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SARS-Cov-2 pneumonia and concurrent myelodysplasia complicated by Pseudomonas aeruginosa over-infection

Aldo Pezzuto [a,*], Antonella Tammaro [b], Giuseppe Tonini [c], Giulia Conforti [d], Francesca Falangone [d], Valerio Spuntarelli [d], Antonella Teggi [e], Alfredo Pennica [e]

[a] Cardiovascular-Respiratory Science Department, Sant'Andrea Hospital-Sapienza University, Via di Grottarossa, 1035/39, 00189, Rome, Italy
[b] Department of Neurosciences, Mental Health and Sensory Organs [NESMOS], Sapienza University of Rome, Via di Grottarossa 1035, 00189, Rome, Italy
[c] Oncology Department, University Campus-Medico, via Alvaro Del Portillo, 00128, Roma, Italy
[d] Internal Medicine Department Sant'Andrea Hospital, Sapienza University, 00189, Rome, Italy
[e] Infectious Disease Unit-S Andrea Hospital, Sapienza University, Rome, Italy

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ABSTRACT

The new virus called severe acute respiratory syndrome coronavirus 2 (SARSCov-2) causing Coronavirus disease 2019 (COVID-19) has spread quickly in several countries and it has become pandemic. Different types of clinical manifestations are attributed to this infection.

Some mechanisms related to the infection regarding the immune response are not still elucidated.

Herein we reported a case of a 66-years-old patient affected by myelodysplasia who was referred to our hospital because of clinical and radiological manifestations of viral pneumonia. The clinical course has become complicated due to bacterial secondary over-infection by Pseudomonas aeruginosa during stay in internal medicine unit whilst a persistent positive oral and naso-pharyngeal swab test was reported up to 100 days of admission. The patient had a fast clinical and radiological worsening that led her to be admitted to an intensive care unit. Despite intubation and mechanical ventilation she died in a few days.

1. Introduction

The Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) which is responsible of different clinical pictures.

The foremost clinical symptoms are fever, dry cough, weakness, sore-throat and shortness of breath frequently associated with radiological interstitial pneumonia (Huang et al., 2020).

Different clinical manifestations may be caused by this viral infection with a possible multi-organ involvement (Tammaro et al., 2020).

Herein we report a case of a female patient with a positive oral and nasal-pharyngeal swab test and multiple outbreaks of pneumonia at chest CT scan complicated by Pseudomonas aeruginosa secondary over-infection in a condition of immunodeficiency due to the concurrent presence of myelodysplasia. The swab test was performed three times every 10 days with rRT-PCR assay and remained positive for a very long time. The patient had a fast worsening of clinical and radiological parameters despite the use of anti-viral agents and specific antibiotics.

2. Case presentation

A 66-year-old female presented at the emergency department of our hospital with fever 38.1 °C and a respiratory rate of 25 breaths per minute and pulse rate of 90 beats per minute. It occurred on March 30th 2020. The oxygen hemoglobin saturation was 86 % at room temperature. The rate PaO2/FiO2 was 200, the respiratory rate was 35 beats/minute. The patient also complained with sore throat, cough, dyspnea at rest.

A myelodysplastic syndrome was reported as a matter of her recent clinical history. The patient wasn't on chemotherapy because it was a recent finding but in the meantime she had fallen ill with viral infection.

Other comorbidities were chronic obstructive pulmonary disease (COPD), hypertension. The patient reported being a former smoker with pack-year 30.

* Corresponding author at: Sant'Andrea Hospital, Sapienza University, Rome, Via Grottarossa, 1035, Italy.
E-mail addresses: pezzutoaldo@libero.it (A. Pezzuto), antonella.tammaro@uniroma1.it (A. Tammaro), g.tonini@unicampus.it (G. Tonini), giulia.conforti@uniroma1.it (G. Conforti), francesca.falangone@uniroma1.it (F. Falangone), valerio.spuntarelli@uniroma1.it (V. Spuntarelli), antonella.teggi@ospedalesantandrea.it (A. Teggi), alfredo.pennica@uniroma1.it (A. Pennica).

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On March the 30th the first nasal and pharyngeal swab was positive and chest CT scan (Fig. 1) showed confluent infiltrates with interstitial thickness mainly located in the lower lobes.

Therefore she was admitted to an internal medicine isolation unit. Her chemistries were the following: hemoglobin 8.3 g/dl, platelets 23,000/μl, white blood cells 600/μl of which 200 lymphocytes and 250 neutrophils. The lymphocyte typing revealed a low level of all subtypes among which T CD3 80/μl, B lymphocytes 25/μl, NK cells 29/μl, T helper CD3+/CD4 + 33/μl.

The other chemical analysis were the following: vitamin D deficiency with a dosage of 10 ng/mL, C reactive protein (CRP) 15.9 mg/dl, procalcitonin 0.47 ng/mL which is indicative of sepsis, kidney function and electrolytes level were normal, D-dimer value was 889 ng/mL. The electrocardiogram was normal.

On day 7 of admission a treatment with hydroxychloroquine and lopinavir/ritonavir was started as off-label prescription.

The patient needed a blood transfusion of erythrocytes with a rise of hemoglobin up to 9 g/dl.

The oral and nasal-pharyngeal swab test performed with reverse-transcriptase–polymerase-chain-reaction (RT-PCR) assay was still positive after 20 days after admission.

At the beginning the patient felt better without fever and cough but she still reported dyspnea at rest.

At one month of admission a new febrile episode occurred that was followed by dry cough, worsening of dyspnea and wheezing. Then steroid therapy was started with methyl-prednisolone 20 mg twice a day.

An antibiotic therapy was started with ceftazidime and linezolid according to a culture examination with antibiogram performed on sputum revealing a Pseudomonas aeruginosa infection. This finding was consistent with the result of a blood culture and the evidence of an increase of the lung patchy consolidations at CT scan check (Fig. 2). A new blood check revealed a further decrease of neutrophils up to 150/μl. An increase of D-dimer up to 1,000, a reduction of sodium level (135 mmol/l) were also detected. A peripheral blood smear was performed revealing the presence of 50 % of dysplastic neutrophils characterized by hypogranulation and nuclear abnormalities.

Three months of admission a new oral and nasal-pharyngeal swab test was performed that was still positive. The inflammatory markers worsened with an increase of CRP up to 19 mg/dl and high level of ferritin detection (2 μg/mL) and D-dimer increased up to 1400 ng/mL and a normalization of lymphocytes count was not achieved. The patient respiratory symptoms and parameters were also worsened leading to the need of intubation. Notably the rate PaO2/FiO2 was decreased up to 150. The patient was eventually transferred to an intensive care unit for the application of mechanical ventilation. Afterwards despite intubation and high-dose steroid therapy administered the patient died a few days after the transfer.

Fig. 1. Baseline CT scan of the chest showing infiltrates located in the lower lobes.

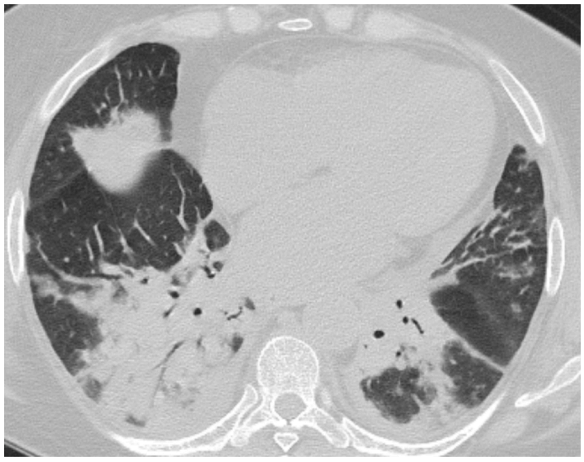

Fig. 2. Following CT scan of the chest after 7 days from the first check showing a significant increase of lung multifocal patchy consolidations.

3. Discussion

The mortality rate of SARS-CoV infection is 10 %, and the outbreak has been spreading in several countries.

The clinical manifestations range from sore-throat to mild or severe pneumonia, and lung failure with a possible multi-organ involvement (Huang et al., 2020).

Some drugs normally used to treat malaria and rheumatoid conditions such as arthritis were used in covid-19 infection during the first wave phase as off-label prescription.

Hydroxychloroquine indeed demonstrated antiviral activity, being able to modify the activity of the immune system, inhibiting autophagosome-lysosome fusion and inactivating enzymes that the virus needs for replication (Ferner and Aronson, 2020). Anti-viral agents normally used for the treatment of human immunodeficiency virus (HIV) have demonstrated to be active in coronavirus treatment, too (Nutho et al., 2020). Notably, ritonavir and lopinavir have been demonstrated to be indeed effective by a strong binding to hydrogen residues of the virus. During the second wave the above reported anti-viral agents were not approved for the treatment of Covid-19 because of an unfavorable ratio of efficacy to side effects.

The case we reported is unusual because the patient was affected aside from covid-19 pneumonia, by an important comorbidity such as myelodysplasia characterized by a reduction of all blood cells resulting in a dysregulation of the immune system. That comorbidity is a very rare finding among the comorbidities associated with SARS-Cov-2 infection.

A worsening of clinical condition was observed along with a long duration of positivity to the swab test despite the use of anti-retroviral agents leading to lung failure and the need for intubation with mechanical respiratory support. The radiological picture worsened due to a secondary bacterial infection by Pseudomonas aeruginosa. The bacterial infection occurred during the stay in the internal medicine unit and not in the intensive care unit.

The latter is ubiquitous and it has the ability to survive under a variety of environmental conditions. Such bacterium not only causes disease in plants and animals, but also in humans, causing serious immunodeficiency condition. In the present report P. Aeruginosa was sensitive only to ceftazidime and linezolid (Wang et al., 2006). The uncommon bacterial pneumonia over-infection that occurred in an internal medicine and not in an intensive care unit was also favored by the chronic inflammatory state of the airways owing to the presence of

COPD in the same way as other atypical pneumonia (Bruno et al., 2011).

The clinical symptoms and inflammatory markers worsened quickly despite the therapy was reinforced with antibiotics, and a concurrent increase of the inflammatory opacities was observed at chest CT scan.

Concerning the swab test for SARS-cov-2, it was performed at different time point and continued to be still positive 100 days after the admission. No serology for antibodies detection was used. The long-time positivity of the swab test was probably due to the concomitant immunodeficiency of the patient since the T cell immunity is very important to fight against a viral infection.

We know that the swab test specificity and sensitivity are increased performing both oral and nasal-pharyngeal. Conversely the use of serology for antibody detection is controversial (Xie et al., 2020).

The present case reported aside from comorbidities such as COPD and history of smoking the presence of altered blood cells with a reduction of T -lymphocytes subtypes due to the myelodysplasia (Liu et al., 2020; Pezzuto and Carico, 2020). Notably an altered level of natural killer cells, T helper and T suppressor subtypes was found. This condition resulted in a weakened immune response and favored bacterial over-infection, consistent with previous studies reporting an association of myelodisplasia with bacterial infection (Pagano and Caira, 2012; Qin et al., 2020).

Our case report confirms that the variability of clinical presentations and prognosis both depend upon the physiopathology of this viral infection and the interaction with the immune system (Okba et al., 2020). The bacterial over-infection that we observed in the present case is a rare occurrence in an internal medicine unit as we know from the literature (Langford et al., 2020a). The super-infection was subsequent to the viral infection because it occurred one month after the finding of the first positive swab test for SARS-Cov-2. We know from the literature that we can found a co-infection or a secondary infection following a viral infection (Langford et al., 2020b; Mirzaei et al., 2020).

The deficit of lymphocytes that probably favored the long-lasting of the disease and the poor outcome suggests us that an immunotherapy could be the next scenario about the treatment approach to the disease. The latter used for other viral chronic infections may play an important role alongside antiviral agents, since the infection alters by itself the immune-system defenses (Hedge et al., 2009).

Data availability

Data will be made available on request.

Ethical approval

Informed consent was obtained by the patient

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Authors' contribution

Conceptualization and writing: Aldo Pezzuto, Antonella Tammaro

Data Curation: Giuseppe Tonini, Giulia Conforti, Francesca Falangone, Valerio Spuntarelli, Antonella Teggi, Alfredo Pennica.

Author statement

Conceptualization and writing: Aldo Pezzuto, Antonella Tammaro.

Data Curation: Giuseppe Tonini, Giulia Conforti, Francesca Falangone, Valerio Spuntarelli, Antonella Teggi, Alfredo Pennica.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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