

Specific Morphological Changes of Peripheral Immunocompetent Members in Sars-Cov-2

1. Xoshimov B.L.
2. Allaberganov D. Sh

Received 2nd Mar 2022,
Accepted 3rd Apr 2022,
Online 11th May 2022

^{1,2}Tashkent Medical Academy

Annotation: Specific morphological changes of immune organs in Covid-19 depend on the general reactivity of the organism, age, sex and the degree of development of the pathological process, if the process develops chronically; many sclerotic and atrophic changes develop in immune organs. In this study, SARS-CoV-2 was characterized by the development of specific sclerotic and atrophic changes in the active areas of the spleen and lymph nodes. In particular, a decrease in lymphocytes in the T and V areas of the lymph node and in the lymphoid follicles of the spleen and a quantitative decrease in the number of T lymphocytes around the pulp arteries were studied. These morphological changes, in turn, lead to a decrease in immunocompetent cells, low local detection of T and V lymphocytes, and the development of mixed-type cellular and humoral immunodeficiency.

Key words: SARS-CoV-2, spleen, lymphocytes, lymphoid follicles, immune organs.

INTRODUCTION

Covid-19 (SARS-CoV-2) has been studied in the form of various degrees of respiratory distress syndromes. Interaction of SARS-CoV-2 with target cells leads to dysfunction of immune cells [1]. As a result, the disease manifests itself with a sharp development. As a result, necrosis of many cells is observed, and the production of many cytokines by immune cells (cytokine storm) leads to a systemic response of all vascular components [2,3,4]. These changes are clinically observed in sudden vasodilation, drop in blood pressure, development of varying degrees of shock, and eventual death in 22.8% of cases leading to SIRS [5,6]. These vasoparalytic changes are observed in the liver, heart, lungs, kidneys, and spleen. At the same time is manifested by a violation of acute perfusion of immune organs (hyperemia) and compression suppression of immune cells, a sharp suppression and deficiency of lymphoid follicular areas.

In our study, an increase in volume as a result of macroscopically developed fullness in the spleen, an increase in spleen weight by 2–2.5 times above normal, leads to compression of lymphoid follicles and compression of immunocompetent areas. Macroscopically, the appearance of many lattice structures on the surface of the blade in the cross-section of the spleen is a clear proof of our opinion. Tension of

the splenic capsule, resistance of arteries located in the cavity of the trabecular system, creating a feedback effect, an increase in intra-arterial pressure in the area of the spleen, and in response to an increase in clinical blood pressure, an increase in pulse rate. These changes, in turn, lead to an increase in systolic pressure in the cavity of all arteries in the spleen and the fullness of the pulpal artery networks. The appearance of numerous reticular structures in the splenic stroma on macroscopic examination at the expense of the resulting completeness is a clear proof of this.

Thus, the disease is clinically very severe, manifested in the form of acute circulatory disorders (at the capillary level) and poly organic insufficiency in vital organs, lungs, heart, kidneys, pancreas, adrenal glands and immune organs, high mortality, bleeding in the peak stages of the disease. In order to further increase the clinical efficacy in the restoration of circulation, the study of specific general and local morphological changes in the splenic tissue, which are considered to be immune organs in these studies, is relevant at the present time [9].

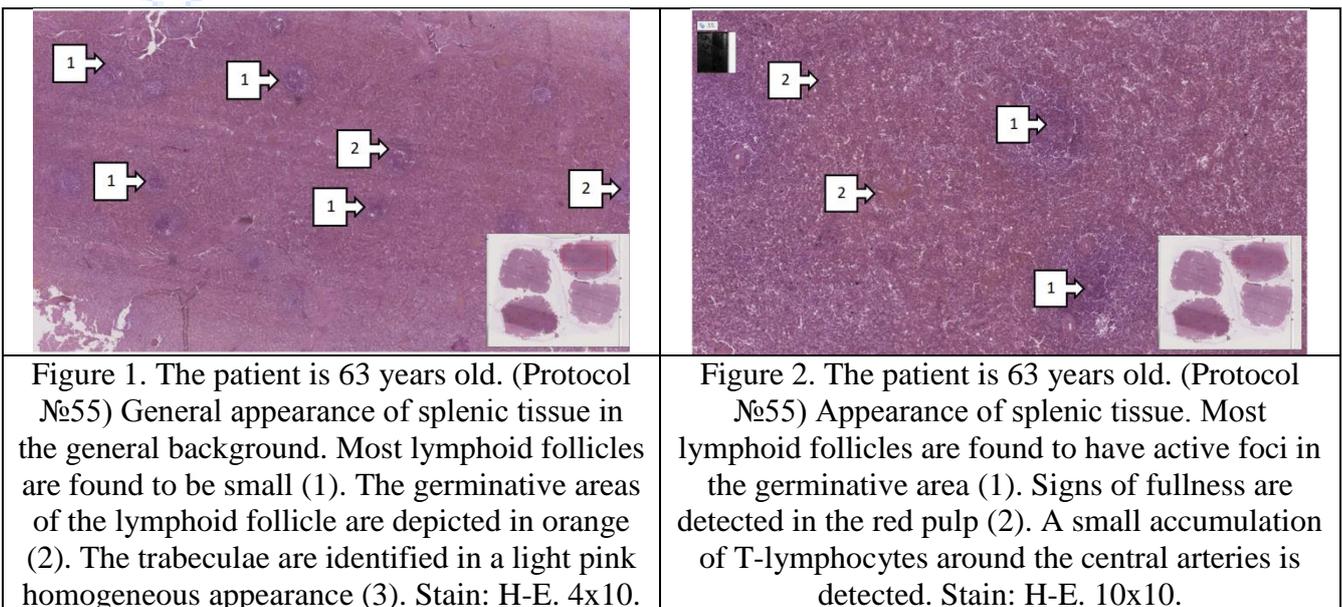
The aim of the study was to study the morphological changes in the tissue of the spleen and visceral lymph nodes isolated at autopsy of patients who died from Kovid-19 and to apply them in the development of practical recommendations.

MATERIALS AND METHODS

Spleen and lymph node tissue of those who died with the diagnosis of Covid-19 encountered in RPAC practice in 2020-2021 was studied by macroscopic, microscopic, and morphological methods. Clinical-anamnestic data were studied as a result of analysis of medical history and autopsy protocol. Histological incisions were made from paraffin bricks made from spleen and lymph node tissue obtained during autopsy and stained with hematoxylin-eosin stain. Histological preparations were examined under a binocular light microscope, and micropreparations were obtained from the required sites.

RESULTS AND DISCUSSION

The results of the study showed that changes in the spleen and lymph nodes when examined by hematoxylin-eosin staining showed a decrease in the size of lymphoid follicles, acute fullness of the pulp vessels, a decrease in lymphocytes in the T and V areas, chaotic location of lymphocytes in the cortical and paracortical areas. cystosis was manifested by the development of enlarged foci.

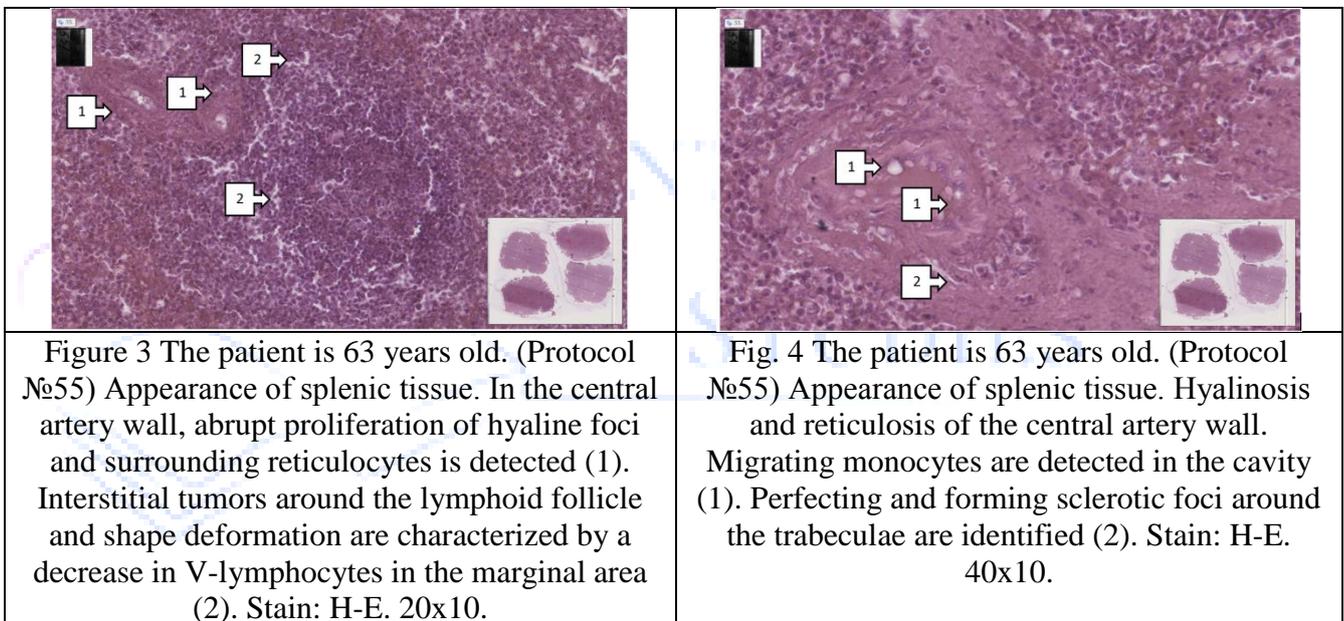


Microscopic examination of splenic tissue reveals no abrupt thickening of the spleen capsule. Hyalinosis of the wall of trabeculae growing in the splenic parenchyma, and abrupt proliferation of reticulocytes in the peritrabekular areas are detected. It is in the cavities of the central arterial network from which the trabeculae are found that the presence of blood clot, which are formed to varying degrees and recanalized, is detected.

Diapedesis foci of hemorrhage are identified as a result of the sudden filling of the capillaries arising from these vessels.

In response to secondary infections associated with SARS-CoV-2 around the central arteries, varying degrees of hyperplasia of some T-areas, many in the remaining areas, and a sharp decrease in T-lymphocytes in the T-areas are detected (Fig. 1). These morphological changes are considered to be changes resulting from comorbid diseases.

Most lymphoid follicles were found to have atrophic changes in the visual field, flattening of V-lymphocytes in the marginal area, low number of hypermutated plasma cells in the germinative area, and large accumulation of macrophages and histiocytes around them indicating a weakened immune system response (Figure 2).



In the stroma of splenic tissue, many trabecular structures are composed of coarse fibrous structures, with increased proliferative activity of reticulocytes, detected in 4/3 of patients with SARS-CoV-2, and in 4/1, fullness in the red pulp of the spleen, the formation of secondary follicles in lymphoid follicles occurs depending on age. In particular, examination of the spleen tissue of patients diagnosed with SARS-CoV-2 at the age of 25-45 years revealed the development of hyperplasia of lymphoid follicles. These changes are mainly explained by the fact that the wall structures of the central arteries, which enter through the splenic trabeculae, are not changed, hyaline and sclerotic changes are not developed. This is because the sudden accumulation of T-lymphocytes in the bare perivascular area of the central artery around the lymphoid follicles serves as a key factor for antigen-dependent lymphocyte proliferation and migration to the greater circulation through the postcapillary venules. If the patient is 50 years of age or older, a violation of wall permeability is observed as a result of hyalinosis and abrupt proliferation of reticulocytes around most arterial vessels and trabeculae in the spleen.

These morphological changes, in turn, may be the basis for the development of different degrees of cellular immunodeficiency.

Accumulation of interdigitating cells around V-lymphocytes in the paracortical area of the lymph node, abrupt proliferation of antigen-dependent lymphocytes, accumulation of CD4 + and CD5 + antigenic lymphocytes in the marginal areas of lymphoid follicles were detected. The majority of T-lymphocytes occupying the coronary trajectory around the paracortical areas have a relative decrease in antigen-dependent proliferation, enlargement of the interstitial spaces due to damage to the cellular immune system, and decreased formation of unformed CD20 +, CD25 + marker lymphocytes in these areas. The varying degrees of fullness of the postcapillary venules in the paracortical area, the defective appearance of the walls of the upper membrane endothelial cells, indicate that the migration of T-lymphocytes through the transendothelial route is paralyzed. The proliferation of pericytes around the endothelium of most postcapillary venules may be grounds for a sharp decrease in cellular immune response due to a sharp increase in sparse fibrous connective tissue components, inhibition of vascular wall permeability, and inhibition of antigen-dependent lymphocyte migration.

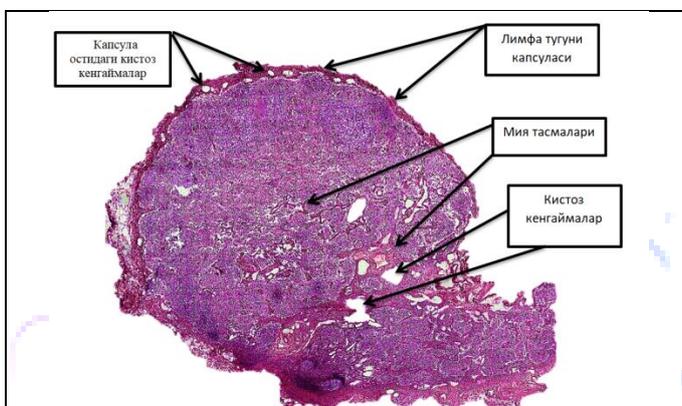


Fig. 1 The patient is 47 years old (Protocol 176 VI). Covid -19 approved. General view of the lymph node. The lymph node capsule is thicker than usual. Subcapsular cavities are almost indistinguishable. Many subcapsular cystic enlarged foci are detected. The boundaries of the cortex and paracortex are clearly defined. Many stripped pathological enlargements are detected in the area of the cerebral cortex. The stain is hematoxylin-eosin. Size 2x10.

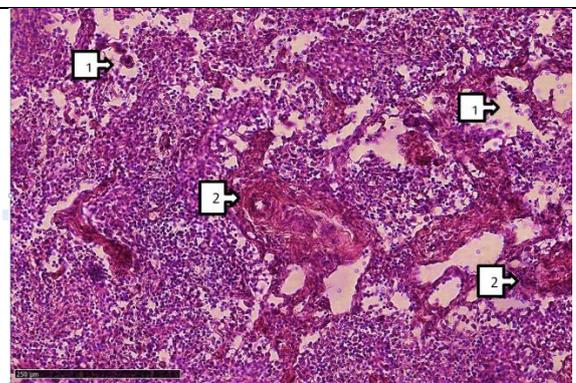


Fig 2. The patient is 47 years old (Protocol 176 VI). Acute proliferation of pericytes around the vascular wall around the cerebral cortex, sclerosis, and proliferation of reticulocytes (2). Too many cystic enlargements are detected (1). Different levels of interstitial tumors. A variable mixture of very small amounts of T and V lymphocytes is detected around the cerebral cortex. Stain: Hematoxylin-eosin. Size 10x10.

At the same time it was found that abrupt stripping of the lymph node around the cerebral cortex of the lymph nodes, the parenchyma of the lymph node, decreased proliferation of lymphocytes, impaired feedback continue with the development of reticulosis (Fig. 2). As a result, the accumulation of many metaplastically altered macrophages in the area of the cerebral cortex was detected. Reticulocytosis and interstitial edema have been found to lead to macroscopic deformation of the lymph nodes and clinically non-palpation of the lymph nodes, in some cases leading to swelling of the lymph nodes.

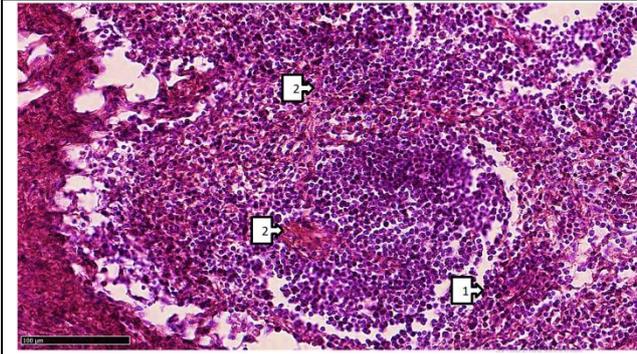


Fig. 3 The patient is 47 years old (Protocol 176 VI). Proliferation and accumulation of V-lymphocytes in the marginal areas of the lymphoid follicle were detected (1). Most of the reddish-pink reticular structures are found to have developed sclerotic changes in the stroma (2). The stain is hematoxylin-eosin. Size 10x10.

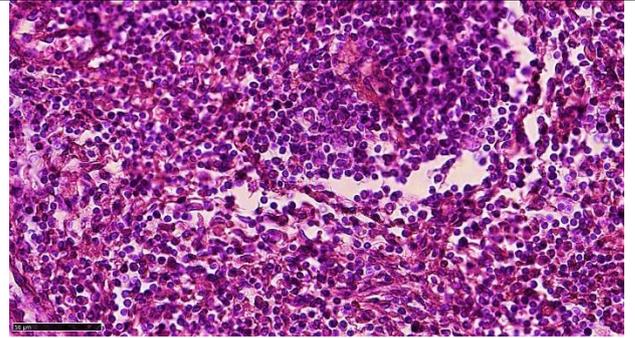


Fig. 4 The patient is 47 years old (Protocol 176 VI). On a larger scale, most lymphocytes are found to be about the same size. The enlargement of the interstitial spaces, the sharp development of the process of reticulocytosis and histiocytosis are detected by the inhibition of the migration of most lymphocytes (indicated by arrows). The stain is hematoxylin-eosin. Size 10x40

Lymph node reticulosis in the area of the cerebral cortex leads to a shift of the vascular network to the periphery and a relative blockage of lymph fluid movement, and stagnation in the cerebral cortex and lymph node portal area and the appearance of cystic enlarged foci on histological examination. When these foci are measured morphometrically, it is found that most are 45–75 μm in size. Normally, cystic enlargements of this size are not detected in the lymph node in the cerebral cortex (Figures 3 and 4). This, in turn, has been found to be the basis for our conclusion based on these changes that impaired lymph dynamics leads to clinical lung cancer.

CONCLUSION

Thus, in conclusion, morphological changes in splenic tissue, which are considered immune organs of patients with SARS-CoV-2, are mainly determined by the fullness of pulp vessels, diapedesis bleeding around the central arteries and proliferation of many macrophages and reticulocytes in the stroma. Hyperplasia of lymphoid follicles is of varying degrees, mainly explained by a sharp decrease in the structures of the V-area marginal area, the presence of weak secondary lymphoid follicles formed in the generative area. In T-site lymphocytes in patients aged 50 years and older, there is a decrease in T-lymphocytes in the spleen, sclerosis and hyalinosis of the central arteries, impaired intravascular migration of T-lymphocytes from the perivascular area through the postcapillary venules and the development of various levels of cellular immunological found its proof in investigations. Acute proliferation of macrophages and reticulocytes around lymphocytes in the T-field, increased proliferative activity of connective cells from the lymph node stroma-vascular structures, thickening of the vessel wall, disruption of T-lymphocyte migration from the postcapillary venules (microangiostclerosis), followed by intravenous lymphatic fluid dynamics the appearance of expanded foci was detected. Clinically, these changes are characterized by acute deficiency of cellular components of the immune system and the addition of secondary infectious factors, paralysis of lymphatic drainage function in vital organs, mainly the formation of mixed-type lung tumors (nocardogenic and lymphostasis) in lung tissue.

LIST OF REFERENCES

1. Fedorov D.N., Korosteleva P.A., Zybin D.I., Popov M.A., Tyurina V.M., Varlamov A.V. Morphological and immunohistochemically characteristics of changes in the lymphatic system of the bronchopulmonary group in patients with new coronavirus infection COVID-19 (according to the results of autopsy studies). *Almanac of Clinical Medicine*. 2020; 48: pp. 37-42.
2. Semenov V.M., Pashinskaya E.S., Pobyarjin V.V., Subbotina I.A., Shlyaxunov E.A., Veremey I.S., Semenov S.V. Immunohistochemical and molecular-genetic methods of diagnostics of oncological diseases *Bulletin of Vitebsk State Medical University*, 2017, Tom 16, №2 pp.15-25
3. Morphological diagnostics of lymphatic pathology // Wright D., Eddis B., Leong E. Moscow, Meditsinskaya literatura, 2008, 176 p.
4. Park WB, Kwon NJ, Choi SJ, Kang CK, Choe PG, Kim JY, Yun J, Lee GW, Seong MW, Kim NJ, Seo JS, Oh MD. Virus Isolation from the First Patient with SARS-CoV-2 in Korea. *J Korean Med Sci*. 2020;35(7): p. 84.
5. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, Schiergens TS, Herrler G, Wu NH, Nitsche A, Müller MA, Drosten C, Pöhlmann S. SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. *Cell*. 2020;181(2):271–80.
6. Wang K, Chen W, Zhou YS, Lian JQ, Zhang Z, Du P, Gong L, Zhang Y, Cui HY, Geng JJ, Wang B, Sun XX, Wang CF, Yang X. SARS-CoV-2 invades host cells via a novel route: CD147-spike protein [Internet].
7. Walls A C, Park YJ, Tortorici MA, Wall A, McGuire AT, Veesler D. Structure, Function, and Antigenicity of the SARS-CoV-2 Spike Glycoprotein. *Cell*. 2020;181(2):281–p.92.
8. Perrella A, Trama U, Bernardi FF, Russo G, Monastra L, Frangranza F, Orlando V, Co. Brancatella A, Ricci D, Viola N, et al. Subacute thyroiditis after SARS-CoV-2 infection. *J. Clin Endocrinol Metab*. 2020;105(7): p. 276.
9. Stafford V V. Use of an immunohistochemical method in diagnostics. *RJOAS*. 2016 Aug;8(56): pp. 18-21.