

On the issue of post COVID-19 condition in patients with rheumatic diseases

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Actual problems of rheumatology include the possibility of developing a wide range of long-term consequences of COVID-19, so-called post-COVID syndrome (PCS). The results of our own research are presented, during which among 45 patients over 18 years with rheumatic diseases (RD) PCS was detected in 20% cases: 6 of them had ANCA-associated vasculitis (AAV) and one each for rheumatoid arthritis, juvenile arthritis and osteoarthritis. In AAV cases PCS was more severe and varied than in other RD: lung lesions according to computed tomography (up to the damage 75% of the lung parenchyma), skin and nervous (Guillain – Barré syndrome) lesions, myalgias, arthralgias were present. In most patients PCS ended in recovery, sudden death occurred only in the patient with AAV. The frequency of RD's relapses in patients with PCS was 9%. Relapses were not noted in AAV, against the background of anti-B cell therapy with rituximab.

Our own results and literature data indicate that patients with RD after COVID-19 need careful continuous monitoring to detect long-term complications of coronavirus infection and early diagnosis of relapses of the underlying disease.

Key words: post-COVID syndrome, long-COVID, COVID-19, coronavirus disease 2019, rheumatic diseases, ANCA-associated vasculitis

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К ВОПРОСУ ПОЗДНИХ ОСЛОЖНЕНИЙ COVID-19 У ПАЦИЕНТОВ С РЕВМАТИЧЕСКИМИ ЗАБОЛЕВАНИЯМИ

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Среди актуальных проблем ревматологии рассматривается возможность развития широкого спектра отдаленных последствий COVID-19, так называемого постковидного синдрома (ПКС). Представлены результаты собственного исследования, в ходе которого среди 45 пациентов старше 18 лет с различными ревматическими заболеваниями (РЗ) ПКС выявлен в 20% случаев (6 пациентов с АНЦА-ассоциированным системным васкулитом (АНЦА-СВ), 1 – с ревматоидным артритом, 1 – с ювенильным артритом, 1 – с остеоартритом). ПКС при АНЦА-СВ протекал тяжелее и многообразнее, чем при других РЗ: чаще отмечались изменения легких по данным компьютерной томографии (вплоть до поражения 75% легочной паренхимы), присутствовали миалгии, артралгии, выявлены случаи поражения кожи и нервной системы (синдром Гийена – Барре). В большинстве случаев ПКС закончился выздоровлением, у одного пациента с АНЦА-СВ наступила внезапная сердечно-сосудистая смерть. Частота рецидивов РЗ у пациентов с ПКС составила 9%, при АНЦА-СВ на фоне анти-В-клеточной терапии ритуксимабом рецидивы не отмечены. Собственные результаты и данные литературы свидетельствуют о том, что пациенты с РЗ, перенесшие COVID-19, требуют тщательного продолжительного мониторинга для выявления отдаленных осложнений коронавирусной инфекции и ранней диагностики рецидива основного заболевания.

Ключевые слова: постковидный синдром, лонг-ковид, COVID-19, коронавирусная болезнь 2019, ревматические заболевания, АНЦА-ассоциированные системные васкулиты

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Over the last year, the Journal «Rheumatology Science and Practice» has widely discussed the issues of coronavirus disease 2019 (coronavirus disease 2019; COVID-19) in patients with rheumatic diseases (RD) [1, 2]. One of the problems is the possibility of developing wide clinical spectrum of long-term consequences COVID-19 (so-called post-COVID syndrome, PCS), including vessels' thrombosis of various sizes and types, avascular necrosis of bones, dermatological and musculo-articular symptoms, etc [3–6]. Although are of interest the classifications developed by C. Fernandez-de-Las Penas et al. and R. Becker [7, 8], today a generally accepted definition and a unified nomenclature of PCS has not been formulated.

We would like to bring further evidence regarding this point by providing data from our own study, the purpose of which was estimate the prevalence of PCS in patients with RD over 18 years of age and to characterize the features of its clinical course. A telephone/online survey of COVID-19 patients with rheumatic diseases has been conducted to detect lung and other organ damage 40 days or more after the coronavirus infection. If it necessary, additional examination was carried out. The inclusion criterion was the laboratory confirmation of SARS-CoV-2 virus and/or undoubted data of chest computed tomography (CT) and/or hospitalization in COVID-19 hospitals. Our group

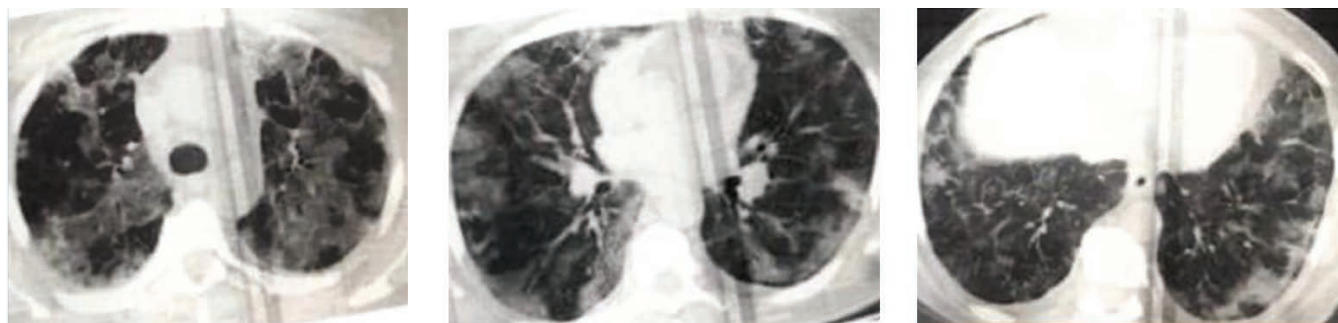


Fig. 1. Lung changes on CT scan in patient 69-year-old with GPA in remission in GPA 90 days after COVID-19 onset

included 45 patients: 24 had ANCA-associated vasculitis (AAV), 10 – systemic sclerosis, 3 – rheumatoid arthritis (RA), 2 – polymyalgia rheumatic (PMR), 1 – systemic lupus erythematosus (with antiphospholipid syndrome) and 4 – osteoarthritis. The study was focused on somatic pathology, psychiatric disorders have not been studied.

Long-term complications of COVID-19 (which are classified as PCS) have been detected in 9 (20%) patients: 6 of them had AAV (3 – granulomatosis with polyangiitis (GPA); 2 – with eosinophilic granulomatosis with polyangiitis (EGPA); 1 – with microscopic polyangiitis (MPA)) and one each for RA, juvenile arthritis and osteoarthritis. Median age was 41 (20–69) years, 78% women. In all cases there was no detected activity of the main disease, and other infections were excluded. In 5 patients with AAV (2 – GPA, 2 – EGPA, 1 – MPA) long-term consequences of COVID-19 included lung involvement (changes on CT scan with 25–75% damage of lung parenchyma noted 70–150 days after acute COVID-19; 5/5 – ground-glass opacity, 2/5 – fibrosis; fig. 1). All patients with lung injury underwent hospital examination and treatment methylprednisolone 8–24 mg per day with subsequent positive dynamics or complete resolution of changes according to CT data. On 42 day after the onset of COVID-19 one patient with MPA and lung involvement (CT 45% damage with frosted glass symptom) developed a clinical presentation of Guillain-Barré syndrome, the protein content in the cerebrospinal fluid was 0.46 g/L. After the addition of high doses of intravenous human immunoglobulin against the background of a decrease in the dose of methylprednisolone, recovery was achieved with CT normalization and complete reverse development of neurological symptoms. Two cases of dermatological manifestations developed in one GPA with severe dermatitis by type toxicoderma (60 days after COVID-19) and in one osteoarthritis with itchy epithemic rash on the legs. Three patients had myalgias (1 – GPA, 1 – EGPA, 1 – RA). Also detected cases of headache (with juvenile arthritis), anosmia and sleep disturbance (RA), arthralgia (EGPA). Hypersensitivity pneumonitis development cannot be excluded in two patients with EGPA, considering the polypharmacy.

In most patients, PCS ended in recovery. Sudden death occurred 6 months later only in the patient with GPA without a history of heart disease against the background of anticoagulant therapy's withdrawal, prescribed during the period of coronavirus infection. The frequency of RD's relapses in PCS patients was 9% (2 – RA and 2 – PMR, one of them with developing clinics of giant cell arthritis). Relapses were



Fig. 2. Dermatitis in patient 59-year-old with GPA in remission 60 days after COVID-19 onset

not noted in AAV, against the background of anti-B-cell therapy with rituximab.

PCS in cases of AAV was more severe and varied than in other RD: bilateral lung lesions involving 45–75% of the lung parenchyma, skin and nervous (Guillain – Barré syndrome) lesions, myalgias, arthralgias were present. The features of AAV are a high frequency of lesions of the respiratory organs, generalized necrotizing lesions of small vessels of various organs and systems, pathologically associated with immune-mediated activation of neutrophils [9]. Severe COVID-19 is characterized by endothelitis, pathological activation of neutrophils, activation of the alternative/leptin pathway of the complement system, autoantibody production, and the phenomenon of immunothrombosis, which is also characteristic of immunoinflammatory RD [1, 10, 11]. The proximity of the pathogenetic mechanisms of COVID-19 and immunoinflammatory RD, primarily AAV, may contribute to the development of long-term consequences of COVID-19 [1]. It should be noted that recently reports of a possible connection between the development of AAV and vaccination against coronavirus were appeared [12].

In addition to PCS, it is necessary to discuss the possibility of RD's relapses against the background of drug withdrawal during COVID-19. In our own group, relapses were noted in two patients with PMR and two with RA. However, among patients with AAV, who received anti-B-cell therapy with rituximab, relapses were not observed. These data underline the high efficacy of B-cell depletion therapy in AAV.

Thereby, our observations and literature data indicate that patients with immunoinflammatory RD, primarily AAV, after COVID-19 (or after coronavirus vaccination) need careful continuous monitoring to detect long-term complications of coronavirus infection and early diagnosis of relapses of the underlying disease.

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