CORRESPONDENCE

Letters to the Editor

The Characteristics of 50 Hospitalized COVID-19 Patients With and Without ARDS

by Michael Dreher, Alexander Kersten, Johannes Bickenbach, Paul Balfanz, Bojan Hartmann, Christian Cornelissen, Ayham Daher, Robert Stöhr, Michael Kleines, Sebastian W. Lemmen, Jörg Christian Brokmann, Tobias Müller, Dirk Müller-Wieland, Gernot Marx, and Nikolaus Marx in issue 16/2020

Liver Involvement

In the article (1), we noticed that significant differences were reported between patients with acute respiratory distress syndrome (ARDS) and those with non-ARDS for laboratory parameters such as CRP, IL-6, LDH, CK, and D-dimer, but that no increases in serum levels of liver function markers and/or of liver function impairment were observed. However, a number of scientific studies have already shown that, in the context of COVID-19, liver can be involved in 16%–53% of cases, especially if there is a severe SARS-CoV-2 infection (2, 3). For a large number of these cases, only an asymptomatic increase in transaminases, but no significant increase in bilirubin or liver function impairment, was described. However, there have also been reports of severe liver damage during SARS-CoV-2 infection (4). We therefore recommend that, in addition to the laboratory parameters proposed by Dreher et al., the serum levels of liver enzymes are also closely monitored, especially in the case of a severe course with ARDS.

DOI: 10.3238/arztebl.2020.0717a

References

1. Dreher M, Kersten A, Bickenbach J, et al.: The characteristics of 50 hospitalized COVID-19 patients with and without ARDS. *Dtsch Arztebl Int* 2020; 117: 271–8.
2. Zhang C, Shi L, Wang FS: Liver injury in COVID-19: management and challenges. *Lancet Gastroenterol Hepatol* 2020; 5: 428–30.
3. Ong J, Young BE, Ong S: COVID-19 in gastroenterology: a clinical perspective. *Gut* 2020; 69: 1144–5.
4. Weber S, Mayerle J, Irlbeck M, Gerbes AL: Severe liver failure during SARS-CoV-2 infection. *Gut* 2020; 69: 1365–7.

Prof. Dr. Alexander L. Gerbes
Dr. med. Sabine Weber
University Hospital Munich
Department of Medicine II
Liver Centre Munich, Germany
Sabine.Weber@med.uni-muenchen.de

Conflict of interest statement

The authors declare that no conflict of interest exists.

Ambiguities

The authors report on a first case series of patients with COVID-19 and compare 24 cases with acute respiratory distress syndrome (ARDS) to 26 cases with non-ARDS (1). The data are important and have therefore been published extremely quickly, as there is currently little scientific knowledge about the clinical characteristics of the disease, especially in Germany. However, the article presents some ambiguities, which are however important for interpretation of the data.

First, the authors describe that in addition to bronchial secretions and sputum, “serum, urine, and stool were also tested for SARS-CoV-2”. Serum is then also listed in Table 2 under “virus

detection”. It is not clear what this means. So far, it has been assumed in particular that SARS-CoV-2 is not transmitted through blood, and live viruses have not yet been detected in stool (2). Are the authors referring to antibody detection, or did they actually discover virus antigens in blood?

Furthermore, detailed information on patient selection is missing. It is stated that these patients were the first 50 to be treated at the hospital, yet 16 (14 with ARDS) had been transferred there. It can therefore be assumed that the non-ARDS group does not represent an appropriate comparison group in the scientific sense, as it was selected differently; therefore, certain characteristics of the ARDS group could be overestimated.

Finally, under the key messages, the authors state that “COVID-19 patients without ARDS also require longer hospitalization [...]”. This general statement cannot be derived from the data, as only a small number of hospitalized COVID-19 cases were investigated. In fact, our experience (3) shows that most patients who first presented to the emergency room can be treated on an outpatient basis, although the proportion of patients who then require inpatient treatment at a later point in time is still the subject of ongoing investigations.

DOI: 10.3238/arztebl.2020.0717b

References

1. Dreher M, Kersten A, Bickenbach J, et al.: The characteristics of 50 hospitalized COVID-19 patients with and without ARDS. *Dtsch Arztebl Int* 2020; 117: 271–8.
2. Wölfel R, Corman VM, Guggemos W, et al.: Virological assessment of hospitalized patients with COVID-2019. *Nature* 2020; 581: 465–9.
3. Möckel M, Bachmann U, Behringer W, Pfäfflin F, Stegemann MS: How emergency departments prepare for virus disease outbreaks like COVID-19. *Eur J Emerg Med* 2020; 27: 161–2.

Prof. Dr. med. Martin Möckel, FESC, FAHA

Departments of Emergency and Acute Medicine and Chest Pain Units, Campus Charité Mitte and Campus Virchow-Klinikum, Charité – Universitätsmedizin Berlin, Germany
martin.moekel@charite.de

Conflict of interest statement

The author declares that no conflict of interest exists.

In Reply:

The suggestion from Dr. Weber and Prof. Gerber, that not only the mentioned laboratory parameters but also the serum levels of liver function markers should be closely monitored, is indeed important on the basis of initial indications. Transaminase levels as well as other liver-specific laboratory parameters were of course recorded in our collective, with the median showing no or only slightly increased values in the total collective at the time of admission: aspartate aminotransferase (AST), 48 (31–77) U/L; alanine aminotransferase (ALT), 30 (19–55) U/L; and total bilirubin, 0.6 (0.4–0.8) mg/dL. The median gamma-GT and alkaline

phosphatase (AP) remained in the normal range, at 35 (23–74) U/L, and 56 (44–78) U/L, respectively.

Additionally, Prof. Möckel asked about the implied meaning of our statement “serum, urine, and stool was tested for SARS-CoV-2”. This explicitly does not refer to antibody detection, but indeed to virus detection in the blood in 53% of patients using polymerase chain reaction (PCR). It is true that a large number of our patients in the intensive care unit were transferred in from other hospitals. As an ECMO center (ECMO, extracorporeal membrane oxygenation), we also accept many patients with acute respiratory distress from other hospitals independent of the SARS-CoV-2 pandemic. Of course, this situation made it difficult to compare patients with ARDS in the intensive care unit to those who could be treated in a normal ward. For this reason, and in view of the small number of cases, we deliberately decided against a statistical evaluation of the significance.

Patients who were hospitalized due to COVID-19 but who were not transferred to the intensive care unit indeed required long periods of inpatient treatment. In addition to a strong inflammatory reaction and long-lasting fever, another reason for this was that almost all of them required supplemental oxygen. A newer analysis of our data showed that oxygen-dependent patients were hospitalized for a median of 12 (7–29) days. Oxygen

administration was required for 8 (5–13) days, and the patients had an elevated body temperature for 7 (2–11) days. Needless to say, many patients who are SARS-CoV-2 positive and present to the emergency room do not need to be hospitalized. However, these patients are not described in our collective.

DOI: 10.3238/arztebl.2020.0717c

Reference

1. Dreher M, Kersten A, Bickenbach J, et al.: The characteristics of 50 hospitalized COVID-19 patients with and without ARDS. *Dtsch Arztebl Int* 2020; 117: 271–8.

On behalf of the authors:

Prof. Dr. med. Michael Dreher

Uniklinik RWTH Aachen

Department of Pneumology and Intensive Care Medicine

Medical Clinic V, Aachen, Germany

mdreher@ukaachen.de

Paul Balfanz

Dr. med. Dirk Müller-Wieland

Prof. Dr. med. Nikolaus Marx

Uniklinik RWTH Aachen

Department of Cardiology, Angiology and Internal Intensive

Medicine, Medical Clinic I, Aachen, Germany

Conflict of interest statement

Prof. Dreher has served as a paid consultant for GSK and has received speaking honoraria from AstraZeneca and Novartis.

The remaining authors declare that no conflict of interest exists.

CLINICAL SNAPSHOT

Shiitake Dermatitis

A 70-year-old man presented with an approximately 2-day history of itching striate skin lesions on the trunk and extremities with no general symptoms (*Figure*). On inquiry, he stated that he had eaten an Asian meal around 2 to 3 days before the onset of symptoms. He had consumed various fungi, including shiitake mushrooms. Shiitake dermatitis is described quite frequently in Asia, and the number of case reports in western countries is constantly increasing. Typically, the consumption of shiitake mushrooms is followed by a delayed striate cutaneous reaction resembling the flagellate dermatitis that can be induced by bleomycin (Latin *flagellum*: scourge, whip). The skin lesion is thought to represent a toxic reaction to the heat-labile protein lentinan; for this reason, the mushrooms should always be properly cooked before being eaten. Further allergological investigations such as skin tests or determination of specific IgE in serum bring no further benefit. Apart from bleomycin dermatitis, the differential diagnoses, depending on the clinical findings, include drug reactions or contact allergy. The recommended treatment is topical steroids, supplemented with antihistamines if required. The lesions usually resolve without scarring.

Dr. med. Andre Heineke, Dr. med. Hans Joachim Mußgnug, Prof. Dr. med. Michael Tronnier

Klinik für Dermatologie, Venerologie und Allergologie, Helios Klinikum Hildesheim, andre.heineke@helios-gesundheit.de

Conflict of interest statement: The authors declare that no conflict of interest exists.

Translated from the original German by David Roseveare.

Cite this as: Heineke A, Mußgnug HJ, Tronnier M: Shiitake dermatitis. *Dtsch Arztebl Int* 2020; 117: 718. DOI: 10.3238/arztebl.2020.0718