develops [13].

Changes on CT often prevail in the lower lobes of lungs and are represented by the “tree in buds” pattern and centrilobular nodules of various densities. Both unilateral changes (more often right-sided due to a more vertical course of right lower lobe bronchus) and bilateral lesions are possible (Fig. 6). Concomitant extra-pulmonary findings, such as diseases of the esophagus,

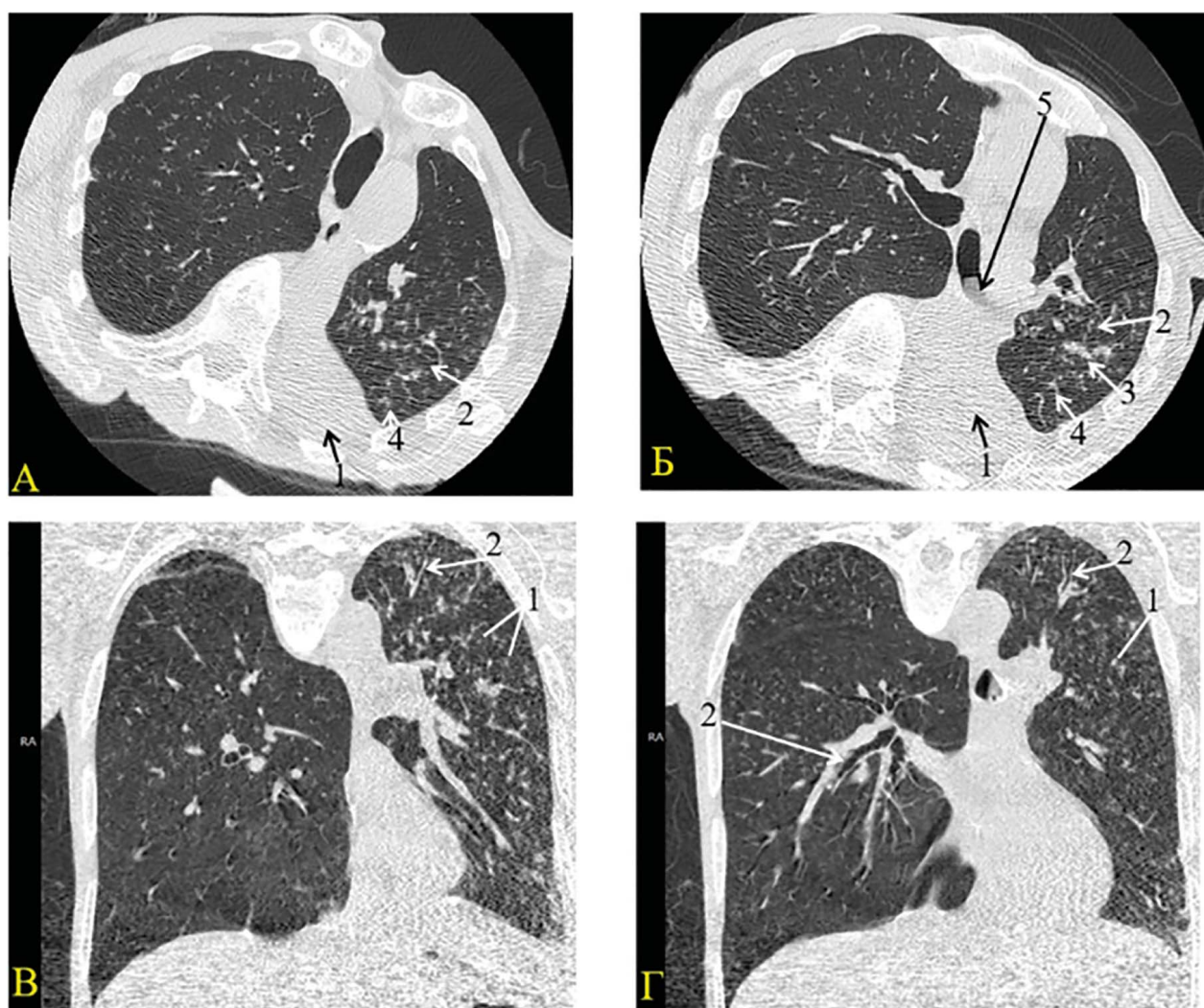


Figure 6. CT of a 59-year-old woman with aspiration bronchiolitis. The patient has left-sided spastic hemiplegia, pseudobulbar syndrome, symptomatic epilepsy as a result of an ischemic stroke

A, B. In S6 of the left lung, the focus of consolidation (1). There are centrilobular nodules of ground-glass (2), with a tendency to merge (3), more on the left, a «tree-in-bud» pattern (4). The lumen of the left main bronchus is filled with pathological contents (5).
C, D. Reconstruction in the coronary plane. Determined a decrease in the volume of the lower lobe of the left lung. In both lungs, more on the left, centrilobular nodules of ground-glass are visualized (1). The walls of the bronchi are thickened and thickened (2)

mass lesions in the neck or mediastinum, significantly facilitate differential diagnosis. It highlights the need for a thorough analysis not only of the zone of interest, but also of all the anatomical structures that are included in the visible area by the radiologist [15, 16].

Diffuse Panbronchiolitis

Diffuse panbronchiolitis is much less common than other forms of cellular bronchiolitis. Its first ("classic") cases were described among residents of Asian countries. But to date, diffuse panbronchiolitis has spread to other regions. Diffuse panbronchiolitis is a steadily progressing pathological process of cryptogenic etiology in the upper and lower respiratory tract. Apparently, there is a genetic predisposition to this disease [2].

Morphological examination revealed peribronchiolar infiltration by inflammatory cells with hyperplasia of bronchoalveolar lymphoid tissue and accumulation of foamy macrophages in interstitium and alveolar spaces [2, 9]. The only clinical signs of diffuse panbronchiolitis are chronic sinusitis, cough and gradually increased dyspnea with the development of obstructive disorders.

Early CT signs include common centrilobular nodules and "tree in buds" with predominance in the lower lobes of lungs. Later, bronchiectasis and bronchiolectasis also appear, air traps and air cysts are formed with a mosaic pattern of lung attenuation. It should be noted that *P. aeruginosa* infection is typical for this group of patients, with the pattern of starting pneumonia on CT [2, 9].

Conclusion

Using the example of three types of cellular bronchiolitis with similar patterns on CT, the importance of a multidisciplinary approach to diagnosis was demonstrated, along with the required analysis of clinical and medical history data and the results of instrumental examinations in total.

It should be remembered that bronchiolitis in adult patients often develops with pulmonary comorbidity. Therefore, analysis of results should include a thorough evaluation of all visible structures using such image post-processing methods as maximum and minimum intensity projection. Upon findings that are not typical for bronchiolitis presentation, the doctor should think about a concomitant disease in the patient, including that of extrapulmonary etiology, and should conduct a diagnostic search in this direction.

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