

SARS-COV-2 INFECTION: A CASE FAMILY REPORT

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ABSTRACT

From the beginning of 2020 in the World there was a tragic spread of infection by SARS-CoV-2 that for the number of infection, speed of diffusion and high mortality it has been elevated to a pandemic event.

Actually, after more than one year since the starting of pandemic, there is no cure and the virus has increased its speed of spread through its new variants, despite the fact that 5 vaccines were produced

marketed and are now in use. In particular, among SARS-CoV-2 variants, the most common is the one called B.1.1.7. It has been isolated in United Kingdom and is spreading in Europe.

Here, we described a case of an Italian family, consisting of 5 people; one of them, was already vaccinated, while all the other four people were infected by SARS-CoV-2. In particular, we report the history of the infection within the family, the symptoms, the drug treatments received and the evolution of the infection. This case demonstrates the randomness, with which people can be infected, the speed of infection and the effectiveness of vaccines.

General Terms: SARS-CoV-2 infection, case report

Keywords: SARS-CoV-2; SARS-CoV-2 variant; symptoms; medical treatment

1. INTRODUCTION

In no other case of disease or pandemic, such extraordinary results have been achieved in over a year as in the case of SARS-CoV-2.

To date, more than 180 vaccines, at different developmental stages, have been generated and 5 of them have been licensed and used since December 2020 [1, 2], and at least 2 more are in the final approval phase. Although, there is no cure for SARS-CoV-2, many aspects have been clarified and several drugs have been successfully used to reduce the effects of the infection and shorten patients' hospital stays [3, 4].

Despite these excellent results, SARS-CoV-2 is still considered very dangerous and for this reason, in many countries, large areas are still in lock down to limit the virus spreading.

The last data from the World Health Organization indicate that, from the beginning of the pandemic until the end of March 2021, more than 140 million people have been infected, and about 3 million have died for COVID-19 (https://www.who.int).

Furthermore, in the recent months, several virus variants have been isolated. The most widespread variant has been the one called B.1.1.7, isolated in the United Kingdom in September 2020; currently it is still most widespread virus in the UK and it has also been detected in Europe with a frequency of 40-50% of total reported cases [5]. Other variants showing great transmissibility as the B.1.1.7 one, have been isolated in South Africa, in August 2020, the B.1.351 variant, [6], and successively in Brazil, (December 2020), the B.1.1.28.1 variant, [7]. However, the current licensed vaccines appear also to be effective against these new virus variants [8].

2. CLINICAL ASPECTS

Typical SARS-CoV-2 infection begins after an incubation period of approximately 4 days (range: 2-14 days). It is characterized by dry cough and low-grade fever within 3 days from infection $(38-39^{\circ}C \text{ or } 100,5-102,1^{\circ}F)$, often accompanied by other symptoms [9].

In most patients, COVID-19 infection remains mild or moderate, symptoms resolve within a week, and patients typically recover at home. Around 10% of patients remain symptomatic through the second week of infection. Patients admitted to the Intensive Care Unit (ICU) show a longer persistence of the symptoms, associated with a greater risk of developing a more severe COVID-19 disease. Many symptoms associated with COVID-19 infection have been described, however, the main clusters concern: respiratory [10], musculoskeletal [11], gastrointestinal [12], cutaneous [13], and nervous systems [14, 15].

Table 1 shows the most common symptoms observed in SARS-CoV-2 patients. However, other rare symptoms have also been reported, particularly, at the nervous system level [14], such as Guillain-Barre syndrome [16], as well as at the cardiovascular level [17].

AFFECTED	SYMPTOMS						
SYSTEM	COMMON	LESS COMMON	SEVERE				
Respiratory S.	Fever; sputum; cough	Conjunctivitis; sore throat.	Shortness of breath;				
Kespiratory 5.	r ever, sputum, cougn	Conjunctivitis, sole unoat.	chest tightness				
Musculoskeletal S.	Fatigue; headache	Myalgia; join pain					
Gastrointestinal S.	Abdominal pain	Diarrhoea; vomiting	Intestinal inflammation				
Cutaneous S.		Erythema multiforme; chilblaine-like acral rash	Chickenpox-like rash				
Nervous S.	Anosmia/dysgeusia	Myalgia	Loss of speech or movemen				

 Table 1. Symptoms associated with COVID-19. Here, we reported the more common symptoms associated with SARS-CoV-2 infection.

3. SARS-CoV-2 VARIANT(S) SPREADING IN ITALY

Starting from January 2021, there has been an increase in the number of infected people, in Italy; this number has been attributed to B.1.1.7 variant, which seems to be the one more easily transmitted [5].

Data from the Italian Healthy Institute (Istituto Superiore di Sanità; http://www.iss.it) reported that, since 18 February 2021, in Italy, there were up to 54% of B.1.1.7 variant, 5% of the Brazilian one and 0.5% of the South African one. These data were obtained from the sequencing of about 1300 samples, recorded throughout the national territory, in order to guarantee geographical representativeness, as well as considering the different age groups. In particular, in northern Italy the spread of B.1.1.7. variant was over 70%, while in the Naples urban area (southern Italy, Campania region) the spread was about 30%. After 2 weeks, at the beginning of March 2021, the data indicated that the percentage of B.1.1.7 variant increased by about 20%, reaching about 50% of the "actual infected" individuals in Campania (http://www.regione.campania.it).

4. CASE FAMILY REPORT

Here, we describe a well-documented case of an Italian family of SARS-CoV-2 infection, from the Naples urban area. All family members give their consent for their personal data treatment. However, it was not possible to obtain information about the variant responsible of their infection. This family consists of 5 people: father, mother and three children (two boys and one girl). One of them (the mother), working in a hospital, completed the two-dose vaccination (Pfizer/BioNTech COVID-19 vaccine) in early February and was tested for her ability to produce antibodies against SARS-CoV-2. Data showed a high antibody titer against COVID19. She was the only one of all family members who was not infected by SARS-CoV-2. The first one of all family members to be infected was the girl (**Table 2**). She showed the first symptoms on February 19, 2021. On the first day, she suffered from headaches. Then, the following day, she showed fever up to 38.5 °C and on the same day she was subjected to a molecular swab to detect SARS-CoV-2. She resulted positive to the test. At this point, quarantine protocols were adopted from each component of the family. Everyone was isolated in different rooms of the apartment, used the mask at all times and maintained strict hygiene measures in the house. Probably, the girl was infected between February 15 and 16, during lunch in a public area, and when she showed the first symptoms, she had already infected other members of the family. In fact, during the following week other 3 members showed the same symptoms (headache and fever). The same pharmacological treatment, based on antibiotics and cortisone, was adopted for all the infected family members. SARS-CoV-2 positivity was confirmed for all of them by molecular swab analysis (**Table 2**).

All family members showed fever for a day, and then moderate dry cough, in the following 2-3 days. Interestingly, after 1 week from the fever, the girl, boy 1 and father presented anosmia and dysgeusia (**Table 2**). After 2 days from anosmia and dysgeusia only the girl and the father showed erythema multiform-like rush, as shown in **Figure 1**.

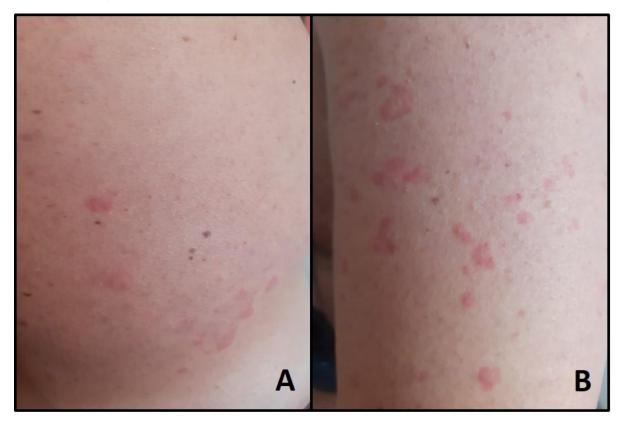


Figure 1. Erythema multiforme observed in the patient. A) Shoulder; B) Arm. (the patients give us signed consent to the publication of these images).

This symptom was treated with delta-cortene, another type of cortisone, for 5-8 days from the erythema onset. Differently, Boy 2 and Boy 1 showed only dry-cough, starting from February 27 and March 1, respectively, and both for 2 days. The data and the timeline of infection are reported in **Table 2**.

Table 2. Data related to the people, the infection timeline and symptoms. The first infection was calculated around February 15-16, 2021. The presence of SARS-CV-2 was confirmed by RT-PCR, performed at the Italian National Health System (Azienda Ospedaliera dei Colli- UOC Microbiologia e Virologia- Naples, Italy).

Sex	Age	Vaccine	Possible Infection Time	Swab Time and Result	First Symptom s	Second Symptom s	Swab Time and Result	Third Symptom s	End of Symptom	Swab Time- and Results
Woma n	52	yes	//	no	//	//	02/03 negative	//	//	10/03 negative
Man	52	no	19-20 February	no	Headache fever	anosmia dysgeusia	02/03 positive	erythema- like rash	10 March	12/03 positive
Girl	15	no	15-16 February	20/02 positive	Headache fever	anosmia dysgeusia	02/03 positive	erythema- like rash	05 March	12/03 negative
Boy 1	20	no	22-23 February	no	Headache fever	anosmia dysgeusia	02/03 positive	dry cough	11 March	12/03 positive

Boy 2	10 no	19-20 February	no	fever	dry cough	02/03 positive	//	03 March	12/03 negative
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The sequence and the type of symptoms were very similar for all the members of the family, with duration of about 3 weeks, despite only two members showed erythema-like rash and two dry-cough. Moreover, the Father and Boy 1 still resulted positive to the swab on March 22 (about 28 days from infection), although they had shown no symptoms for about ten days. They resulted negative to the presence of SAR-CoV-2 virus only on April 5.

The average period of positivity to SARS-CoV-2 infection in patients has been reported to be about 18 days [18], while cases of longterm infection have been described up to 6 weeks, but these case were referred to hospitalized patients presenting severe symptoms [18]. Here, we observed for two family members the presence of SARS-CoV-2 up to 5 weeks, even if no symptoms were present during the last two weeks.

All the family members presenting symptoms had pharmacological therapies. The therapy was proposed by the Italian Ministry of Health (www.salute.gov.it, in "circolare 30 November 2020"). In particular, the drug therapy to take care of the infection is reported in **Table 3**. The drug prescription was made by the attending physician.

Table 3. Drug therapy. Here, are reported the active molecules used for each symptom, the quantities and methods of intake.

 SYMPTOMS

	SYMPTOMS							
DRUG	FEVER	DRY COUGH	ERYTHEMA-like RASH					
paracetamol	Up to 3 gr for day							
azitromicin	500 mg/day for 3 days							
betasone disodium phosphate	2 mg/day for 5 days							
delta cortene		25 mg/day for 3 days	50 mg/day for 6 days					
cetirizine dichloridate			20 mg/day for 6 days					

All family members were tested for antibodies against SARS-CoV-2 two weeks after the negative swab to the presence of the virus, results are reported in **Table 4**.

Table 4. Analysis for the presence of antibodies (IgG and IgM) against SARS-CoV-2. Antibodies were monitored by chemiluminescence, and values <1000 indicates absence of antibodies, whereas values >1000 indicates the presence of antibodies against SARS-CoV-2; N.D. indicated not detected antibodies. Analysis was performed at "Laboratori Coleman SpA-Medicina Futura Group", Naples, Italy.

	IgG	IgM
Mother	2900 U/ml	N.D.
Father	2350 U/ml	N.D.
Girl	2320 U/ml	N.D.
Boy 1	1100 U/ml	N.D.
Boy 2	5150 U/ml	N.D.

The presence of the IgM antibodies indicates ongoing viral infection, whereas the presence of IgG indicates that people have already been infected and generated an immune response during the infection. In this case, all family member produced antibodies IgG against SARS-CoV-2, in particular the best immune response was for the young Boy 2 (10 years-old), while Boy 1 showed a weaker immune response.

5. CONCLUSIONS

The pandemic caused by SARS-CoV-2 had tragic effects on many global aspects: about 3 million of victims; millions of people had serious economic problems; many restrictions of personal freedom have been necessary to block virus spreading. But from a medical and scientific point of view, there was a period of extraordinary collaboration among countries, international and national health and no profit organizations, pharmaceutical companies and the medical and scientific communities, because they had the same goal: to be able to neutralize the pandemic progression. This allowed in less than one year to have different vaccines, all equally effective, and different drug therapies aimed at reducing the problems associated with the infection.

There are consolidated data that indicate 30-40% on the total number of SARS-CoV-2 positive tested are asymptomatic; about 50% are moderate symptomatic, showing a variable range of symptoms; and about 10% have severe symptoms, that require hospitalization.

Here, we describe a case of family infection, where it was possible to follow the timeline of infection from the onset of symptoms.

The first important information coming out from this case report is that the only one family member receiving immunogenic therapy remained negative, indicating that the vaccines are safe and effective.

The second information concerns the symptoms, which usually appear more than one (at least 4 have been observed, **Table 2**), they do not occur at the same time but they follow each other over the time. Moreover, in this reported case, at least 3 weeks were necessary to obtain the disappearance of the symptoms and the virus; during this time no hospitalization was necessary for any family members. The Father and Boy 1 were longer positive in absence of other symptoms; in fact, their positivity to the presence of SARS-CoV-2 was about 5 weeks. This observation could be explained by the use of steroids for 8-10 days due to the presence of erythema (Father) and cough (Boy 1), in fact it has been observed that patients in early stage of infection may be disadvantaged by the administration of steroids, that potentially cause a delay in the clearance of the virus and inhibit the proliferation of lymphocytes [19]. For this reason, starting from the end of April 2021 the Italian Ministry of Health give a new pharmacological indication in case of not severe SARS-CoV-2 patients, by using only paracetamol and/or non-steroidal anti-inflammatory drugs. This indicated that "The use of early steroid therapy proved useless if not harmful as it can affect the development of an adequate immune response" (www.salute.gov.it, in "circolare 26 April 2021").

As positive consequence of the infection all the family members have developed antibodies against SARS-CoV-2 (Table 4).

The last observation concerns the youngest family subject (10 years); the symptoms were moderate and faster (**Table 2**), and he showed the best immune response than the others (**Table 4**). This data is in line with the observation in previous studies [20], but we also think that the adequate use of drugs avoided the appearance of more serious symptoms.

In conclusion, the only way to go out from the pandemic emergency is to extend vaccine strategy to the world population.

Authors contributions

Authors contributed equally in the design of the study, the preparation and analysis of the data, and drafted the manuscript.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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REFERENCES

- [1] Krammer, F. (2020) SARS-CoV-2 vaccines in development. Nature, 586:516-527.
- [2] Castells, M.C, Phillips, E.J. (2020) Maintaining Safety with SARS-CoV-2 Vaccines. N Engl J Med, NEJMra2035343.
- [3] Trougakos, I.P., Stamatelopoulos, K., Terpos, E., Tsitsilonis, O.E., Aivalioti, E., Paraskevis, D., Kastritis, E., Pavlakis, G.N., Dimopoulos, M.A. (2021) Insights to SARS-CoV-2 life cycle, pathophysiology, and rationalized treatments that target COVID-19 clinical complications. *J Biomed Sci*, 28: 9.
- [4] Tsai, S.C., Lu, C.C., Bau, D.-T., Chiu, Y.-J., Yen, Y.-T., Hsu, Y.-M., Fu, C.-W., Kuo, S.-C., Lo, Y.-S., Chiu, H.-Y., Juan, Y.-N., Tsai, F.-J., Yang, J.-S. (2021) Approaches towards fighting the COVID-19 pandemic. *Int J Mol Med*, 47(1): 3–22.
- [5] Davies, N.G., Abbott, S., Barnard, R.C., Jarvis, C.I., Kucharski, A.J., Munday, J.D., Pearson, C.A.B. Russell, T.W., Tully, D.C., Washburne, A.D., Wenseleers, T., Gimma, A., Waites, W., Wong, K.L.M., van Zandvoort, K., Silverman, J.D., CMMID COVID-19 Working Group; COVID-19 Genomics UK (COG-UK) Consortium, Diaz-Ordaz, K., Keogh, R., Eggo, R.M., Funk, S., Jit, M., Atkins, K.E., Edmunds, W.J. (2021) Estimated transmissibility and impact of SARS-CoV-2 lineage B.1.1.7 in England. *Science*, eabg3055. doi: 10.1126/science.abg3055.
- [6] Tegally, H., Wilkinson, E., Giovanetti, M., Iranzadeh, A., Fonseca, V., Giandhari, J., Doolabh, D., Pillay, S., San, E.J., Msomi, N. (2020) Emergence and rapid spread of a new severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) lineage with multiple spike mutations in South Africa. *medRxiv*, doi: 10.1101/2020.12.21.20248640.
- [7] Faria, N.R., Morales Claro, I., Candido, D., Moyses Franco, L.A., Andrade, P.S., Coletti, T.M., Silva, C.A.M., Sales, F.C., Manuli, E.R., Aguiar, R.S., Gaburo, N., da C. Camilo, C., Fraiji, N.A., Esashika Crispim, M.A., do Perpétuo S.S. Carvalho, M., Rambaut, A., Loman, N., Pybus, O.G., Sabino, E.C., on behalf of CADDE Genomic Network. (2021) Genomic characterisation of an emergent SARS-CoV-2 lineage in Manaus: preliminary findings https://virological.org/t/genomiccharacterisation-of-an-emergent-sars-cov-2-lineage-in-manaus-preliminary-findings/586.
- [8] Burioni, R., Topol, E.J. (2021) Assessing the human immune response to SARS-CoV-2 variants. *Nat Med*, https://doi.org/10.1038/s41591-021-01290-0
- [9] Lauer, S.A., Grantz, K.H., Bi, Q., Jones, F.K., Zheng, Q., Meredith, H.R., Azman, A.S., Nicholas Reich, G., Lessler, J. (2020) The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application. *Annal of Internal Medicine*, https://doi.org/10.7326/M20-0504.
- [10] Gupta, A., Madhavan, M.V., Sehgal, K., Nair, N., Mahajan, S., Sehrawat, T.S., Bikdeli, B., Ahluwalia, N., Ausiello, J.C., Wan1, E.Y., Freedberg, D.E., Kirtane, A.J., Parikh, S.A., Maurer, M.S., Nordvig, A.S., Accili, D., Bathon, J.M., Mohan, S., Bauer, K.A., Leon, M.B., Krumholz, H.M., Uriell, N., Mehra, M.R., Elkind, M.S.V., Stone, G.W., Schwartz, A., Ho, D.H., Bilezikian, J.P., Landry, D.W. (2020) Extrapulmonary manifestations of COVID-19. *Nature Medicine*, 26: 1017-1032.
- [11] Wiersinga, W.J., Rhodes, A., Cheng, A.C., Peacock, S.J., Prescott, H.C. (2020) Transmission, Diagnosis, and Treatment of Coronavirus Disease 2019 (COVID-19): A Review. *Pathophysiology, JAMA*, **324**(8):782-793. doi:10.1001/jama.2020.12839
- [12] Villapol, S. (2020) Gastrointestinal symptoms associated with COVID-19: impact on the gut microbiome. *Transl Res*, 226:57-69. doi: 10.1016/j.trsl.2020.08.004.
- [13] Wollina, U., Karadağ, A.S., Rowland-Payne, C., Chiriac, A., Torello Lotti, T. (2020) Cutaneous signs in COVID-19 patients: A review. *Dermatol Ther*, **33**(5): e13549. doi: 10.1111/dth.13549. Epub 2020 May 29.
- [14] Berger, J.R. (2020) COVID-19 and the nervous system. J Neurovirol, 26(2):143-148. doi: 10.1007/s13365-020-00840-5.
- [15] Zahra, S.A, Iddawela, S., Pillai, K., Choudhury, R.Y., Harky, A. (2020) Can symptoms of anosmia and dysgeusia be diagnostic for COVID-19? Brain Behav, 10(11): e01839. doi: 10.1002/brb3.1839. Epub 2020 Sep 16.
- [16] Abu-Rumeileh, S., Abdelhak, A., Fosch, M., Tumani, H., Otto, M. (2020) Guillain-Barre syndrome spectrum associated with COVID-19: an up-to-date systematic review of 73 cases. *J Neurol*, 25:1-38. doi: 10.1007/s00415-020-10124-x.
- [17] Kurz, D.J., Eberli, F.R. (2020) Cardiovascular aspects of COVID-19. *Swiss Med Wkly*, 150:w20417. doi: 10.4414/smw.2020.20417. eCollection 2020 Dec 14.
- [18] Lin, L., Luo, S., Qin, R., Yang, M., Wang, X., Yang, Q., Zhang, Y., Wang, Q., Zhu, R., Fan, H., Wang, H., Hu, Y., Wang, L., Hu, D. (2020) Long-term infection of SARS-CoV-2 changed the body's immune status. *Clin Immunol*, 218: 108524. doi:10.1016/j.clim.2020.108524.
- [19] Solinas, C., Perra, L., Aiello, M., Migliori, E., Petrosillo, N. (2020) A critical evaluation of glucocorticoids in the management of severe COVID-19. *Cytokine Growth Factor Rev*, 54: 8-23.
- [20] Gautret, P., Million, M., Jarrot, P.A., Camoin-Jau, L., Colson, P., Fenollar, F., Leone, M., La Scola, B., Devaux, C., Gaubert, J.Y., Mege, J.L., Vitte, J., Melenotte, C., Rolain, J.M., Parola, P., Lagier, J.C., Brouqui, P., Raoult, D. (2020) Natural history of COVID-19 and therapeutic options. *Expert Rev Clin Immunol*, 16(12):1159-1184. doi: 10.1080/1744666X.2021.1847640.