https://doi.org/10.18093/0869-0189-2020-30-5-709-714

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An unusual course of COVID-19 infection with late increase in C-reactive protein (clinical case reports)

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Abstract

Clinical signs of COVID-19 infection are non-specific and diagnosis is typically based on comprehensive evaluation of the patient's history, clinical status, radiological and laboratory findings. A common finding in COVID-19 patients is increased C-reactive protein (CRP), though in some patients, CRP remains within normal range notwithstanding the presence of other criteria of severe disease. We describe two clinical cases of COVID-19 with severe bilateral pneumonia and late increase in CRP. Similar cases re quite challenging for making the diagnosis and indicating the antiinflammatory therapy.

Key words: COVID-19, C-reactive protein, "cytokine storm", coronavirus infection.

Conflict of interests. The authors declare the absence of conflict of interests.

For citation: Chikina S.Yu., Brovko M.Yu., Royuk V.V., Avdeev S.N. An unusual course of COVID-19 infection with late increase in C-reactive protein (clinical case reports). *Pul'monologiya*. 2020; 30 (5): 709–714 (in Russian). DOI: 10.18093/0869-0189-2020-30-5-709-714

Нетипичное течение новой коронавирусной инфекции COVID-19 с поздним повышением уровня С-реактивного белка (клинические наблюдения)

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Резюме

Клинические проявления COVID-19 неспецифичны, при этом основу диагностики составляет комплексная оценка данных. Одним из характерных лабораторных признаков, отражающих тяжесть течения COVID-19, является повышение уровня С-реактивного белка (СРБ). Однако в некоторых случаях уровень СРБ в течение длительного времени может оставаться в пределах нормальных значений, несмотря на присутствие других признаков тяжелого течения заболевания. В статье представлены два клинических наблюдения тяжелого течения двусторонней пневмонии, ассоциированной с COVID-19, у пациентов с поздним повышением уровня СРБ. Такие больные могут представлять определенные трудности при оценке тяжести течения и подборе патогенетической терапии.

Ключевые слова: COVID-19, С-реактивный белок, «цитокиновый шторм», коронавирусная инфекция.

Конфликт интересов. Авторы заявляют об отсутствии конфликта интересов.

Для цитирования: Чикина С.Ю., Бровко М.Ю., Роюк В.В., Авдеев С.Н. Нетипичное течение новой коронавирусной инфекции COVID-19 с поздним повышением уровня С-реактивного белка (клинические наблюдения). *Пульмонология*. 2020; 30 (5): 709–714. DOI: 10.18093/0869-0189-2020-30-5-709-714

The novel coronavirus infection COVID-19 has been investigated worldwide since December 2019. The disease is caused by SARS-CoV-2 virus. Clinical signs of COVID-19 infection are non-specific and the diagnosis is typically based on the comprehensive evaluation of clinical, laboratory, and CT findings. One of the most typical laboratory signs of COVID-19 is increased level of C-reactive protein (CRP). According to international data, CRP strongly correlates with severity of the disease, the extension of lung injury based on CT findings, prognosis and progression of COVID-19 [1–4]. CRP is produced by the liver and, according to *G.Ponti et al.*, CRP can be associated with systemic angiitis in COVID-19 patients [1]. Other laboratory markers of the disease are lymphopenia [5, 6] that can reflect immune defense abnormalities [6]; thrombocytopenia associated with disseminated intravascular coagulation [5, 6]; increased D-dimer related to coagulation activation [5, 6]; and increased serum interleukin-6 (IL-6) and ferritin reflecting the severity of systemic inflammation. Excessive release of various cytokines, such as IL-6, IL-1β, IL-18, interferon gamma, and tumour necrosis factor-alpha, is called as "cytokine storm". The key markers of "cytokine storm" in real clinical practice are CRP and ferritin [1, 7]. CRP is increased in 75 – 93% of COVID-19 patients in the first days of the disease [8] and is used by physicians as one of the most significant markers of the disease severity [9]. Nevertheless, CRP can grow more slowly in some COVID-19 patients and remains within the normal range for a long time despite the presence of other signs of severe course of COVID-19. Thus, physicians could be chal-

lenged while assessing the disease severity and choosing the therapy for such patients. We describe two clinical cases of COVID-19 with late CRP increase.

Case 1

32-year old male who lived in Moscow was admitted to a hospital on the 4th of May, 2020, with fever for past 5 days, diarrhea and vomiting for past 3 days. At home, the patient took paracetamol and aspirin. Previously, he had a history of gastroesophageal reflux disease, pollinosis (allergic rhinitis and allergic conjunctivitis during birch pollution) and angioedema after eating nuts. The patient is a current smoker of hookan quite daily during past 3 or 4 years; he was not exposed to other hazards. He did not have the history of drug intolerance. The patient did not have a close contact to anyone infected by SARS-CoV-2 virus during the previous two weeks.

At presentation, he was febrile to 38.3 °C. Vital signs at the time of presentation revealed normal respiratory rate (RR, 18/min), mild tachycardia (heart rate, 90/min), normal blood pressure (BP, 130/80 mm Hg), normal oxygen saturation (SpO_2, 95%) at the room air; no peripheral oedema, no cyanosis. Lung auscultation was not performed.

Initial laboratory data showed lymphopenia (0.92×10^9/L) with normal white cell (WBC) count (5.79×10^9/L); moderately increased aspartate aminotransferase (AST) and alanine aminotransferase (ALT) to 62 and 84 U/L, respectively; and moderately increased creatinine (133 μmol/L). The baseline CRP was 2 mg/L. Chest computed tomography (CT) demonstrated bilateral multifocal, mostly bronchocentric ground glass opacities; an overall right lung involvement score was < 25 %; an overall left lung involvement score was 25 to 50% (CT-2 [9]) (Figure 1A). Nasal and oropharyngeal smears for SARS-CoV-2 virus were positive.

The initial therapy included mefloquine (7 days, the standard regimen), oral azithromycin 500 mg daily, oral lopinavir/ritonavir 400/100 mg daily, paracetamol, fraxiparine 0.4 mg daily. The fever remained at 38.5 °C. On day 3 of admission, the diarrhoea worsened and a sharp increase in hepatic transaminases (AST, 233 U/L; ALT, 234 U/L; gamma-glutamyl transpeptidase (GGT), 112 U/L) and lactate dehydrogenase (LDH) (up to 1,069 U/L) was revealed. By this reason, azithromycin, mefloquine, and ritonavir/lopinavir were withdrawn. From day 5 of admission (day 10 from disease onset), the temperature decreased to 37.5 °C, but hypoxia occurred with the decrease in SpO_2 to 94 – 91% at room air. Supplemental oxygen therapy was initiated via nasal prongs followed by a face mask because the oxygen flow gradually increased to 8 – 10 L/min. Dexamethasone 24 mg/day i.v. was added. Repeated chest CT (day 10 after disease onset) showed further extension of ground glass opacities and the appearance of consolidation areas in both lungs. The total lung involvement increased to 50 – 75% for each lung (Figure 1B).

CRP remained low during first 12 days of the disease (1.9 – 5.27 mg/L) and increased to 42.7 mg/L by day 13. Serum ferritin remained normal as well (127 – 166 μg/L; normal value is > 200 μg/L). IL-6 was measured on day 13 and was 2.5 times higher than normal (15.4 pg/mL; normal value is > 6 pg/mL).

On day 13 of admission, the low-grade fever remains; the patient had mild respiratory failure (SpO_2 80 – 84% at room air with the increase to 96% when using supplemental oxygen 6 L/min via a face mask).

Considering the respiratory failure, slow but progressive increase in CRP level and the liver damage with unsuccessful treatment with previous drugs including systemic steroids, sarilumab (human anti-IL-6R monoclonal IgG1 antibody) 200 mg was administered. This was followed by a rapid decrease in CRP to 10 – 16 mg/L and in the body temperature to 36.4 °C. SpO_2 improved until after the physical rehabilitation was started. To day 21 of the disease, SpO_2 reached 92% at room air and the supplemental oxygen flow was reduced to 3 L/min via nasal prongs. The changes in key markers of systemic inflammation, such as CRP, fibrinogen, IL-6, and lymphocytes, were shown in Figure 2. AST, ALT, GGT and LDH reduced gradually, but were still increased at the patient's discharge from the hospital.

The patient was discharged on day 20 of hospitalisation (day 25 from disease onset) with normal body temperature and SpO_2 of 95% at room air. Chest CT follow-up in a month after the discharge showed mild ground glass opacities and no consolidation (Figure 1C).

Case 2

39-year old male who lived in Moscow was admitted to a hospital on the 30th of April, 2020, on day 6 of disease onset with fever (39 °C), diarrhea, and sore throat. The initial treatment before admission with hydroxychloroquine 200 mg b.i.d. and azithro-

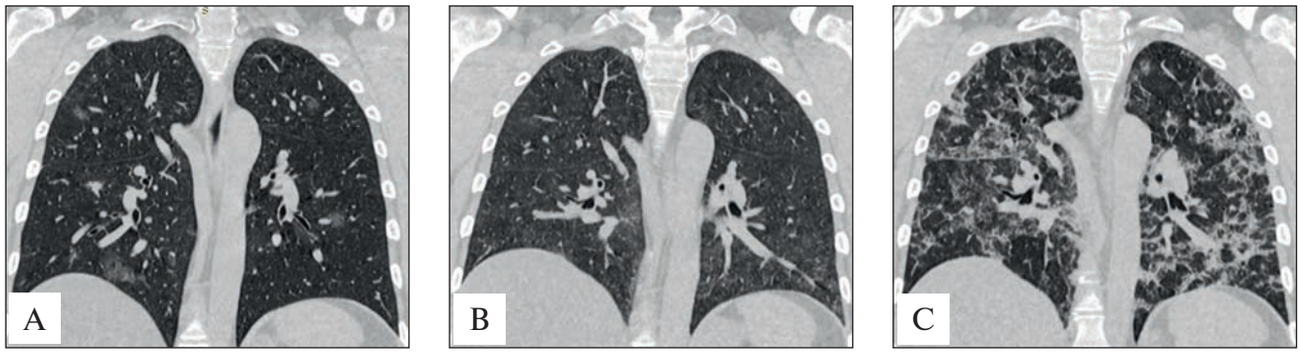

Figure 1. Computer tomogram of the patient's lungs (clinical observation No.1): A, on the 5th day from the onset of the disease (upon admission to the hospital); B, on the 22nd day from the onset of the disease (upon discharge from the hospital); C, 1 month after discharge from hospital

Рис. 1. Компьютерная томограмма легких больного (клиническое наблюдение № 1): А – на 5-е сутки от начала заболевания (при поступлении в стационар); В – на 22-е сутки от начала заболевания (при выписке из стационара); С – через 1 мес. после выписки из стационара

mycin 500 mg q.d. was unsuccessful. The patient did not have previous chronic diseases or hazardous exposure. No history of allergic reactions or drug intolerance.

At admission, the patient was febrile to 38.7 °C. He was overweight with body mass index of 30.9 kg/m^2. Vital signs at the time of admission revealed normal RR (19/min), moderate tachycardia (heart rate, 101 beats/min) and slightly decreased BP (108/66 mm Hg). SpO_2 was 96% at room air at rest. No peripheral oedema and no cyanosis were found. Lung auscultation was not performed.

Laboratory data at baseline showed low WBC (3.1 × 10^9/L), lymphopenia 0.7 × 10^9/L, and mild thrombocytopenia (118 × 10^9/L). CRP was increased to 32 mg/L. Liver transaminases were within normal ranges. Chest CT at baseline showed multiple bilateral diffusive ground glass opacities with reticular changes. The overall lung involvement was 25 to 50% in both lungs (CT-2 [9]). Nasal and oropharyngeal smears for SARS-CoV-2 were positive.

Therapy with lopinavir/ritonavir 800/200 mg/day, interferon-β-1b, and enoxaparin was started at admission. Hydroxychloroquine 400 mg/day was continued. On day 4 after admission, the patient was still febrile with the body temperature of 39 °C and SpO_2 fell to 92% at room air. CRP grew from 32 to 48 mg/L. Supplemental oxygen 6 L/min was initiated via nasal prongs resulting in the SpO_2 improvement to 96%.

On day 5 of hospitalisation (day 11 of disease), the fever became low-grade, but dyspnea worsened. SpO_2 reduced to 87 – 88% at room air. This required to increase the oxygen flow up to 10 L/min with improvement in SpO_2 to 91 – 92%. CRP continued growing to 82 – 113 mg/L. Leukopenia and lymphopenia worsened to 2.9 × 10^9/L and 0.34 × 10^9/L, respectively. There was an increase in LDH to 1,253 U/L, AST to 244 U/L, ALT to 552 U/L, total bilirubin to 21.8 μmol/L, and fibrinogen to 5.73 g/L (the normal value is < 4.00 g/L). Chest CT demonstrated further extension of ground glass opacities to 50 – 75% in each lung corresponding to CT-3.

The patient was transferred to intensive care unit (ICU) on day 5 of hospitalisation (day 11 of disease onset) for non-invasive ventilation (NIV) with CPAP mode (10 cm H_2O, FiO_2 50%). Given the growing CRP, progressive respiratory failure and liver damage, tocilizumab 480 mg was administered i.v.; the dose of enoxaparin was increased to 0.8 mL b.i.d.; lopinavir/ritonavir and hydroxychloroquine were withdrawn.

The temperature dropped to 37.4 °C several hours after tocilizumab infusion and became normal a day later. CRP reduced to 47 mg/L in the next day after tocilizumab infusion with further decrease to 8 – 5 – 2 mg/L. NIV allowed to keep SpO_2 at 95 – 96%. Liver transaminases also reduced, but had not reached the normal level to the time of the patient's discharge from the hospital (Figure 2).

On day 8 of hospitalisation, the patient was weaned from NIV to supplemental oxygen 10 L/min via a face mask and was transferred from ICU to a general ward. The patient was discharged on day 19 of hospitalisation after clinical and laboratory stability was achieved. Chest CT at the end of hospitalisation showed linear and patchy consolidation; the overall right lung involvement reduced to 25% and the overall left lung involvement reduced to 25 – 50% compared to the baseline; this corresponded to CT-2 [9].

Discussion

Clinical cases of COVID-19 with severe bilateral pneumonia were described in this article. A particular feature of these cases was late increase in CRP. The respiratory failure worsened together with CRP growth.

Development of "cytokine storm" requires administration of monoclonal antibodies against ILs or IL receptors. Clinically, these drugs should be used in patients with significant lung injury (50 – 75%) and at least two of the following signs: low SpO_2, CRP as high as > 60 mg/L or 3-fold growth in CRP on days 8 – 14 of disease; fever of > 38 °C during 5 days, WBC < 3.0 × 10^9/L, blood lymphocyte count < 1 × 10^9 /L and/or < 15% [9]. However, physicians are often guided by CRP level and underestimate these clinical criteria.

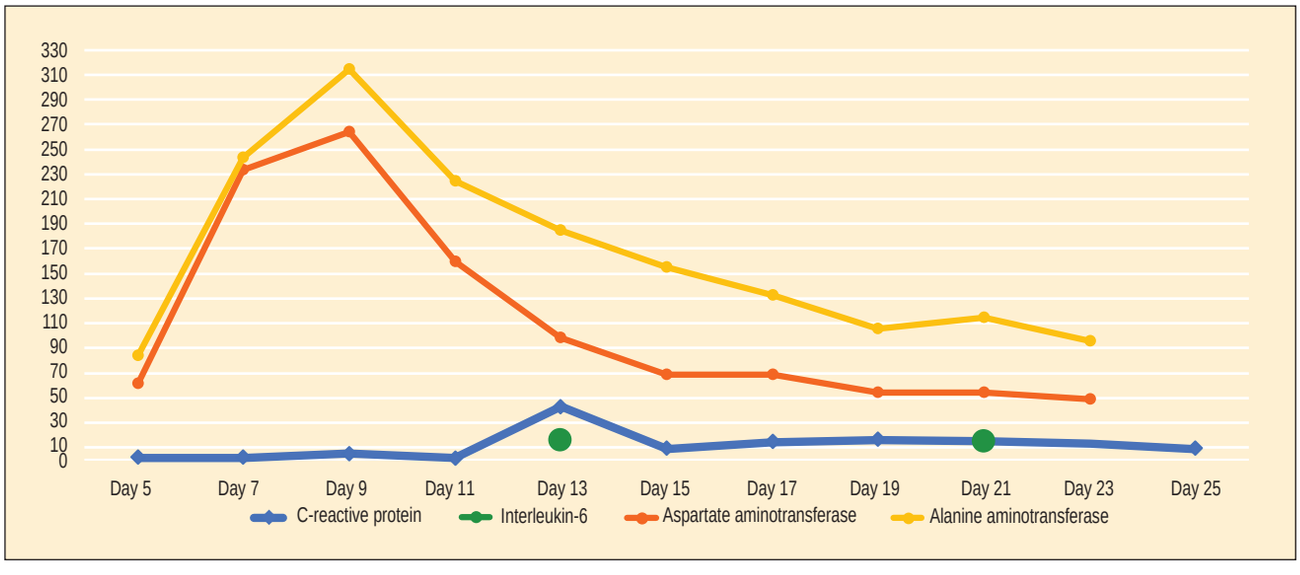

Figure 2. Dynamics of the main laboratory parameters (clinical observation No.1)

Рис. 2. Основные лабораторные показатели в динамике (клиническое наблюдение № 1)

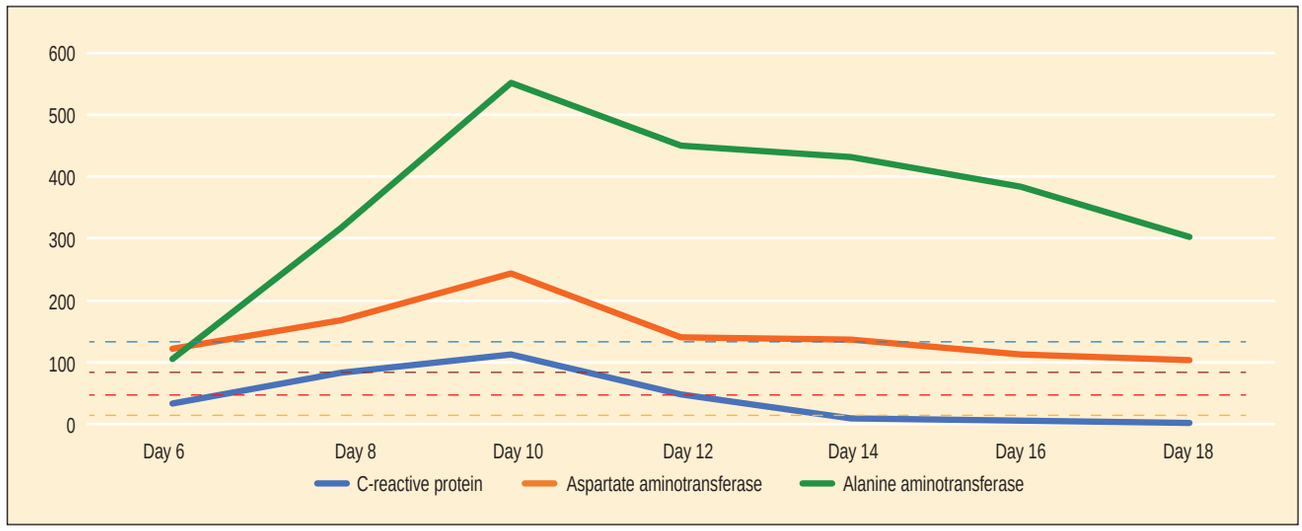

Figure 3. Dynamics of the main laboratory parameters (clinical observation No.2)
Рис. 3. Основные лабораторные показатели в динамике (клиническое наблюдение № 2)

Both patients described were febrile and had low blood lymphocyte count. The patient 2 had also low WBC count. However, the lung involvement in both patients was not extensive enough to suspect the "cytokine storm". When the lung involvement enlarged, the fever, another important clinical sign of "cytokine storm", surprisingly reduced to low-grade level.

In patient 1, CRP has not reached the threshold of 60 mg/L during all the course of the disease and 3-fold growth was found on day 13 only (from 5.27 to 42.7 mg/L). Dexamethasone did not impact significantly on the clinical presentation. In patient 2, CRP exceeded 60 mg/L to day 11 of disease only and 3-fold increase in CRP level occurred much more later (Figure 3).

Therefore, "cytokine storm" is not always associated with contemporary CRP growth to high values in real clinical practice. The measurement of another marker of "cytokine storm", IL-6, is not available everywhere.

Of note, both patients had significantly increased liver transaminases. A rise of liver transaminases could be seen in 20 – 35% of COVID-19 patients; this could reflect acute liver injury associated with COVID-19 [10–12]. Liver damage can be caused by SARS-CoV-2 virus itself that binds to angiotension-converting enzyme (ACE II) receptor in order to enter an epithelial cell. ACE II receptors are expressed on epithelial cells of bile ducts in hepatic tissue and, to a lesser extent, on hepatocytes [10, 11]. An increase in liver transaminases was demonstrated to correlate directly with COVID-19 severity [10, 12]. On the other hand the majority of drugs used to treat the novel coronavirus infection COVID-19, such as ritonavir/lopinavir and hydroxychloroquine, can damage the liver. Both patients received aminoquinolines (mefloquine or hydroxychloroquine) and lopinavir/ritonavir from day 1 of admission. Therefore, it is hard to say whether the increase in transaminases level was associated with COVID-19 severity (in this case, high AST and ALT, similarly to CRP, are features of disease severity) or with drug-induced liver injury. The former thesis is supported by the fact that the liver transaminases begun rising three days after the therapy was started and remained at a high level for 2 – 3 weeks after drugs had been withdrawn.

CRP is produced in the liver [1], therefore, It could be assumed that virus-induced liver damage could dysregulate synthetic liver function followed by lowering CRP level. However, some authors report that an increase in liver transaminases was associated with more severe systemic inflammation in COVID-19 [13, 14]. *Q.Cai et al.* found that hospitalized COVID-19 patients are at higher risk of drug-induced liver injury, primarily due to use of lopinavir/ritonavir which increases this risk in 4 times [15]. Many authors describe a direct association between the increase in liver transaminases and the severity of COVID-19 [13, 15, 16].

Conclusion

In conclusion, COVID-19 patients with higher liver transaminase level should be considered as patients with potentially severe course of COVID-19, even if CRP is normal or slightly increased. We suppose that increased liver transaminases in a patient with chest CT typical for COVID-19 and long-lasting fever should be considered as an indication for administration of anti-IL monoclonal antibodies.

References

1. Ponti G., Maccaferri M., Ruini C. et al. Biomarkers associated with COVID-19 disease progression. *Crit. Rev. Clin. Lab. Sci.* 2020; 57 (6): 389–399. DOI: 10.1080/ 10408363. 2020.1770685.
2. Tan C., Huang Y., Shi F. et a. C-reactive protein correlates with computed tomographic findings and predicts severe COVID-19 early. *J. Med. Virol.* 2020; 92 (7): 856–862. DOI: 10.1002/jmv.25871.
3. Gao Y., Li T., Han M. et al. Diagnostic utility of clinical laboratory data determinations for patients with the severe

COVID-19. *J. Med. Virol.* 2020; 92 (7): 791–796. DOI: 10.1002/jmv.25770.
4. Liu F., Li L., Da Xu M. et al. Prognostic value of interleukin-6, C-reactive protein, and procalcitonin in patients with COVID-19. *J. Clin. Virol.* 2020; 127: 104370. DOI: 10.1016/j.jcv.2020.104370.
5. Sorayaa G.V., Ulhaq Z.S. Crucial laboratory parameters in COVID-19 diagnosis and prognosis: An updated meta-analysis. *Med Clin (Barc.)*. 2020; 155 (4): 143–151. DOI: 10.1016/j.medcli.2020.05.017.
6. Frater J.L., Zini G., d'Onofrio G. et al. COVID-19 and the clinical hematology laboratory. *Int. J. Lab. Hematol.* 2020; 42 (1): 11–18. DOI: 10.1111/ijlh.13229.
7. McGonagle D., Sharif K., O'Regan A. et al. COVID-19 induced pneumonia and macrophage activation syndrome-like disease. *Autoimmun. Rev*. 2020; 19 (6): 102537. DOI: 10.1016/j.autrev.2020.102537.
8. Lippi G., Plebani M. Laboratory abnormalities in patients with COVID-2019 infection. *Clin. Chem. Lab. Med*. 2020; 58 (7): 1131–1134. DOI: 10.1515/cclm-2020-0198.
9. Ministry of Health of the Russian Federation. [Temporary guidelines: Prevention, diagnosis and treatment of new coronavirus infection (COVID-19). Version 7 (03.06.2020)]. Available at: *https://static-0.rosminzdrav.ru/system/attachments/attaches/000/050/584/original/03062020_%D0%9CR_COVID-19_v7.pdf* (in Russian).
10. Xie H., Zhao J., Lian N. et al. Clinical characteristics of non-ICU hospitalized patients with coronavirus disease 2019 and liver injury: A retrospective study. *Liver Int.* 2020; 40 (6): 1321–1326. DOI: 10.1111/liv.14449.
11. Zhang Ch., Shi L., Wang F.Sh. Liver injury in COVID-19: management and challenges. *Lancet Gastroenterol. Hepatol.* 2020; 5 (5): 428–430. DOI: 10.1016/S2468-1253(20)30057-1.
12. Agarwal A., Chen A., Ravindran N. et al. gastrointestinal and liver manifestations of COVID-19. *J. Clin. Exp. Hepatol.* 2020; 10 (3): 263–265. DOI: 10.1016/j.jceh.2020.03.001.
13. Fan Zh., Chen L., Li J. et al. Clinical features of COVID-19-related liver functional abnormality. *Clin. Gastroenterol. Hepatol.* 2020; 18 (7): 1561–1566. DOI: 10.1016/j.cgh.2020.04.002.
14. Duan P., Chen Y., Zhang J. et al. Clinical characteristics and mechanism of liver injury in patients with severe acute respiratory syndrome. *Zhonghua Gan Zang Bing Za Zhi.* 2003; 11: 493–496.
15. Cai Q., Huang D., Yu H. et al. COVID-19: Abnormal liver function tests. *J. Hepatol.* 2020; 73 (3): 566–574. DOI: 10.1016/j.jhep.2020.04.006.
16. Garrido I., Liberal R., Macedo G. Review article: COVID-19 and liver disease-what we know on 1st May 2020. *Aliment. Pharmacol. Ther.* 2020; 52 (2): 267–275. DOI: 10.1111/apt.15813.

Received: August 03, 2020

Литература

1. Ponti G., Maccaferri M., Ruini C. et al. Biomarkers associated with COVID-19 disease progression. *Crit. Rev. Clin. Lab. Sci*. 2020; 57 (6): 389–399. DOI: 10.1080/ 10408363.2020.1770685.
2. Tan C., Huang Y., Shi F. et a. C-reactive protein correlates with computed tomographic findings and predicts severe COVID-19 early. *J. Med. Virol.* 2020; 92 (7): 856–862. DOI: 10.1002/jmv.25871.
3. Gao Y., Li T., Han M. et al. Diagnostic utility of clinical laboratory data determinations for patients with the severe COVID-19. *J. Med. Virol*. 2020; 92 (7): 791–796. DOI: 10.1002/jmv.25770.
4. Liu F., Li L., Da Xu M. et al. Prognostic value of interleukin-6, C-reactive protein, and procalcitonin in patients with COVID-19. *J. Clin. Virol.* 2020; 127: 104370. DOI: 10.1016/j.jcv.2020.104370.
5. Sorayaa G.V., Ulhaq Z.S. Crucial laboratory parameters in COVID-19 diagnosis and prognosis: An updated meta-analysis. *Med Clin (Barc.)*. 2020; 155 (4): 143–151. DOI: 10.1016/j.medcli.2020.05.017.
6. Frater J.L., Zini G., d'Onofrio G. et al. COVID-19 and the clinical hematology laboratory. *Int. J. Lab. Hematol.* 2020; 42 (1): 11–18. DOI: 10.1111/ijlh.13229.
7. McGonagle D., Sharif K., O'Regan A. et al. COVID-19 induced pneumonia and macrophage activation syndrome-like disease. *Autoimmun. Rev*. 2020; 19 (6): 102537. DOI: 10.1016/j.autrev.2020.102537.
8. Lippi G., Plebani M. Laboratory abnormalities in patients with COVID-2019 infection. *Clin. Chem. Lab. Med*. 2020; 58 (7): 1131–1134. DOI: 10.1515/cclm-2020-0198.
9. Министерство здравоохранения Российской Федерации. Временные методические рекомендации: Профилактика, диагностика и лечение новой коронавирусной инфекции (COVID-19). Версия 7 (03.06.2020). Доступно на: *https://static-0.rosminzdrav.ru/system/attachments/attaches/000/050/584/original/03062020_%D0%9CR_COVID-19_v7.pdf*
10. Xie H., Zhao J., Lian N. et al. Clinical characteristics of non-ICU hospitalized patients with coronavirus disease 2019 and liver injury: A retrospective study. *Liver Int.* 2020; 40 (6): 1321–1326. DOI: 10.1111/liv.14449.
11. Zhang Ch., Shi L., Wang F.Sh. Liver injury in COVID-19: management and challenges. *Lancet Gastroenterol. Hepatol.* 2020; 5 (5): 428–430. DOI: 10.1016/S2468-1253(20)30057-1.
12. Agarwal A., Chen A., Ravindran N. et al. gastrointestinal and liver manifestations of COVID-19. *J. Clin. Exp. Hepatol.* 2020; 10 (3): 263–265. DOI: 10.1016/j.jceh.2020.03.001.
13. Fan Zh., Chen L., Li J. et al. Clinical features of COVID-19-related liver functional abnormality. *Clin. Gastroenterol. Hepatol.* 2020; 18 (7): 1561–1566. DOI: 10.1016/j.cgh.2020.04.002.
14. Duan P., Chen Y., Zhang J. et al. Clinical characteristics and mechanism of liver injury in patients with severe acute respiratory syndrome. *Zhonghua Gan Zang Bing Za Zhi.* 2003; 11: 493–496.
15. Cai Q., Huang D., Yu H. et al. COVID-19: Abnormal liver function tests. *J. Hepatol.* 2020; 73 (3): 566–574. DOI: 10.1016/j.jhep.2020.04.006.
16. Garrido I., Liberal R., Macedo G. Review article: COVID-19 and liver disease-what we know on 1st May 2020. *Aliment. Pharmacol. Ther.* 2020; 52 (2): 267–275. DOI: 10.1111/apt.15813.

Поступила 03.08.2020

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