

Therapeutic approach to Sars-COV-2 in early treatment of patient not-hospitalized: a case report.

Daniela Marasco

Service Biotech srl <https://orcid.org/0000-0003-0540-623X>

Salvatore Del Prete (✉ saldelp@gmail.com)

Service Biotech srl <https://orcid.org/0000-0001-6004-7781>

Rosalaura Sabetta

2Dipartimento di Salute Mentale e Fisica e Medicina Preventiva, Università degli Studi della Campania Luigi Vanvitelli, Naples, Italy

Arturo Armone Caruso

AIAS Afragola

Guido Consolmagno

School of Medicine and Surgery Università degli Studi della Campania Luigi Vanvitelli, Naples, Italy

Antonio Del Prete

Department of Neurosciences and Reproductive and Dentistry Sciences, School of Medicine and Surgery, University of Naples Federico II <https://orcid.org/0000-0002-4884-0274>

Case Report

Keywords: SARS coronavirus, < Virus classification, Hand, foot and mouth disease virus < Virus classification, Herpesvirus< use of corticosteroids in pretreatment of not hospitalized covid patients

DOI: <https://doi.org/10.21203/rs.3.rs-53046/v2>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background: Sars-CoV-2 induces a massive inflammatory response mediated by macrophages, activated thanks to IFN γ secreted by T lymphocytes. Viral Spanish influenza has been reported that it could have the similar inflammatory mechanism that we can observe in COVID-19 patients¹⁶). We tested this theory on a 55-year-old male patient, Sars-COV-2 positive.

Case presentation: We treated our patient using clinical data and therapeutic approaches from a team of Chinese researchers, established during the beginning of the epidemic in December 2019. The new member of the human coronavirus, officially called SARS - CoV - 2 (severe acute respiratory syndrome coronavirus 2) by the International Committee on Taxonomy of Viruses (ICTV) is a new RNA virus strain that has not been previously identified in humans (1). This patient showed a Sars Cov-2 infection and was treated early with glucocorticoids. The patient immediately showed a regression of fever and an improvement of symptoms.

Conclusions: We hypothesize that the initial stages of the infection can be treated with glucocorticoid therapy.

Background

SARS-Cov2 induce a middle infection into the young children but the mortality is more high in to the adult population: this way of infection it isn't a classic way because the child doesn't have a strong immune response, therefore this atypical response. In patients with severe disease, viral clearance was delayed, with a persistent elevation of pro-inflammatory cytokines and associated multiorgan damage despite antiviral therapy². Furthermore, a lower serum IgG2 level appeared to be associated with a mild severity of disease, especially in pregnant patients. Severe disease and lung pathology were associated with the deposition of immune complexes. Another important aspect in the pathogenesis of SARS-CoV-2 is the cytokine storm^{6,13}. SARS Cov-2 have some similarity in the pathogenesis with other class of viruses that can stimulate immune response regulated by cytokine IL-6, IL-1, IL-8^{8,10,12,13}. In the early hours of a viral infection, the cytokines produced by cells infected or coming into contact with viral products are vital in promoting of the innate immune response¹⁸ and of infection^{14,15}. On the basis of the similar pathogenetic pathway in the MASs (macrophage activation syndromes)¹³ where we can find the presence of an altered immune response making by an higher expression of inflammatory cytokine (IL-6,IL-1, IL-18), responsible to generate a respiratory distress, that we can find also in other pathology with altered immune response i.e. rheumatoid arthritis In literature we can find many links between virus and altered immune response, i.e. EBV and sHLH¹². On this wake we can speculate that Covid-19 positive patient with high fever and not responsive at paracetamol and with dyspnoea at the fourth day of manifestation of symptoms could start therapy 3x3x3 with cortisone. That patient showed an improvement in ten days from the beginning of the therapy. In literature we note that treatment of sHLH from EBV in **early step** making an improvement of the treated patient¹².

Case Presentation

Therapy approach

We based our treatment, on clinical action of Sars COV-2^{8,16}, and for this patient M.A. male of 53 years old with an history of hypertension and hypercholesterolemia, authorized us treating this virus¹⁶, trying to intervene on cytokine storm. Our patient showed high fever 39,5°C, general exhaustion with persistent cough; in a first clinical approach the patient was treated with paracetamol 1000mg each 12 hours and supracef in pills one each day for 4 days; after 4 days of treatment we observe a constant fever at 39 °C and increase of cough and an initial dyspnea, with an increasing general exhaustion. We recommended sampling with swab on nose mucosa for Sars COV-2, as it is recommended by guidelines, the swab was positive for Sars COV-2. The patient began immediately a therapy with betametasone (bentelan) 1mg x 3 times a day for 3 days, then 2 times a day for 3 days and 1 time a day for 3 days and we administered, although claritromycin 500mg 1 pill a day for 7 days for reducing possibility of over infection; we suggest also a correct disinfection of oral mucosa with gargling with peroxid 3% 10 vol. each 12 hours. We retain to administer also some integration with complex of vitamins and mineral salts. After three days of this treatment the patient improved with reducing all symptoms, cough, Exhaustion and fever, that reducing from 39,5 °C to 37°C. At the day five the patient didn't show fever anymore and cough; we notice a persistence of general exhaustion. At day seven the patient showed slight hoarseness treated with bronchodilator mixed low level of cortisone in spray solution; after 15 days the patient's repeat swab was negative for Sars COV-2.

Discussion And Conclusions

Our Hypothesis is that Sars-COV-2 has a capacity to stimulate a cytokine storm^{8,16}, guided us to cure Patient M.A. with short therapy with cortisone; it's obvious that this kind of treatment could be applied just in the onset of the pathology after first step of therapy with paracetamol was negative. This therapy could be useful in the first steps because we try to break out the initial increasing of the immune response in fact we try to intervene on macrophages¹³ and monocyte response at the virus. As other studies show the glucocorticoid regulate the central cytokine release and regulate in negative sense the release of IL-6 and macrophages¹⁸. The Interleukins have the principal role in the cytokine storm development and blocking it we can solve in early time the increasing of a great part of the symptoms shows in this Sars COV-2 infection; this therapy could be used to control viruses symptoms and it avoid the ICU admission of the patient.

Declarations

Funding: No funding was received for this study.

Conflict of Interest declaration.

Conflict of Interest: Del Prete Salvatore; Marasco Daniela; Rosalaura Sabetta; Caruso Armone Arturo; Guido Consolmagno and Del Prete Antonio, declare that they have no conflict of interest.

Compliance with Ethical Standards:

This study did not receive funding.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

The patient consented to participate and have their clinical data published as a case report.

References

1. Zhang JJ¹, Dong X¹, Cao YY², Yuan YD³, Yang YB⁴, Yan YQ⁵, Akdis CA⁶, Gao YD¹ Clinical characteristics of 140 patients infected by SARS-CoV-2 in Wuhan, China. 2020 Feb 19. doi: 10.1111/all.14238. [Epub ahead of print].
2. Vincent C. C. Cheng,^{a,b,*} Kelvin K. W. To,^{a,c,*} Herman Tse,^{a,c,*} Ivan F. N. Hung,^{c,d,*} and Kwok-Yung Yuen. Two Years after Pandemic Influenza A/2009/H1N1: What Have We Learned? *Clin Microbiol Rev.* 2012 Apr; 25(2): 223–263.
3. Cui J¹, Li F², Shi ZL³ Origin and evolution of pathogenic coronaviruses. *Nat Rev Microbiol.* 2019 Mar; 17(3): 181–192. doi: 10.1038/s41579-018-0118-9.
4. Oldstone Lessons learned and concepts formed from study of the pathogenesis of the two negative-strand viruses lymphocytic choriomeningitis and influenza PNAS March 12, 2013 110 (11) 4180–4183; <https://doi.org/10.1073/pnas.1222025110> Contributed by Michael B. A. Oldstone, December 20, 2012 (sent for review December 5, 2012)
5. Michael B. A. Oldstone^{a,1}, Brian C. Warea^a, Lucy E. Hortona^a, Megan J. Welcha^a, Roberto Aiolfi^b, Alessandro Zarpelloni^b, Zaverio M. Ruggeri^b, and Brian M. Sullivan^a Lymphocytic choriomeningitis virus Clone 13 infection causes either persistence or acute death dependent on IFN-1, cytotoxic T lymphocytes (CTLs), and host genetics (sent for review March 19, 2018; reviewed by Ralph S. Baric and Allan J. Zajac)
6. Xu K^{1,2}, Cai H¹, Shen Y¹, Ni Q^{1,2}, Chen Y¹, Hu S¹, Li J¹, Wang H¹, Yu L^{1,2}, Huang H¹, Qiu Y¹, Wei G¹, Fang Q¹, Zhou J¹, Sheng J^{1,2}, Liang T¹, Li L^{1,2} Management of corona virus disease-19 (COVID-19): the Zhejiang experience]. *Zhejiang Da Xue Xue Bao Yi Xue Ban.* 2020 Feb 21; 49(1): 0. [Article in Chinese]
7. Xia S¹, Zhu Y², Liu M³, Lan Q¹, Xu W¹, Wu Y¹, Ying T¹, Liu S⁴, Shi Z³, Jiang S^{5,6}, Lu L⁷. Fusion mechanism of 2019-nCoV and fusion inhibitors targeting HR1 domain in spike protein. *Cell*

- [Mol Immunol](#). 2020 Feb 11. doi: 10.1038/s41423-020-0374-2. [Epub ahead of print]
8. Marasco Daniela, Del Prete Salvatore and Sabetta Rosalaura, Hypothesis about pathogenic action of Sars-COV-2 06 March 2020. DOI: 10.29328/journal.ijcv.1001009
 9. Na YJ, Choi KJ, Park SB, Sung HR, Jung WH, Kim HY, Rhee SD, Kim KY. [Protective effects of carbenoxolone, an 11 \$\beta\$ -HSD1 inhibitor, against chemical induced dry eye syndrome](#). *Apoptosis*. 2017 Nov;22(11):1441-1453. doi: 10.1007/s10495-017-1419-6. PMID:28887719
 10. Slominski RM¹, Tuckey RC², Manna PR³, Jetten AM⁴, Postlethwaite A^{5,6}, Raman C¹, Slominski AT^{7,8,9} Extra-adrenal glucocorticoid biosynthesis: implications for autoimmune and inflammatory disorders. *Genes Immun*.2020 Mar 23. doi: 10.1038/s41435-020-0096-6
 11. Wu D¹, Yang XO². TH17 responses in cytokine storm of COVID-19: An emerging target of JAK2 inhibitor Fedratinib. *J Microbiol Immunol Infect*. 2020 Mar 11. pii: S1684-1182(20)30065-7. doi: 10.1016/j.jmii.2020.03.005.
 12. Mărginean MO¹, Molnar E², Chinceșan MI¹. Epstein-Barr virus-associated hemophagocytic lymphohistiocytosis in a small child: A case report. *Medicine (Baltimore)*.2020 Jan;99(3):e18759. doi: 10.1097/MD.00000000000018759.
 13. McGonagle D¹, Sharif K², O'Regan A³, Bridgewood C⁴. Interleukin-6 use in COVID-19 pneumonia related macrophage activation syndrome. *Autoimmun Rev*.2020 Apr 3:102537. doi: 10.1016/j.autrev.2020.102537.
 14. Ellermann-Eriksen S, Liberto MC, Iannello D, Mogensen SC: X-linkage of the early in vitro alpha/beta interferon response of mouse peritoneal macrophages to herpes simplex virus type 2. *J Gen Virol* 1986, 67: 1025-1033.
 15. Zawatzky R, Gresser I, De Mayer E, Kirchner H: The role of interferon in the resistance of C57BL/6 mice to various doses of herpes simplex virus type 1. *J Infect Dis* 1982, 146: 405-410.
 16. Xing X^{1,2}, Hu S³, Chen M⁴, Zhan F⁵, Liu H⁶, Chen Z³, Zhang H³, Zeng G³, Xu Q³, Zhang H³, Liu M⁵, Liu H⁵, Gao L⁷, Zhang L⁸. Severe acute respiratory infection risk following glucocorticosteroid treatment in uncomplicated influenza-like illness resulting from pH1N1 influenza infection: a case control study. *BMC Infect Dis*.2019 Dec 26;19(1):1080. doi: 10.1186/s12879-019-4669-9.
 17. Jean-Philippe Bastard, Claude Jardel, Jacques Delattre, Bernard Hainque et al., [Evidence for a Link Between Adipose Tissue Interleukin-6 Content and Serum C-Reactive Protein Concentrations in Obese Subjects](#), in *Circulation*, vol. 99, n° 16, 1999, pp. 2219–2222, DOI:1161/01.CIR.99.16.2219.c.
 18. Gauthier A¹, Fisch A², Seuwen K³, Baumgarten B³, Ruffner H³, Aebi A³, Rausch M⁴, Kiessling F⁵, Bartneck M⁶, Weiskirchen R⁷, Tacke F⁶, Storm G⁸, Lammers T⁹, Ludwig MG¹⁰. Glucocorticoid-loaded liposomes induce a pro-resolution phenotype in human primary macrophages to support chronic wound healing. 2018 Sep;178:481-495. doi: 10.1016/j.biomaterials.2018.04.006. Epub 2018 Apr 5.
 19. **Robin George Manappallil¹ A Case of Macrophage Activation Syndrome with Acute Respiratory Distress Syndrome** *J Clin Diagn Res*. 2016 Sep; 10(9): OD11–OD12. Published online 2016 Sep

1. doi: [7860/JCDR/2016/20902.8518](https://doi.org/10.7860/JCDR/2016/20902.8518)