THE ROLE OF RADIOLOGICAL RESEARCH METHODS IN THE DIAGNOSIS OF RARE FORMS OF INTERSTITIAL LUNG DISEASES IN NEWBORNS

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ANNOTATION. Introduction. Interstitial lung diseases in newborns, associated with a diffuse disorder of lung development, represent a complex diagnostic task, since they are rare conditions, form in the early stages of embryonic development, and clinically manifest in the first hours of life as severe respiratory distress syndrome of newborns. Target. Reflect the role of radiation research methods and the difficulties of differential diagnosis of rare forms of interstitial lung diseases associated with diffuse impairment of lung development. Materials and methods. Clinical cases of congenital alveolar dysplasia and alveolar-capillary dysplasia with abnormal location of the pulmonary veins are described in detail. Data from radiological research methods, confirmed by histological studies, are presented. Results. Specific changes in interstitial lung diseases in newborns associated with diffuse impairment of lung development are not determined by radiography in the first day of life, but progressive negative dynamics are noted. Computed tomography of the lungs allows for a detailed diagnosis of structural changes in the lung parenchyma, their severity and extent. Issues of differential diagnosis of diffuse disorders of lung development in newborns are discussed; Our own results correlate with literature data. Conclusion. Currently, histological examination is the "gold standard" in the diagnosis of interstitial lung diseases associated with diffuse disorders of lung development in newborns, but is most often performed at autopsy. The role of radiation methods in the algorithmic diagnostic approach is increasing due to accumulated data and improved quality of detection and recognition of rare variants of interstitial lung diseases in newborns according to computed tomography of the chest.

Key words: congenital alveolar dysplasia, alveolar-capillary dysplasia with abnormal location of the pulmonary veins, alveolar amplification , interstitial lung diseases in children, computed tomography

Introduction. Interstitial lung diseases (ILD), associated with diffuse impairment of lung development, are a heterogeneous group of diseases that predominantly affect the alveoli and are characterized by remodeling of pulmonary structures with thickening of the alveolar-capillary membrane and interalveolar septa, and associated disturbances in pulmonary gas exchange and hypoxemia [1]. There are differences in the forms, course, histological features, and prognosis of ILD in children and adults. Children have forms of ILD that are not found in adults, such as diffuse disorders of lung development and growth, infantile neuroendocrine hyperplasia, pulmonary interstitial glycogenosis, and other disorders described in recent decades [2]. Historically, these diseases were defined based on histopathological findings at autopsy or lung biopsy. However, recent advances have facilitated the expansion of noninvasive diagnosis through the use of chest computed

tomography (CT) and genetic testing. The evaluation of children with suspected ILD often requires a multidisciplinary approach, as the clinical presentation of neonates and infants with ILD can be highly variable. For the diagnosis of nosological forms related to ILD, careful collection and meaningful analysis of anamnestic data (medical history, family history, newborn screening results, laboratory data) are of great importance. However, as is known from practical experience, recognizing ILD at the stages of primary diagnosis causes significant difficulties, since their clinical manifestations are largely similar. Cyanosis and symptoms of respiratory failure (RF), requiring transfer of the child to artificial ventilation (ALV) with various parameters, a progressive course, tachypnea is observed in 80% of patients [3, 4]. Currently, the most convenient for use is the classification of ILD in children, proposed by experts of the American Thoracic Society (ATS) in 2013 (table), based on data from a histological examination of biopsy material from 259 patients [4, 5]. Of greatest interest to us are ILDs characteristic of newborns and infants associated with diffuse disorders of lung development: congenital alveolar dysplasia (CAD), alveolar-capillary dysplasia with abnormal location of the pulmonary veins (ACD). These pathologies are interesting for their rarity in clinical practice and the associated difficulties in the algorithmic approach to their diagnosis. The authors of the article suggest that the low incidence of VAD and ACD may be associated with a low degree of detection and the fact that these pathologies are often misinterpreted as severe bronchopulmonary dysplasia (BPD) or diffuse lung disease associated with intra-amniotic infection. The difficulty of diagnosis is also due to the fact that in most cases children are born premature, some of them with low body weight, and are on mechanical ventilation for a long time in a specialized neonatal intensive care unit. Despite the fact that histological examination of the lung remains the “gold standard” for diagnosing ILD, in this review we highlight the role of radiation methods in the diagnostic search and present clinical observation data from our practice.

According to radiography performed on the first day of life, there was an uneven asymmetrical (D<S) increase in the airiness of the lung parenchyma, a diffuse increase in the pulmonary pattern with its mesh transformation (Fig. 1). On the second day of life, bilateral pneumothorax was clinically suspected and radiologically confirmed (Fig. 1, b). After installing drains in the pleural cavities on both sides, a diffuse decrease in pneumatization and an increase in the pulmonary pattern with its more pronounced mesh transformation remain (Figure 1, c). It was not possible to stabilize the child's condition. Episodes of short-term stabilization were followed by deterioration. Against the background of the course of the underlying disease, mechanical ventilation with strict parameters, the child’s condition worsened, bilateral pneumothorax increased, which required additional thoracentesis on both sides (Fig. 2). Severe refractory pulmonary hypertension continued to dominate the clinical picture. Resuscitation measures were ineffective. At the age of three days from birth, the child died. According to the official guidelines of the American Thoracic Society for the diagnosis and treatment of ILD in children, thin-section multislice computed tomography (MSCT) of the chest is recommended for newborns with diffuse lung disease syndrome in order to assess the nature and extent of changes in the lungs [4]. However, in this clinical case, due to the

rapidly deteriorating condition of the newborn and the impossibility of transporting him, MSCT was not performed. It is also known from the anamnesis that this was the second pregnancy for the woman (mother of the newborn). Earlier, from the first pregnancy, a girl was born. The condition at birth was satisfactory; she was staying with her mother. A few hours after birth, the child had diffuse cyanosis, irregular breathing, muffled heart sounds, and bradycardia. The child was intubated , transferred to mechanical ventilation, and was treated in the neonatal intensive care unit. The child's condition was extremely serious; hemodynamic support was provided with high doses of inotropes . According to cardiac ultrasound, high PH remained. On the third day of life, the child's condition worsened, bradycardia and cardiac arrest developed. Taking into account the obstetric history and similar parallels in the medical history of both siblings, the early development of PH, X-ray data of a male newborn, and, including, early death, despite the treatment measures, ILD was suspected in both newborns. Among other reasons, emphasis was placed on diffuse disorders of lung development (VAD, ADC).

Currently, approximately 200 cases of ACD have been described worldwide. Most of them are sporadic, and only in 10% of cases is the familial nature of this pathology noted with a presumed autosomal recessive mode of inheritance. In reported cases, there was a slight predominance (60%) of male neonates [8, 11]. More than 90% of affected children are born at term [12, 13], and in more than 60% of cases, cyanosis and DN appear within 48 hours after birth [14, 15]. 80% of sick newborns have concomitant anomalies of the cardiovascular system, gastrointestinal and urogenital tracts, the most common of which are hypoplasia of the left ventricle in combination with hypoplasia or coarctation of the aorta and incomplete intestinal rotation [8, 16]. Histological examination of the lung remains the gold standard for diagnosing ACD. According to published data by J. Miranda et al ., 90% of reported cases of ACD were diagnosed at autopsy, and 10% of diagnoses were made from lung tissue obtained during lung biopsy ante mortem [17, 18]. A mouse model of FOX1 deficiency was developed in Chicago in 2001 in the laboratory of Robert Costa. Homozygous FOX1-deficient mouse embryos all died 8.5 days postcoital due to pulmonary vascular abnormalities. Interestingly, of the heterozygous mice, half lived asymptomatically as normal mice, while the rest had abnormal alveolar development and died later from pulmonary hemorrhage due to severe alveolar defects and vasculogenesis [19, 21]. The histopathological changes in the mouse lungs included some, but not all, of those observed in infants with ACD. Because of this incomplete combination, the connection with the AKD was not established at that time. A chest radiograph is a standard part of the initial diagnostic evaluation of any infant with respiratory symptoms, in terms of low radiation dose, low cost, ease of performance, and availability. However, detectable changes on chest radiographs, such as heterogeneous diffuse opacification of the lung fields on both sides, with areas of swelling, as well as pneumothorax, are not specific for ACD. Additional information about the nature and distribution of the disease is obtained based on MSCT data. MSCT of the lungs is a non-invasive method that allows detailed diagnosis of structural changes in the lung parenchyma, their severity and prevalence, and is considered a more sensitive method for diagnosing various ILDs, including those associated with developmental disorders,

compared to traditional radiography. In children with ACD, MSCT usually reveals a variety of changes: bilateral diffuse areas of compaction of the lung parenchyma like "ground glass", diffuse disturbance of the architectonics with fine mesh deformation and coarse compaction of the peribronchial, perivascular and interlobar interstitium , depleted vascular pattern, pleuropulmonary adhesions and multiple areas of swelling. Interpretation of MSCT data is most often difficult due to a combination of changes characteristic of ACD, as well as the phenomena of hypoventilation , respiratory artifacts and air traps, characteristic of children who are on mechanical ventilation at the time of the study. To effectively describe MSCT findings, it is recommended to use standardized terms such as ground glass, honeycomb lung, reticular striation or cobblestone, etc., as defined in the Fleischner Society Glossary of Thoracic Imaging Terms [20]. Currently, ACD is a disease with a poor prognosis, requiring significant medical expenses and without any specific treatment. The diagnosis can be confirmed only with the help of intravital lung biopsy, and the only treatment method can be considered lung transplantation [24]. In clinical practice, attempts have been made to stabilize and treat patients with ACD with extracorporeal membrane oxygenation (ECMO), inhaled nitric oxide and exogenous surfactant therapy , and lung transplantation, but short-term improvement with inhaled nitric oxide support and the ECMO procedure does not lead to long-term improvement. survival rate with ACD [12, 22].

Thus, having similar clinical symptoms with BPD, idiopathic PH of newborns and other interstitial diseases in infants, VAD and ACD are distinguished by the early appearance of RDS, high PH and characteristic pathomorphological changes. Unfortunately, at present, intravital diagnosis of this group of diseases is still limited, and diffuse disorders of lung development are a rare and so far fatal pathology for newborns. However, according to radiological research methods, among which MSCT plays a predominant role, in combination with clinical data, it is possible to diagnose diffuse interstitial changes in the lungs and draw up a differential diagnostic series, as well as localize the area of the greatest changes to select a biopsy site. Establishing a diagnosis is important for parents of newborns with ILD, for planning subsequent pregnancies, and the legal aspect is no less important in the expert assessment of the assistance provided.

Conclusion

ILDs associated with diffuse disorders of lung development represent a heterogeneous group of diseases characterized by remodeling of pulmonary structures with the proliferation of connective tissue in the lungs. In young children, these processes occur in the developing lung, giving them unique characteristics. Histological examination of lung tissue is currently the "gold standard" for diagnosis, but is most often performed at autopsy. Due to the clinical availability of genetic testing and the improvement in the quality of detection and recognition of atypical variants of ILD in newborns according to chest MSCT, less invasive techniques should be considered to make the diagnosis of childhood ILD. Despite the high percentage of deaths that accompany ILD with diffuse impairment of lung development (congenital alveolar dysplasia, alveolar-capillary dysplasia), the diagnosis of these diseases helps not only in

treatment planning and prognosis, but can also be important in prenatal diagnosis for subsequent siblings. In connection with the accumulated data, improving the quality of detection and recognition of rare variants of ILD in newborns, MSCT of the lungs is a non-invasive method that allows detailed diagnosis of structural changes in the lung parenchyma, their severity and prevalence.

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