

ORIGINAL ARTICLE

The clinics of HHV-6 infection in COVID-19 pandemic: Pityriasis rosea and Kawasaki disease

Recep Dursun  | Selami Aykut Temiz 

Department of Dermatology, Necmettin Erbakan University Meram Medical Faculty, Konya, Turkey

Correspondence

Selami Aykut Temiz, Department of Dermatology, Necmettin Erbakan University Meram Medical Faculty, Yunus Emre Mh., Necmettin Erbakan Üniversitesi, 42080 Meram/Konya, Konya, Turkey.
Email: aykutmd42@gmail.com

Abstract

A new type of coronavirus family (SARS-CoV-2), which can be found in humans and animals, with many varieties and clinical symptoms, was first seen in Wuhan, China in late 2019, under the name novel Coronavirus Disease 2019 (COVID-19). In the literature, cutaneous symptoms related to the disease are generally emphasized. However, it is not yet known whether this new SARS-CoV-2 virus, which has entered our lives, plays a role in the etiopathogenesis of dermatological diseases. The patients who were admitted to the dermatology outpatient clinic between 1 April and 15 May 2019, and on 1 April and 15 May 2020 were retrospectively analyzed by searching the hospital automation system and patient files. The reason for the same months to be included in the study was to exclude seasonal effects on the diseases. After pandemic, the number of patients with Pityriasis rosea and Kawasaki disease increased significantly in patients who applied to the dermatology outpatient clinic. Our study is the first study showing Pityriasis rosea increase during the pandemic period. We think that this increase is related to HHV-6 reactivation. Herein, we wanted to draw attention to two diseases in which Human Herpes 6 (HHV-6) was accused in etiopathogenesis: Kawasaki disease and Pityriasis rosea.

KEYWORDS

COVID-19, HHV-6, Kawasaki disease, Pityriasis rosea

1 | INTRODUCTION

A new type of coronavirus family (SARS-CoV-2), which can be found in humans and animals, with many varieties and clinical symptoms, was first seen in Wuhan, China in late 2019, under the name novel Coronavirus Disease 2019 (COVID-19). It spread to the world very quickly, and was accepted as a pandemic on March 11, 2020.¹ Clinical, therapeutic, vaccination, anti-virus, and anti-spreading studies have been initiated all over the world related to this virus, where human immunity was first introduced. Because viral disease was spreading very fast and had a very lethal feature.² It is also reported that there are many patients with COVID-19 disease asymptomatic.

There are many publications about the cutaneous findings of the disease. In the literature, disease-related skin lesions have been reported in approximately 2% to 20% of COVID-19 patients.³ In the

literature, cutaneous symptoms related to the disease are generally emphasized. However, it is not yet known whether this new SARS-CoV-2 virus, which has entered our lives, plays a role in the etiopathogenesis of dermatological diseases.⁴ Herein, we wanted to aim to evaluate whether two diseases (Pityriasis rosea and Kawasaki disease), in which Human Herpesvirus 6 (HHV-6) was held responsible for etiopathogenesis, after the COVID-19 pandemic.

2 | MATERIALS AND METHODS

This study was conducted at the Necmettin Erbakan University Hospital, a major tertiary hospital, and sees over 1 200 000 patients per year. The patients who were admitted to the dermatology outpatient clinic between 1 April and 15 May 2019, and on 1 April and 15 May

2020 were retrospectively analyzed by searching the hospital automation system and patient files. The reason for the same months to be included in the study was to exclude seasonal effects on the diseases. In the evaluation made based on before and after the COVID-19 pandemic, the total number of patients admitted to the outpatient clinic during these periods was determined. The numbers and rates of patients with Pityriasis rosea and Kawasaki disease among the total patients who applied to the outpatient clinic were calculated. Local ethics committee approval was also obtained for the study.

3 | STATISTICAL ANALYSIS

Data analysis was performed using the SPSS 22.0 program. Mean \pm SD and percentage were used for descriptive statistics. Chi-square test was performed and the *P* value of less than .05 was accepted as statistically significant.

4 | RESULTS

The total number of patients admitted to the dermatology outpatient clinic between 1 April and 15 May 2019 was 6467. Female patients had a slight predominance (55.9%). The mean age of patients was 35.7 ± 29.1 . The total number of patients admitted to the dermatology outpatient clinic between 1 April and 15 May 2020 was 1292. Female patients had a slight predominance (54.8%). The mean age of patients was 36.6 ± 30.2 . In terms of age and gender, there was no significant difference in outpatient applications before and after the COVID-19 pandemic. Table 1 shows the distribution of the patients who applied to the dermatology outpatient clinic before and after the pandemic.

Among the patients who applied to the dermatology outpatient clinic between 1 April and 15 May 2019, 52 patients (0.8%) were diagnosed with Pityriasis rosae. Among the patients who applied to

the dermatology outpatient clinic between 1 April and 15 May 2020, 50 patients (3.9%) were diagnosed with Pityriasis rosae. After pandemic, the number of patients with Pityriasis rosea increased significantly in patients who applied to the dermatology outpatient clinic (*P*: .000).

Among the patients who applied to the dermatology outpatient clinic between 1 April and 15 May 2019, 2 patients (0.03%) were diagnosed with Kawasaki disease. Among the patients who applied to the dermatology outpatient clinic between 1 April and 15 May 2020, 4 patients (0.3%) were diagnosed with Kawasaki disease. After pandemic, the number of patients with Kawasaki disease increased significantly in patients who applied to the dermatology outpatient clinic (*P*: .009). Table 2 shows the distribution of patients with Pityriasis rosae and Kawasaki disease before and after the pandemic.

5 | DISCUSSION

COVID-19 has already had many effects on the routine dermatology practice.⁵ However, it is clear that there will be many more developments and new information in the relationship between COVID-19 and dermatology in the following days. SARS-CoV-2, which is the cause of COVID-19 disease, is not actually a dermatotropic virus. However, various cutaneous manifestations associated with the disease have been reported to develop during COVID-19 disease.^{3,6} Cutaneous symptoms can be classified under five main categories (urticarial lesions, livedo and necrosis, maculopapular eruption, vesicular rash, pseudo-chilblain).³ However, dermatological diseases triggered by SARS-CoV-2 remain a mystery for now.

In our study, it was found that the rate of Pityriasis rosae patients who applied to the dermatology outpatient clinic this year during the pandemic period increased approximately five times compared to the same time last year. The fact that there was no significant increase in the total number of Pityriasis rosae patients was attributed to the low number of total admissions to the hospital during the pandemic period. In our opinion, the increase in the rate of Pityriasis rosae patients among polyclinic patients was more important data. Previously, a case of Pityriasis rosea associated with COVID-19 disease has been reported.⁷ Our findings are the first study in the literature showing the increase of Pityriasis rosea patients and their relationship with COVID-19.

Pityriasis rosea has been mostly associated with reactivation of Human Herpesvirus 6 and 7, but other viral etiology, vaccination, psychological stress, and drugs have also been implicated as the cause of this reaction.⁸ HHV-6, a member of the herpes virus family, is usually transmitted in the first 2 years of life (Roseola infantum) and settles in

TABLE 1 The distribution of the patients who applied to the dermatology outpatient clinic before and after the pandemic

The characteristics of patients	Before COVID-19 pandemic	After COVID-19 pandemic
Mean age	35.7 \pm 29.1	36.6 \pm 30.2
Total number of patients	6467	1292
• Female	3612 (55.9%)	708 (54.8%)
• Male	2855 (44.1%)	584 (45.2%)

TABLE 2 The distribution of patients with Pityriasis rosae and Kawasaki disease before and after the pandemic

The characteristics of patients	Before COVID-19 pandemic	After COVID-19 pandemic	<i>P</i> value
Pityriasis rosae patients, n (%)	52 (0.8%)	50 (3.9%)	.000
Kawasaki disease patients, n (%)	2 (0.03%)	4 (0.3%)	.009

the salivary glands, causing a latent infection.⁹ There are two types of HHV-6, A and B.¹⁰ The reactivation of HHV-6 is blamed for many diseases, including Pityriasis rosae.¹¹ It has been argued that one of the factors causing activation of Herpes viruses is coronaviruses.¹² Along with the COVID-19 Pandemic, it was thought that reactivation of HHV-6 could explain this obvious increase in Pityriasis rosea cases. Another possible trigger could be psychological stress caused by the pandemic period.

Kawasaki disease is a systemic vasculitis of childhood that can affect the coronary arteries. The diagnosis of Kawasaki disease is based on clinical features. Cutaneous symptoms with diagnostic criteria are: Erythema of the mouth or pharynx, strawberry tongue, or stomatitis; polymorphous rash; erythema or edema of the hands or feet.¹³ The etiology of Kawasaki disease is still unknown. HHV-6 is one of the accused reasons for the etiology.¹⁴ In a study conducted during the COVID-19 pandemic, Kawasaki disease was found to increase 30-fold compared to previous years.¹⁵ In our study, there was a 10-fold increase in the rate of patients with Kawasaki disease who applied to the dermatology outpatient clinic compared to the previous year. We think that this increase in Kawasaki disease during the COVID-19 pandemic may be due to coronavirus triggering of HHV-6, which is responsible for the etiology.

6 | CONCLUSION

The COVID-19 disease caused by SARS-CoV-2 still contains great mysteries for dermatology. In order to solve the mysteries about the disease, a lot of data are published about the clinical symptoms caused by the disease, the effects and side effects of drug treatments, and the associated diseases.

Kawasaki disease has been reported to increase compared to previous years. However, there is no data to show the increase of Pityriasis rosae patients in which HHV-6 plays a role in etiopathogenesis, as in Kawasaki disease. Our study is the first study showing pityriasis rosea increase during pandemic period. We think that this increase is related to HHV-6 reactivation. Herein, we wanted to draw attention to two diseases in which Human Herpes 6 (HHV-6) was accused in etiopathogenesis: Kawasaki disease and Pityriasis rosae.

6.1 | Limitations

The only limitation in our study was that the PCR test could not be applied to the patients. Already, it was not possible to test every patient who applied to the dermatology outpatient clinic.

ACKNOWLEDGMENT

The authors thank Güllü Eren, MD, for her statistical analysis support.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ORCID

Recep Dursun  <https://orcid.org/0000-0002-1279-574X>

Selami Aykut Temiz  <https://orcid.org/0000-0003-4878-0045>

REFERENCES

- Lu R, Zhao X, Li J, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet*. 2020;395(10224):565-574.
- Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of 2019 novel coronavirus infection in China. *NEJM*. 2020;382(18):1708-1720.
- Galván Casas C, Català A, Carretero Hernández G, et al. Classification of the cutaneous manifestations of COVID-19: a rapid prospective nationwide consensus study in Spain with 375 cases. *Br J Dermatol*. 2020. <https://doi.org/10.1111/bjd.19163>. [Epub ahead of print].
- Su CJ, Lee CH. Viral exanthem in COVID-19, a clinical enigma with biological significance. *J Eur Acad Dermatol Venereol*. 2020. <https://doi.org/10.1111/jdv.16469>. [Epub ahead of print].
- Temiz SA, Dursun R, Daye M, Ataseven A. Evaluation of dermatology consultations in the era of COVID19. *Dermatol Ther*. 2020. <https://doi.org/10.1111/dth.13642>. [Epub ahead of print].
- Estébanez A, Pérez-Santiago L, Silva E, Guillen-Climent S, García-Vázquez A, Ramón MD. Cutaneous manifestations in COVID-19: a new contribution. *J Eur Acad Dermatol Venereol*. 2020. <https://doi.org/10.1111/jdv.16474>. [Epub ahead of print].
- Ehsani AH, Nasimi M, Bigdelo Z. Pityriasis rosea as a cutaneous manifestation of COVID-19 infection. *J Eur Acad Dermatol Venereol*. 2020. <https://doi.org/10.1111/jdv.16579>. [Epub ahead of print].
- Yüksel M. Pityriasis rosea recurrence is much higher than previously known: a prospective study. *Acta Derm Venereol*. 2019;99(7-8):664-667.
- Mukai T, Yamamoto T, Kondo T, et al. Molecular epidemiological studies of human herpesvirus 6 in families. *J Med Virol*. 1994;42(3):224-227.
- Zerr DM, Meier AS, Selke SS, et al. A population-based study of primary human herpesvirus 6 infection. *N Engl J Med*. 2005;352(8):768-776.
- Broccolo F, Drago F, Careddu AM, et al. Additional evidence that pityriasis rosea is associated with reactivation of human herpesvirus-6 and-7. *J Invest Dermatol*. 2005;124(6):1234-1240.
- Hassan ST. Shedding light on the effect of natural anti-herpesvirus alkaloids on SARS-CoV-2: a treatment option for COVID-19. *Viruses*. 2020;12(4):476.
- Bayers S, Shulman ST, Paller AS. Kawasaki disease: part I. Diagnosis, clinical features, and pathogenesis. *J Am Acad Dermatol*. 2013;69(4):501.e1.
- Kawano Y, Kawada JI, Nagai N, Ito Y. Reactivation of human herpesviruses 6 and 7 in Kawasaki disease. *Mod Rheumatol*. 2019;29(4):651-655.
- Verdoni L, Mazza A, Gervasoni A, et al. An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. *Lancet*. 2020;395(6):1771-1778.

How to cite this article: Dursun R, Temiz SA. The clinics of HHV-6 infection in COVID-19 pandemic: Pityriasis rosea and Kawasaki disease. *Dermatologic Therapy*. 2020;33:e13730. <https://doi.org/10.1111/dth.13730>