COVID-19 may present with an itchy erythematous papular rash: a case report

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Abstract
Background: the most commonly reported clinical manifestations of Coronavirus Disease (COVID-19) are: fever, fatigue, dry cough, anorexia, myalgias, dyspnoea and sputum production. Other, rarer, manifestations include headache, sore throat, rhinorrhea, nausea, diarrhoea and olfactory or taste disorders. Two recent small-scale studies suggest the possibility of a skin rash being a clinical presentation of the disease. The purpose of our case report is to bring attention to an atypical presentation of the disease (skin rash) and reflect on the importance of the correct identification of COVID-19 suspicious symptoms as part of the crucial activity of case-finding in primary care.

Case presentation: the patient is an Italian 32 years old female nurse who has had several close contacts to COVID-19 cases during her working shifts. On the 13th March 2020 she developed an itchy erythematous papular rash sparing only her face, scalp and abdomen. One week later she developed fever and diarrhoea. During the first week of remote assessment carried out by her General Practitioner (GP), she gradually developed a dry cough, intermittent fever and diarrhoea. At the time of article submission (31 days after the symptoms onset), she has not completely recovered and is still suffering of a dry cough, headache, fatigue and, occasionally, diarrhoea.

Conclusions: this study suggest that skin manifestations could be an early presentation of COVID-19 and, during outbreaks, they should be taken into proper account by primary care providers as possibly caused by Sars-Cov-2. Early identification of COVID-19 patients is a crucial part of the strategy of case detection and case isolation, which has shown to be crucial in the reduction of incidence and COVID-19-related mortality. Further research is needed to establish frequency, symptoms, signs, pathogenesis and role in case detection of skin manifestations in COVID-19 patients.

Background
Coronavirus disease 2019 (COVID–19) is a respiratory illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV–2), firstly identified in the city of Hubei, Wuhan province, in late December 2019.1
On the 11th of March of 2020, the WHO declared the SARS-CoV-2 outbreak as a pandemic, representing a public health emergency of unprecedented dimension, causing major restriction for the everyday life of millions of inhabitants and pressuring health care systems worldwide.\(^2\) Italy has been the first European country to experience a dramatic increase in the number of cases from February 20, 2020 and is still facing one of the largest clusters of COVID-19 in the world.\(^3\)

Next to the majority of asymptomatic cases, the clinical presentation of COVID-19 could range from a mild respiratory infection (common cold-like illness) to a severe pneumonia leading to ARDS (acute respiratory distress syndrome), which is potentially fatal. The most commonly reported clinical manifestations of SARS-CoV-2 infection include: fever, fatigue, dry cough, anorexia, myalgias, dyspnoea and sputum production. Other respiratory symptoms include headache, sore throat and rhinorrhoea. Gastrointestinal manifestations, such as nausea and diarrhoea, have also been reported as possible symptoms of COVID-19.\(^4\)-\(^6\) Recently, a study reported that, of 59 hospitalized patients affected by COVID-19, 33.9% (n = 20) had olfactory or taste disorders. As stated by the authors, it seems clear that the spectrum of symptoms described until now may “fail to give an account of minor symptoms that may be present at earlier stage of the infection”.\(^7\) This could be possibly due to the hospital setting in which these data have been collected until now and it should be noted that no published studies have described the disease’s course in an outpatient setting. In fact, only two pre-published papers suggest that cutaneous manifestations could be present at the onset of Covid-19, namely: i) a case report about a patient with petechial skin rash that was later identified as being SARS-CoV-2 positive in Thailand;\(^8\) ii) a study that analysed cutaneous involvement of 88 hospitalized Covid19 positive patients in Lecco. In this study, authors found that 20.4% (n = 18) of patients developed cutaneous manifestations and that 44% of them (n = 8) had skin manifestations at the onset. Reported skin manifestations were: erythematous rash, widespread urticarial and chickenpox-like vesicles.\(^9\)

The purpose of our case report is to bring attention to an atypical presentation of the disease and to offer a reflection about how this atypical presentation has influenced the health behaviours of the
patient, which can be of little significance on a small scale but could be of great importance if projected in a population perspective.

Case Presentation
The patient is a 32 years old female nurse of Caucasian ethnicity. She works in a private clinic of Emilia Romagna, a region in northern Italy that borders with Lombardy and is, at the present time, the second Italian region for total number of confirmed cases and deaths. On the day of symptoms’ onset (13th March 2020) in her province, Reggio Emilia, confirmed cases were 299 and at the day of article submission (11th April 2020), last official data reported a total of 3263 confirmed cases.\(^{10,11}\)

On the 13th of March, the patient started to feel a mild sense of fatigue and presented an extremely itchy erythematous rash. Small, folliculocentric papules, associated with pruritus, appeared first at the extremities (hands, feet, forearm, legs and back surface of the ears) and then spread to the whole body, sparing only her face, scalp and abdomen. The itch worsened during the nights, causing difficulties to rest. As psychological factors are known to modulate pruritus, at first the patient herself associated the development of symptoms to her psychological stress and to the changes in the working environment and continued working without asking for medical advice.\(^{12}\)

It was only seven days after the onset of the skin rash that she developed fever (37.5°, axillary) and watery diarrhoea (3 or 4 episodes daily). For this reason she called her General Practitioner (GP), who performed a comprehensive remote telephone assessment and identified her as a suspect-COVID–19 case due to the presence of fever, a typical and well known symptom of COVID–19, and due to her epidemiological high-risk profile, i.e. being a healthcare professional exposed to several COVID–19 patients.

It should be noted that the patient did not suffer from any chronic disease and has no personal or familiar history of autoimmune illness, atopy or other skin problems. Furthermore, she does not take any chronic treatment and in the weeks before the symptoms’ onset, she did not take any new drug.

The GP evaluated the patient’s skin rash during this first remote consultation through pictures the patient took herself (Picture 1 and 2).

The patient was advised for home isolation, appropriate fluid intake and self-medication with
paracetamol 500 mg if needed to manage symptoms. For the skin rash, her GP prescribed an oral H1-antihistamine (cetirizine 10 mg once daily). As the patient was living alone (she already lived in self-isolation in order to reduce the possibility of infection of her family members), her GP started telemonitoring her in scheduled follow-up intervals of three days. During the first week of remote assessment, a dry cough appeared gradually. The fever showed an intermittent trend during the day, higher in the evening but never higher than 37.5°C. The diarrhoea gradually improved (from watery diarrhoea to occasional episodes of unformed stool rushes). The itchy rash improved with the administration of oral H1-antihistamine, gradually disappearing. 13 days after the onset of symptoms and 7 days after the appearance of fever the patient got tested for SARS-CoV-2 infection with oropharyngeal swab (RT-PCR) and was found positive. At the day of the article submission, 31 days after the appearance of rash, she has not completely recovered and is still suffering of dry cough, headache and mild to moderate fatigue. Furthermore, even if she doesn’t present pruritus anymore, she reports the persistence of small papules on the arms imparting a stippled appearance to the skin resembling gooseflesh, similar to keratosis pilaris. However, the patient describes these lesions as distinctly palpable but in the performed remote assessment they were not visible.

Discussion
Our patient reported a severe pruritus that worsened during the night, causing difficulties to rest. A frequent cause of severe pruritus is scabies, a skin infestation caused by the mite *Sarcoptes scabiei*, where pruritus is due to a delayed hypersensitivity response to the mite proteins. However, the patient had no suggestive history for scabies nor the disease-specific linear skin burrows. Therefore, the diagnosis of scabies was readily excluded. Another frequent cause of pruritus is an adverse drug reaction. Almost any drug may induce pruritus by various pathogenic mechanisms: some drugs may cause urticarial or erythematous rashes presenting with acute pruritus, but our patient had no recent drug intake. Moreover, other common causes of itchy skin rashes could be reasonably excluded: the patient has no chronic physical or mental illness, she lives in good hygienic conditions, she did not
use any aggressive soaps or cosmetics and she was not pregnant.\textsuperscript{16}

Despite data about skin manifestation in COVID-19 are still limited in literature, \textit{Recalcati et al} reported that 18 patients developed cutaneous manifestations and, as in our case, 14 of them had erythematous rash.\textsuperscript{9} Since we could exclude other causes of an itchy skin rash and the rash itself is similar to aspecific cutaneous involvement occuring during common viral infections, it is very likely that this skin manifestation is related to coronavirus infection.\textsuperscript{17}

The period of infectivity of an individual affected by Sars-CoV-2 is still uncertain, as is the relationship between viral load, disease severity and transmission rate, but some studies suggests that the viral load could be higher soon after the symptoms onset and, then, decrease.\textsuperscript{18} This means that the transmission rate of the infection could be higher in the early stage of the disease. Therefore, the early identification of COVID-19 symptoms appears to be crucial in the strategy of case detection and isolation.

\textbf{Strength And Limitations}

The present study suggests that skin rash could be an early clinical manifestation of COVID-19. The plausibility of the association between our patient’s skin rash and the SARS-CoV-2 infection is supported by several elements: i) recently published reports of skin manifestations related to COVID-19 are consistent with our observations;\textsuperscript{8,9} ii) the presence of a positive SARS-CoV-2 oropharyngeal swab; iii) the high risk epidemiological profile of the patient.

Nevertheless, some limitations have to be mentioned.

Firstly, the patient is a healthcare professional, therefore part of a professional group that in these days of pandemic outbreak is under a huge amount of social pressure. The feeling of being part of a professional group that in a health emergency has the duty to care for ill people and is therefore responsible for public well being is likely to generate stress and stress-related clinical manifestations.\textsuperscript{19} We can therefore not exclude that psychological stress could have had an influence on the subjective perception of pruritus, worsening it. However, we believe that in the case of our patient the role of stress in worsening her symptoms is limited and an alternative diagnosis, such as
psychogenic itch, is extremely unlikely.\textsuperscript{20} In fact, she has no personal or familiar history of mental illness and the screening questionnaire performed during the follow up period for major depressive disorder (PHQ–9), showed borderline results.\textsuperscript{21}

Secondly, the absence of a comprehensive physical examination, due to the personal protective equipment shortage and the massive conversion to remote assessment of the primary care service, could have limited the diagnostic accuracy of the skin rash. However, teledermatology has shown to be as accurate as in-person care, even if the studies have been performed in a dermatology specialist setting and further studies are needed to compare remote dermatologic assessment to in-person care in a primary care setting performed by general practitioners.\textsuperscript{22}

Thirdly, due to the fact that the patient have had several close contacts to COVID–19 cases, it has not been possible to establish the exact incubation period. She developed the skin rash a few days after the symptoms onset observed in many patients, who were tested positive to Sars-CoV.2, she took care during her shifts. This is consistent with the finding about a mean incubation period of 5.2 days (95\%confidence interval [CI], 4.1 to 7.0) described by Li et al.\textsuperscript{23}

Conclusion
The present study is the first case report of a female patient who developed a skin rash as an early clinical manifestation of COVID–19 and has been diagnosed and managed entirely in a primary care setting.

Further studies in larger cohorts of patients are needed to better understand several aspects of the cutaneous involvement of COVID–19, including: absolute frequency in Sars-CoV–2 infection, frequency of presentation at the onset, association with disease course and severity and transmission rate when skin involvement is the unique manifestation of the disease. A better understanding of the early clinical manifestations of COVID–19 will be helpful, especially for front-line primary care providers, to enhance the crucial activity of case finding and early case isolation.

Take-Home messages
During a Sars-CoV-2 outbreak, the sudden appearance of a skin rash in a patient with no other aetiology that explains the clinical presentation should drive physicians to consider as a possible diagnosis COVID-19, especially in high-risk populations.

The probability of a skin rash hiding an underlying Sars-CoV-2 infection depends on the patient's
epidemiological risk profile and on the local epidemiological situation; Further studies are needed in order to understand if the sudden appearance of an isolated skin rash could justify the prescription of home isolation and further investigation for the detection of Sars-Cov-2 infection.

Declarations

Ethics approval and consent to participate

The ethics committee of Modena (AVEN) was approached, and authors were advised that according to Italian law a formal ethical approval was not necessary.

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of data and materials.

The data that support the findings of this study are available on request from the corresponding author.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

SR, as senior GP of the practice, is responsible for the clinical management. AS and PK collected data and drafted the manuscript. MB contributed in a consultant role and made critical suggestions to address differential diagnosis. All authors red the final version of the manuscript, made relevant amendments and approved the final version of the draft.

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Figures
Figure 1

The sequence of the symptoms’ appearance and its relation with the patients health behaviours. In red, the paucisymptomatic period (NB the patient carried out all her normal activities) In green, the symptomatic period, following the onset of typical symptoms
Figure 2

Picture 1: Picture taken by the patient on the 20th of March showing papulo-erythematous rash on the forearm
Figure 3

Picture 2: Photo taken by the patient on the 20th of March showing papulo-erythematous rash on the forearms