Letter to the Editor

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One disease, different features: COVID-19 laboratory and radiological findings in three Italian patients

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To the Editor,

During the current outbreak of the novel Coronavirus (COVID-19) in Italy, aiming to prevent and/or mitigate the unfavorable consequences of this viral epidemic, effort should be devoted to establishing active surveillance programs and promoting accurate diagnostic tools. It is well known that tests assuring a rapid and accurate identification of this new microorganism by molecular diagnostic assays are necessary [1], but we should not underestimate the contribution that routine laboratory tests and diagnostic imaging could provide.

Regarding these two diagnostic tools, according to the preliminary experience gained in our tertiary center, an interesting discrepancy occurred. Indeed, in our three cases (i.e. all males; 66, 67, and 68 years old, respectively) of COVID-19 microbiologically proven infection, features of a severe bacterial infection were seen at laboratory tests while typical findings of viral infections emerged at initial imaging.

The routine laboratory tests performed at admission and during the first period of hospitalization in the intensive care unit (ICU) were similar in all patients. In particular, we unexpectedly observed neutrophilia with immature granulocytes (myelocytes and metamyelocytes) with or without leukocytosis, instead of lymphocytosis with activated elements or at least an inversed formula, which is usually seen in viral infections. Lymphocyte subset determination by flow cytometry demonstrated an increased CD4/CD8 ratio due to a lowering of CD8+ suppressor T cells and a concomitant rise in the percentage of CD4+ helper T lymphocytes. Conversely, viral infections lead usually to an increase in CD8+ suppressor T cells. These hematological findings were associated with an increase in C-reactive protein (CRP), usually found in acute conditions causing inflammation such as severe bacterial or fungal infections. On the contrary, procalcitonin (PCT) was not elevated at admission, but it raised as the clinical conditions worsened in two patients. Increased levels of lactate dehydrogenase (LDH) and ferritin could be detected in all three patients, while creatine phosphokinase (CPK) was normal. Moreover, the research hematological parameter MDW (monocyte volume distribution width – DxH 900 hematology analyzer, Beckman Coulter, CA, USA) was significantly increased in all patients, especially in the one with the worst clinical condition. Until now, this parameter has been associated with sepsis [2]. The coagulation profile demonstrated high D-dimer, especially in one patient who had a value of 56,708 μg/L at admission in ICU. This relevant finding, already reported in the literature, could be important for the outcome [3].

Our findings are in agreement with the current literature on the most representative laboratory abnormalities of patients affected by COVID-19 [4, 5] regarding the occurrence of lymphopenia and leukocytosis, along with abnormal values of LDH, ferritin, D-dimer and PCT, these last three possibly related with clinical outcome. Otherwise, in contrast to previously published COVID-19 cases, we did not detect a prolonged prothrombin time nor an increase in CPK.

Regarding radiological imaging, two patients performed chest X-rays only and one underwent a chest

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computed tomography (CT) scan at admission. The initial chest X-rays of the two patients showed patchy areas of consolidation (Figure 1). Diffuse, bilateral, and symmetric ground-glass and bronchiectasis were evident at CT (Figure 2). Our radiological findings are in agreement with the literature regarding viral infections in general and also COVID-19 [6–8].

Innate immune system is known to be at first activated by viral infection [9, 10], as it seems even more reasonable in a previously not encountered microbial agent like COVID-19, recruiting neutrophil, monocytes, and natural killer cells and promoting the release of IFN and other proinflammatory cytokines. Interestingly, the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) has already revealed strategies to escape innate immunity and prevent proinflammatory production pattern [11].

Our preliminary experience with COVID-19 is confirming that we are dealing with a multifaceted, chameleonic, and complex viral infection that can have discordant features at different diagnostic tests in its initial phase. Although further studies are necessary to confirm this evidence, it highlights the necessity for a multidisciplinary approach to the disease and opens new possible perspectives regarding the therapeutic approach.

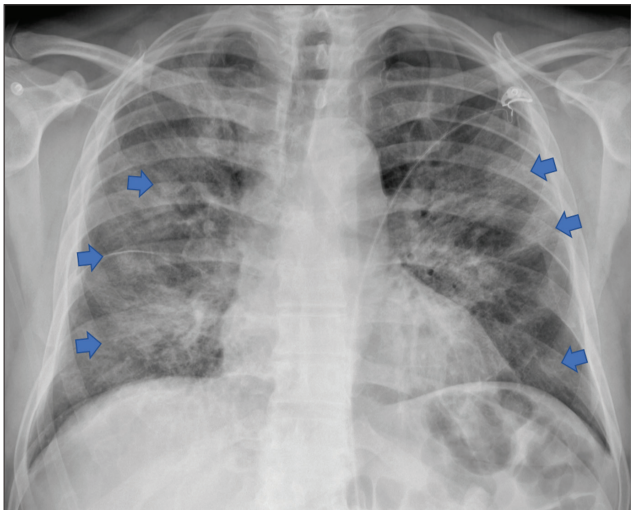

Figure 1: Chest X-ray of a 68-year-old male affected by microbiologically proven COVID-19 performed at admission in the intensive care unit demonstrating bilateral patchy opacities (blue arrows).

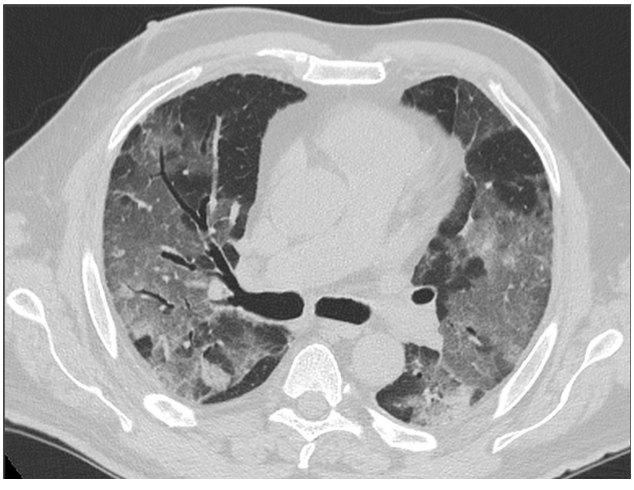

Figure 2: Axial chest computed tomography of a 67-year-old-male affected by COVID-19, showing severe, diffuse, bilateral ground glass opacities and bronchiectasis which are typical features of viral infections.

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References

1. Lippi G, Plebani M. The novel coronavirus (2019-nCoV) outbreak: think the unthinkable and be prepared to face the challenge. Diagnosis (Berl) 2020. DOI: 10.1515/dx-2020-0015. [Epub ahead of print].
2. Crouser ED, Parrillo JE, Seymour C, Angus DC, Bicking K, Tejidor L, et al. Improved early detection of sepsis in the ED with a novel monocyte distribution width biomarker. Chest 2017;152:518–26.
3. Tang N, Li D, Wang X, Sun Z. Abnormal Coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost 2020. DOI: 10.1111/jth.14768 [Epub ahead of print].
4. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. J Am Med Assoc 2020. doi: 10.1001/jama.2020.1585. [Epub ahead of print].
5. Lippi G, Plebani M. Laboratory abnormalities in patients with COVID-2019 infection. Clin Chem Lab Med 2020. DOI: 10.1515/cclm-2020-0198. [Epub ahead of print].
6. Koo HJ, Lim S, Choe J, Choi SH, Sung H, Do KH. Radiographic and CT features of viral pneumonia. Radiographics 2018;38:719–39.
7. Zu ZY, Jiang MD, Xu PP, Chen W, Ni QQ, Lu GM, et al. Coronavirus disease 2019 (COVID19): a perspective from China. Radiology 2020;21:200490.
8. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020;382:727–33.

9. Takeuchi O, Akira S. Innate immunity to virus infection. Immunol Rev 2009;227:75–86.
10. Iwasaki A, Pillai PS. Innate immunity to influenza virus infection. Nat Rev Immunol 2014;14:315–28.
11. Mubarak A, Alturaiki W, Hemida MG. Middle east respiratory syndrome coronavirus (MERS-CoV): infection, immunological response, and vaccine development. J Immunol Res 2019;2019:11.