



FOR MEASURES UNTIL A MONTH PATHOMORPHOLOGICAL CHANGES IN LYMPH GLANDS

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Abstract

In the neonatal period, lymph nodes are not yet fully formed, the boundaries of the cortical and medullary layers are not clearly separated, and manifest with non-specific response reactions to various exogenous and endogenous infections. During this period, the density of lymphocytes in the cortical and paracortical zones in the cortical zone was low, lymphoid follicles were small in size, T-lymphocytes in the paracortical zones were few in number, and a large number of small lymphocytes that had not yet undergone antigen-independent differentiation were found, characterized by a large number of lymphoblasts.

Keywords: Neonatal period, measles, lymph nodes, pathomorphology, depletion.

Introduction

The relevance of the issue: Measles has been an integral companion of human society throughout its entire history. It is widespread everywhere, in all regions, in all climatic zones. The epidemic process of measles was characterized by high morbidity and mortality rates. A high percentage of complications and mortality from the disease causes serious economic and material damage.



In early April 2023, a sharp increase in childhood measles cases was reported in neighboring Kazakhstan. More than 70 cases of the disease have been registered in Almaty alone. After some time,

Measles cases have been officially reported in 44 regions of Russia. It was also noted that due to the fact that the areas where measles is prevalent are mainly in rural areas, it is difficult to consult a doctor in a timely manner and make a diagnosis in a timely manner. This suggests that the situation may be more complex than the official statistics suggest. The World Health Organization warned that European countries are also actively fighting the spread of measles, as 2023 figures exceeded the total number of cases in 2022. The Committee for Sanitary and Epidemiological Well-being and Public Health of Uzbekistan provided an official response to this situation, reporting that 37 cases of measles were confirmed in Uzbekistan during 2023. According to the World Health Organization, in 2021, 40 million children worldwide were excluded from routine vaccination aimed at preventing measles: 25 million children did not receive the first dose, and 14.7 million did not receive the second dose. In the valley regions, this disease is more prevalent than in other regions, and by the end of 2023, 255 patients were being treated in the Namangan region. In the 1st quarter of 2024, 1,819 patients in the Fergana region received treatment for measles at the hospital of the Republican Specialized Scientific and Practical Medical Center for the Prevention and Treatment of Measles, 10 of whom died due to severe complications.

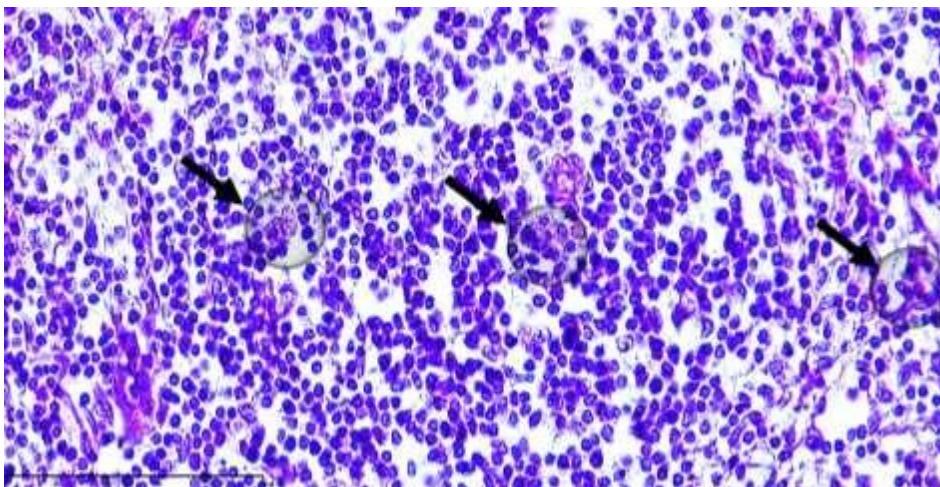
Objective of the study: Features of pathomorphological changes in the lymph nodes of the cervical region in infants who contracted and died of measles in the neonatal period.

Materials and methods of the study: 18 autopsy cases and lymph node tissue materials from those who died from measles were submitted to the Fergana Regional Bureau of Pathological Anatomy. Of these, 9 were male and 9 were female. The prepared fragments are studied morphologically.

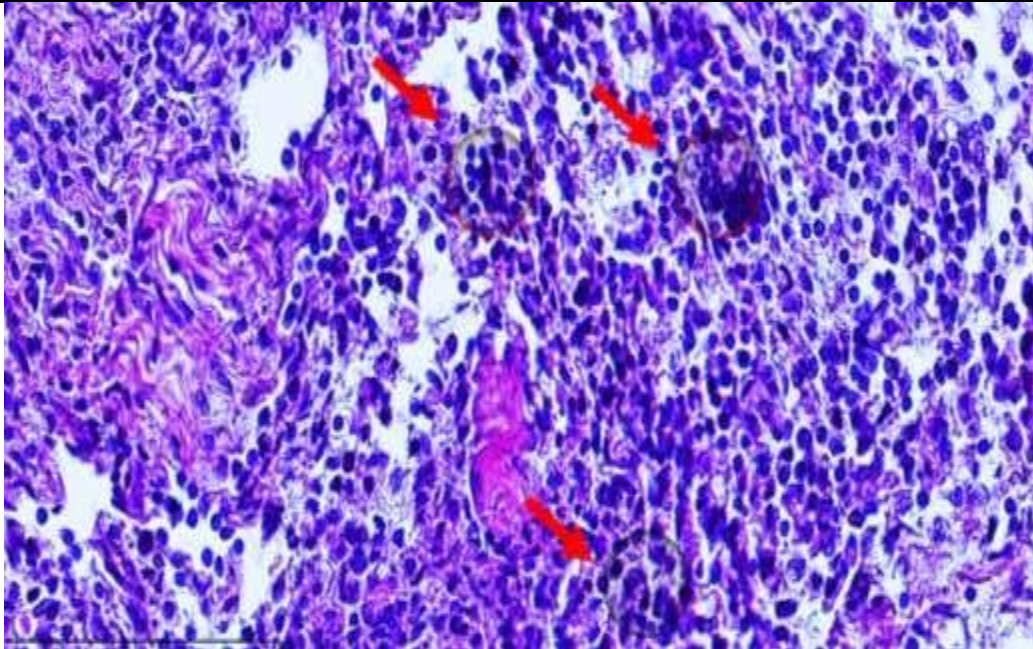
Results and discussion

From birth to 28 days, the specificity of lymph nodes is that they are still in the developmental stage. This period should also be divided into two subgroups. Period 1 - early neonatal period of 0-7 days, Period 2 - late neonatal period of 8-28 days.

1-Period In the medullary layer, a collection of cells is identified, consisting of sparse fibrous brain bands, interspersed with reticulocytes and a variable mixture of a small number of T, B lymphocytes, histiocytes, and macrophages. Dendritic and interdigitating cells are enlarged in size and are found in various locations. During this period, the absence of a response to pathogens in lymphocytes that have not undergone antigen-dependent differentiation develops as a non-specific immune response, leading to the involvement of macrophages in the process.



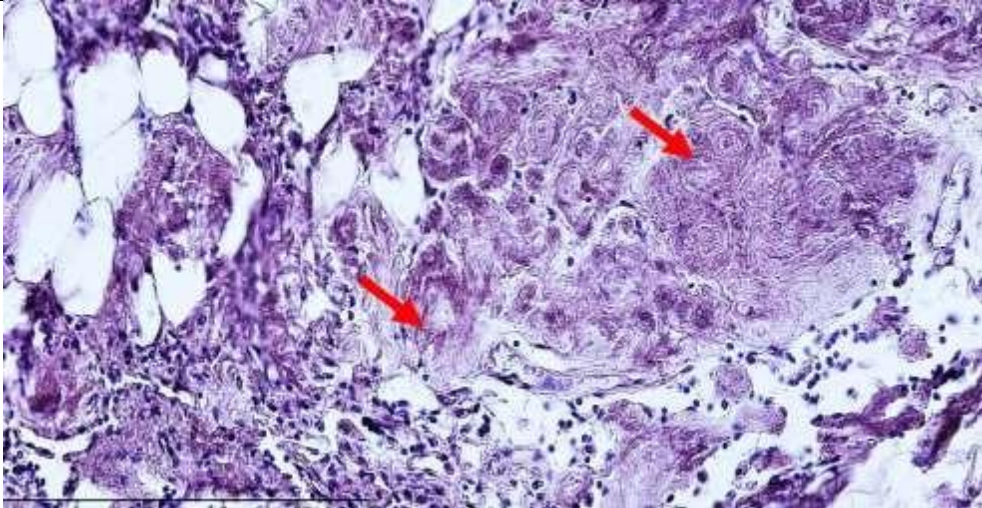
1- Image. 5-day-old infant lymph node. A low number of lymphocytes is detected in the cortical and medullary regions, as well as intermediate edema in the stroma and the development of Wharton-Frinkel cells in the region. Paint G.E. Size 10x10.



2-Image. 7-day-old infant lymph node. On the border of the cortical layer and the subcapsular zone, foci of necrosis and fibrinoid swelling are identified in the reticuloepithelial cells. Interstitial edema and progressive Wharton-Frinkendell cells are detected in the stroma. Paint G.E. Size 10x10.

The causative agent of measles is characterized by the formation of various metaplastic giant cells due to its intracellular activity and damage to macrophages. These changes are primarily characterized by accumulation around reticular bands in the paracortical, corticomedullary, and medullary regions, leading to a decrease in the number of lymphocytes.

Against a general background, the lymph node capsule is tense, there is a decrease in the number of lymphocytes in the subcapsular spaces, an increase in macrophages of various sizes in the space, and the development of signs of congestion in the capsular blood vessels. After infection, the most frequently affected and enlarged nodes are located in the cervical lymph nodes, as they enter through the upper respiratory tract.

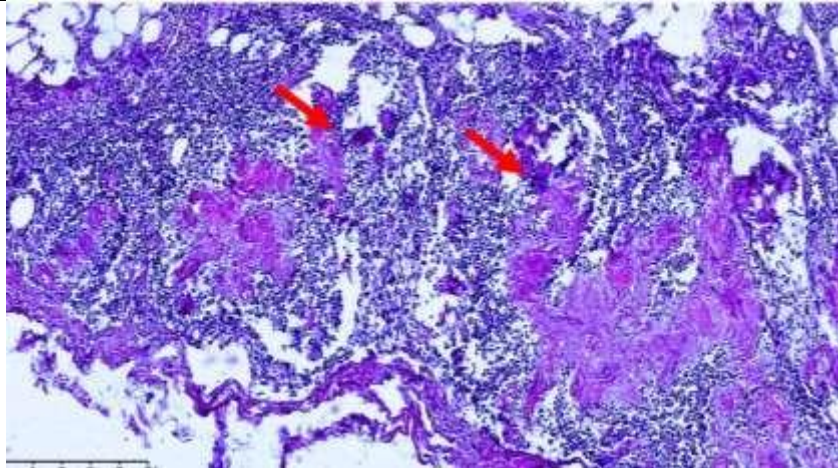


3- Image. A 4-day-old baby. In the subcapsular and cortical layers of the cervical lymph nodes, foci of necrosis and inflammation characteristic of lymphadenitis are identified. Cystic cavities are identified in the interval, which also reveals foci of stromal collapse with massive lymphocyte apoptosis. Paint G.E. Size 10x10.

Posterior and occipital lymph nodes: The swelling and significant enlargement of these nodes is one of the characteristic signs of measles. It is accompanied by inflammatory processes in the submandibular lymph nodes, oral cavity, and throat. Among the tracheobronchial and mesenteric nodes, the parabronchial and pulmonary lymph nodes also exhibit the aforementioned macroscopic signs of redness, enlargement, and other signs.

In infected lymph nodes, the subcapsular spaces of the capsule are initially dilated, macrophages and reticulocytes are abundant in the sinuses, and signs of congestion are detected in the capsule blood vessels. In the early neonatal period, as a result of infection of lymph nodes that are not yet fully formed and the inclusion of a secondary infectious factor in the process, lymphocytic infiltration and a small number of neutrophils in the capsule, and the presence of macrophages and a small number of neutrophils around the postcapillary venules in the paracortical zone, lymphadenitis developed.

means.



4- Image. Six-day-old baby. Foci of necrosis are identified in the subcapsular and cortical layers of the mesenteric lymph nodes. Small-sized multinucleated Wharton-Frinkel cells (indicated by a red arrow) are detected. Cystic cavities with lipomatosis are identified in the interval. Paint G.E. Size 10x10.

Damage to macrophages and reticuloepithelial cells in lymph nodes, the synthesis of various viral inclusions within the cells, and macrophage necrosis, leading to their proliferation in the lymph nodes and subcapsular spaces, lead to the development of necrosis in the lymph nodes. In the areas of maximum macrophage accumulation in the lymph node, there are paracortical zones, while in the brain bands and subcapsular zones, homogeneous protein substrates present with morphological features reminiscent of fibrinoid necrosis. One of the most remarkable aspects is that in measles, macrophages with necrosis and metaplasia of giant cells and reticuloepithelial cells are detected in the lymph nodes, which, in turn, leads to necrosis of these cells. This continues with the formation of secondary inflammatory foci in the lymph nodes, manifesting as secondary immunodeficiency.

In the early neonatal period, the majority of unformed cells in an incompletely formed lymph node consist of macrophages, leading to the formation of 0-

During the 7-day period, the aforementioned cells underwent necrosis, and multicellular macrophages appeared in the form of scattered, still developing, multinucleated Wharton-Frinkel cells, which were very large and contained

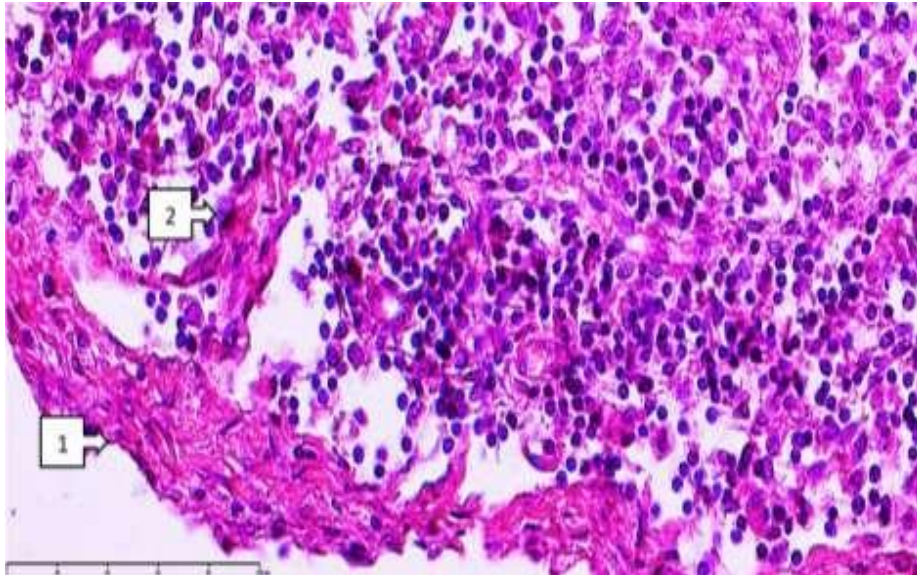


dozens of nuclei. The location of these nuclei is often determined in a variant that resembles the shape of a "grapevine" or a "mulberry" but is not yet fully formed. However, in recent years, foreign scientists have considered these cells to be characteristic not only of measles but also of HIV infection, Kimura's disease (a disease characterized by lymph node edema), systemic lupus erythematosus, and lymphomas (e.g., Hodgkin's lymphoma), one of the main features of which is that these cells are characterized by the appearance of dentritic, macrophage, and reticuloepileptic cells, and rapid apoptosis leads to the intensification of necrotic and purulent processes in the lymph nodes.

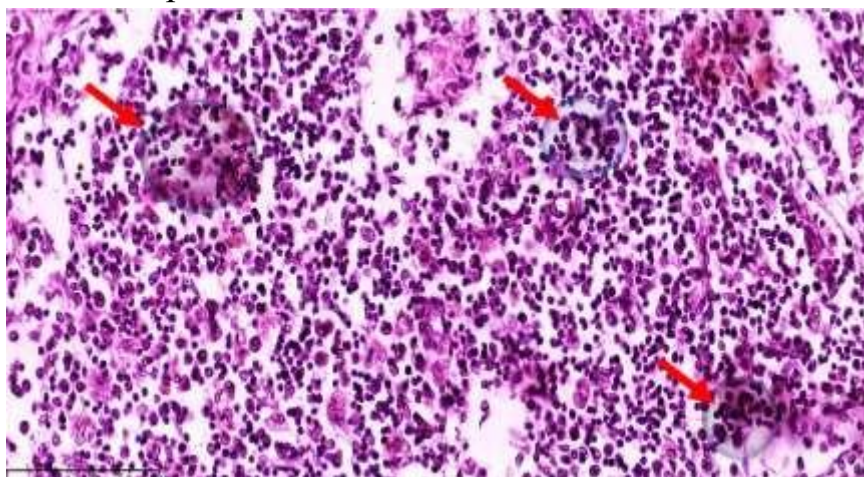
Lymphoid follicles are not yet developed, and a small number of lymphocytes in the paracortical zone indicates a high level of macrophage, dentritic cells, and reticulocyte damage, which leads to increased necrosis and apoptosis in these cells and confirms the high frequency of necrosis processes in lymph nodes.

2-during the late neonatal period, morphological maturity of lymph nodes is determined at 8-28 days compared to the 1st period, the formation of lymphoid follicles of various sizes in the cortical layer, relative maturity of T lymphocytes in the paracortical areas, and sparse fibrous connective tissue with mature brain bands is identified in the medullary layer.

Hypercellularity in the medullary layer is determined by a variable mixture of T- and B-lymphocytes, lymphoblasts, histiocytes, macrophages, and reticulocytes. The fullness of the blood vessels is preserved. The fibrous capsule of the lymph node is relatively thickened, there is fullness in the blood vessels, and the subcapsular cavities have different widths. This is due to measles the following are added to the microscopic changes. Macrophages in the lymph node capsule are characterized by varying sizes, while phagocytically active macrophages are rich in various protein inclusions in the cytoplasm.

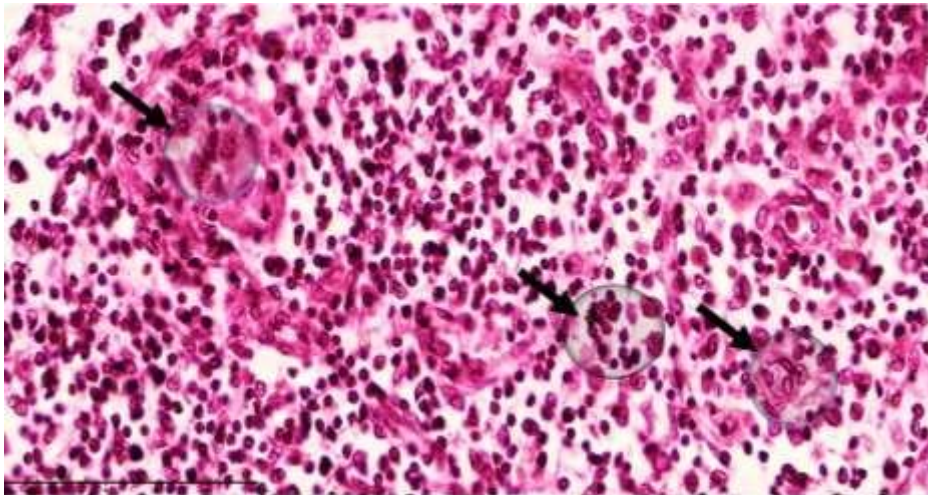


5- Image. 22-day-old baby. The lymph node capsule is thickened (1), hyperplasia of reticulocytes, foci of reticulocytosis, and massive macrophages in the interstitium (2) are identified (a phagocytically active form with cloudy cytoplasm). The subcapsular spaces are dilated, and inflammatory infiltrate is also detected in the capsule wall. Paint G.E. Size 20x10.



6- Image. 25-day-old baby. In the subcapsular zone of the lymph node, a cluster of macrophages and small lymphocytes is detected, along with multinucleated cells in the interstitium. The evolving multinucleate Wharton-

Frinkendell cells are detected. Intermediate edema and foci of reticulocytosis are detected in the stroma. Paint G.E. Size 20x10.

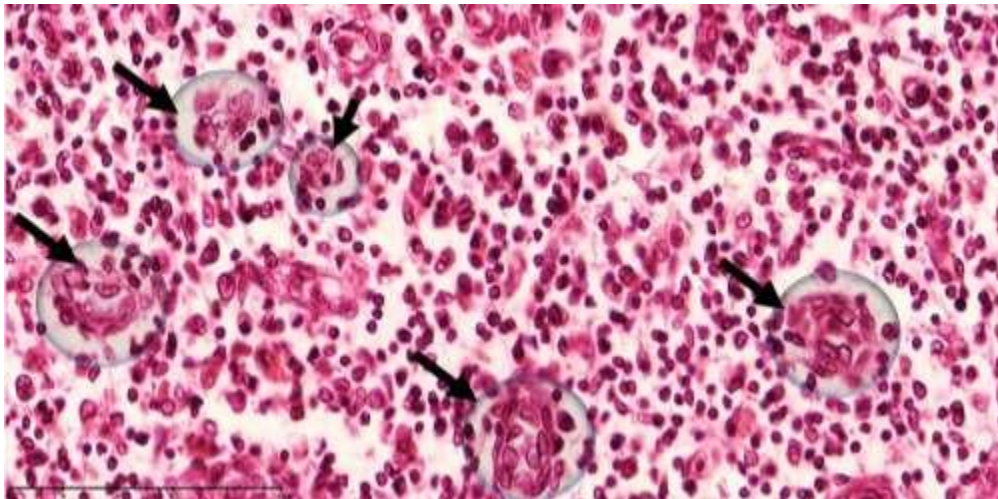


7- Image. Sixteen-day-old baby. In the interstitial cortex, sparse and rough structures are identified in the reticular structures. In reticuloepithelial cells, foci of necrobiosis and fibrinoid swelling are identified. Advanced polynuclear Wharton-Frinkendell cells are identified. Interstitial edema is detected in the stroma. Paint G.E. Size 20x10.

In the late neonatal period, high-reactivity response reactions in the lymph nodes of newborns with measles are manifested as follows: an increase in lymphocytes, primarily in the paracortical zone, and active foci of proliferation are also identified in the germinal centers of lymphoid follicles.

Measles infection in the late neonatal period is characterized by the proliferation of immunoblasts in the paracortical zone, accompanied by follicular hyperplasia. The structure of the nodule is partially altered due to a decrease in lymphocytes and a diffuse layer of immunoblasts. This gives the knot its characteristic spottiness. Among cells and between follicles, various phenotypes of Wharton-Frinkendell cells were identified, which were characterized by a scattered appearance of cells with clusters of nuclei of varying density and number.

view is determined. As a reminder, lymph node biopsy is not performed for measles; the final diagnosis is confirmed by clinical instrumental and laboratory indicators, the most up-to-date PCR analysis, and clinical signs.



8- Image. A 20-day-old baby. In the interstitial cortex, sparse and rough structures are identified within the reticular structures. Exposed light centers are detected in the stroma, indicating an intensified process of apoptosis. Advanced polynuclear Wharton-Frinkendell cells are identified. Interstitial edema is detected in the stroma. Paint G.E. Size 20x10.

In our study, it is necessary to take into account that the diagnosis of measles was confirmed and medication was administered in a medical institution, and the symptoms characteristic of measles in the lymph node are not fully formed, and even if they are formed, the picture is blurred due to necrosis of virus-carrying cells and foci of purulent necrosis developed in the lymph node. In the study, lymph nodes were taken from various areas during the autopsy of infants diagnosed with measles and who died from various secondary complications, and we do not ignore the fact that they undergo pathomorphosis.

In the stage of lymphoid follicular hyperplasia, there are predominantly irregularly located follicles that are clearly visible in the lymph nodes. In the mantle zone, the number of cells is mainly reduced, and in some places they are dead.



it could be. It is possible to identify "naked" breeding centers. In most cases, B-cell hyperplasia of the mantle zone is identified. The presence of a large number of eosinophilic stained protein structures in the lymph node stroma is determined by the presence of macrophages surrounded by residues of necrotic cell and tissue fibrous structures. This means that the proliferation of phagocytically active macrophages increases and T and B lymphocytes, which are immunocompetent cells, lead to a decrease in the number of natural killers.

The parenchyma contains giant, multinucleate cells of the Wharton-Frinkendell type, which are diffusely located within the parenchyma. Lysis of follicles develops due to the infiltration of reproductive centers with small lymphocytes, leading to their destruction. Simultaneously, due to a decrease in the number of cells in the follicles, SHIK-positive substance is accumulated. Accumulation of plasma cells is observed, intensified by follicular lysis.

The lymphocyte depletion stage manifests as a stage of follicular atrophy, a decrease in lymphocyte count, and pronounced vascular proliferation, accompanied by the "terminal stage" of lympho-denitis in measles. The follicles decrease in size, the number of lymphoid cells decreases, and they become vessels with a shell consisting of thick collagen tissue surrounded by SHIC-positive substance. Follicular atrophy can lead to hyalinization; at the same time, a decrease in lymphocytes and severe vascularization are observed in the interfollicular and parafollicular zones. In diffuse fibrosis, the number of plasma cells is high; the presence of such changes everywhere indicates terminal atrophy of the lymph nodes. This means that primary immunodeficiencies occur in the process and lead to death from complications of the secondary infectious factor.

Conclusions

In measles 0-7 days the main features in the lymph nodes of infants are the occurrence of necrosis in the lymph nodes, sharp full-bloodedness multicellular cells are identified that are not yet fully formed and have not reached their classical form. This means that the acute immune response in lymph nodes is very low.



During the 8–28 day period, enlargement of the lymph nodes, interstitial edema, hyperplasia of the lymphoid follicles, varying sizes of Wharton-Frinkendel giant cells and their maturation period, hypercellularity compared to the early neonatal period, and varying degrees of fibrosis and focal sclerosis in the capsule are identified.

This indicates that the process in the lymph node led to reorganization depending on the duration and continued with the formation of secondary lymphoid follicles in the germinal centers of the cortical layer, primarily with a large number of macrophages, reticular cells, and lymphoid follicles. At the same time, it is characterized by the development of lymphadenitis and non-tumor lymphoproliferative changes.

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