УДК [61+615.1] (06)
ББК 5+52.81
А 43
ISBN 978-985-21-1865-1

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МОРФОЛОГИЧЕСКИЕ ИЗМЕНЕНИЯ ПРИ САХАРНОМ ДИАБЕТЕ У ПАЦИЕНТОВ CCOVID-19

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MORPHOLOGICAL CHANGES IN DIABETES MELLITUS IN COVID-19 PATIENTS

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Резюме. COVID-19, вызванный SARS-CoV-2, непропорционально поражает людей с диабетом 2 типа (СД2), ухудшая уже имеющиеся метаболические и сосудистые проблемы. В этом исследовании изучаются морфологические аномалии, наблюдаемые у пациентов с диабетом и COVID-19, с акцентом на микрососудистый тромбоз, иммунологическую дисрегуляцию и органоспецифическое повреждение.

Ключевые слова: COVID-19, сахарный диабет 2 типа, микротромбы, IRF5 путь.

Resume. COVID-19, caused by SARS-CoV-2, disproportionately affects individuals with type 2 diabetes (T2D), worsening pre-existing metabolic and vascular issues. This study investigates the morphological abnormalities observed in diabetic COVID-19 patients, with an emphasis on microvascular thrombosis, immunological dysregulation, and organ-specific damage.

Keywords: COVID-19, type 2 diabetes, microthrombi, IRF5 pathway.

Relevance. The global impact of COVID-19 is disproportionately severe in patients with T2D, who face higher risks of thrombosis, organ failure, and mortality. Understanding the morphological changes in these patients is essential for improving clinical outcomes and developing targeted interventions.

Aim: to analyze the morphological and immunological alterations in diabetic COVID-19 patients and elucidate their pathophysiological mechanisms.

Objectives:

1. Investigate the prevalence and distribution of microthrombi in key organs (lungs, kidneys, liver, heart).
2. Examine the histological features of pulmonary, renal, hepatic, and cardiac damage in diabetic COVID-19 patients.
3. Explore the role of IRF5-driven inflammatory pathways in exacerbating disease severity.

Material and methods. This study reviewed autopsy findings and immunophenotypic data from diabetic COVID-19 patients. Histological analysis included H&E staining of lungs, kidney, liver, and heart tissues. Flow cytometry was used to assess immune cell populations (monocytes, lymphocytes) in peripheral blood.

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Results and their Discussion.

1. **Pulmonary Pathology:**

The lungs of diabetic COVID-19 patients suffered extensive harm, with diffuse alveolar damage (DAD) in all cases. The histological investigation revealed hyaline membranes, desquamated pneumocytes, and hyperplastic alveolar epithelium (Fig.1).

Microthrombi were seen in alveolar capillaries and small vessels in 75% of patients, which contributed to pulmonary infarctions and respiratory failure (Fig. 2). These findings indicate that pre-existing endothelial dysfunction in diabetes exacerbates SARS-CoV-2-induced lung injury.

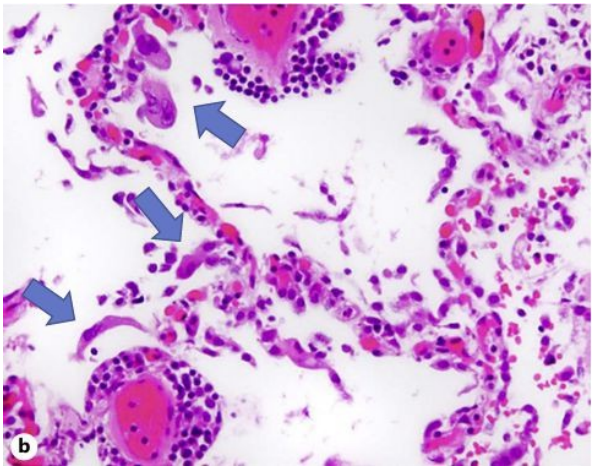

Fig. 1 – Enlarged, atypical pneumocytes with large nuclei in intra-alveolar spaces (arrows). H&E staining. ×400

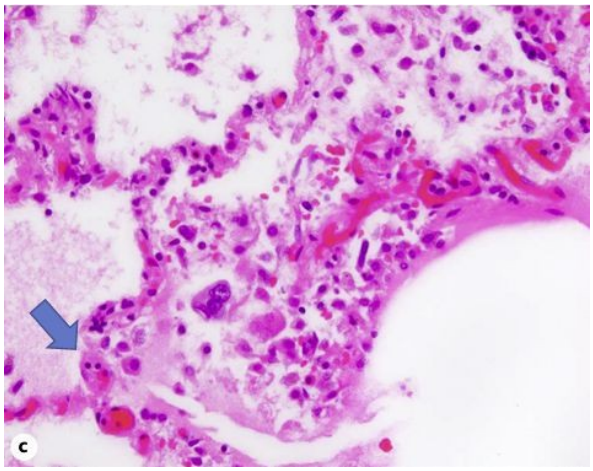

Fig. 2 – Microthrombi in intra-alveolar septa. H&E staining. ×400

2. **Renal Pathology:**

Acute tubular injury (ATI) was a common observation in the kidneys, frequently accompanied by glomerular microthrombi. Patients with pre-existing diabetic nephropathy had impaired renal function, most likely due to ischemia injury from microvascular thrombosis. These alterations illustrate the combined impact of COVID-19 and diabetes on renal pathophysiology.

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3. **Hepatic Changes:**

The liver revealed macro- and microvesicular steatosis, centrilobular congestion, and localized necrosis. Microthrombi were seen being present in hepatic sinusoids, further impairing liver function. These findings are consistent with the recognized metabolic stress caused by both diabetes and COVID-19.

4. **Cardiac Involvement:**

Myocardial fibrosis, which is scarring caused by microthrombi and chronic infarction, and microthrombi in small coronary vessels were found in the cardiac tissue (Fig. 3). Occasional cases of myocarditis were noted, implying direct viral injury or immune-mediated damage. The presence of microthrombi emphasizes the increased thrombotic risk in diabetic COVID-19 patients.

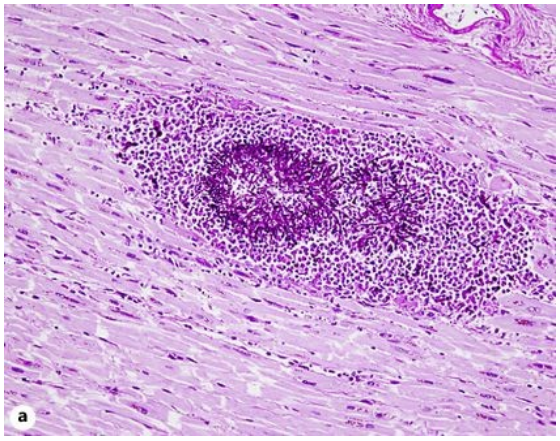

Fig. 3 – Myocardial microabscesses in myocardium. H&E staining. ×200.

5. **Immunological Dysfunction:**

The flow cytometry indicated monocytopenia, including the loss of $CD14^{+}$ classical monocytes and enlarged monocytes (FSC-Hi), indicative of aberrant activation (Fig.4). Elevated levels of IL-6, IL-8, and CCL2 were detected, linked to IRF5-induced hyperinflammatory response connected to cytokine storm (Fig. 5). These immunological changes have been linked to increased disease severity and poor outcomes.

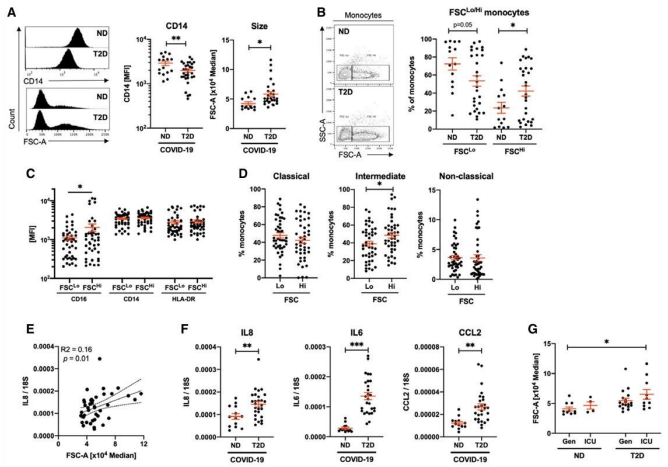

Fig. 4 – Morphologically altered monocytes in type 2 diabetic COVID-19 patients are associated with an aberrant inflammatory response and increased disease severity

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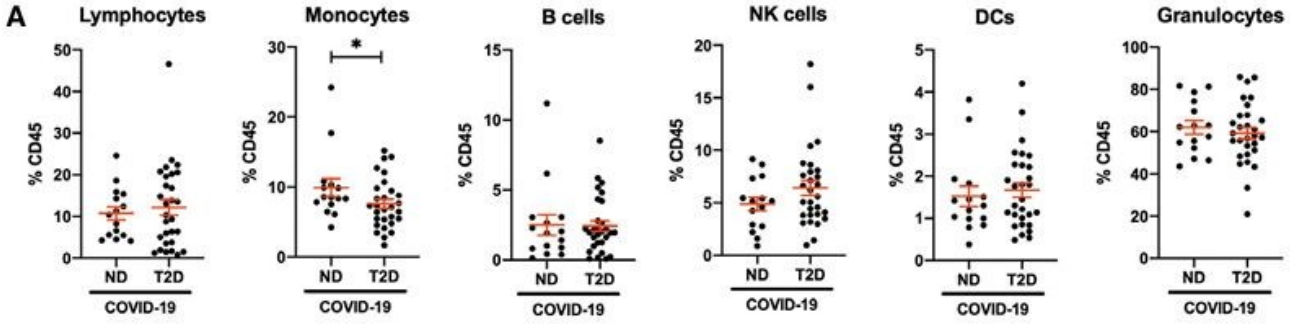

Fig. 5 – Flow cytometric quantification of lymphocytes, monocytes, B cells, natural killer (NK) cells, dendritic cells (DCs) and granulocytes in peripheral venous blood samples from non-diabetic (ND) and type 2 diabetic (T2D) patients with COVID-19

Conclusion:

1. Diabetic COVID-19 patients exhibit severe microvascular thrombosis and organ damage due to synergistic endothelial dysfunction and hyperinflammation.

2. Autopsy findings highlight lungs, heart, and kidney as primary targets of SARS-CoV-2 in diabetics.

3. IRF5-driven immune dysregulation exacerbates disease severity, highlighting potential therapeutic targets.

4. Further research is needed to explore SARS-CoV-2's impact on pancreatic islets and new onset diabetes. In addition to developing targeted therapeutics for immune dysregulation in diabetic COVID-19 patients

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