Int J Biochem Mol Biol 2022;13(5):49-53
www.ijbmb.org /ISSN:2152-4114/IJBMB0144843

Original Article

Concurrent monkeypox and COVID-19: role of interleukin-1 receptor antagonist-like protein mechanism

Rujittika Mungmunpuntipantip[1], Viroj Wiwanitkit[2,3,4,5]

[1]Private Academic Consultant, Bangkok, Thailand; [2]Joseph Ayobaalola University, Ikeji-Arakeji, Nigeria; [3]Dr DY Patil University, Pune, India; [4]Faculty of Medicine, University of Nis, Serbia; [5]Parasitic Disease Research Center, Suranaree University of Technology, Nakhon Ratchasima, Thailand

Received June 18, 2022; Accepted October 8, 2022; Epub October 15, 2022; Published October 30, 2022

Abstract: Objective: In 2022, monkeypox becomes a new global public health threat. Monkeypox has been present in Africa for a very long time. The COVID-19 epidemic has been affecting this region for some years. The outbreak state persists. The coexistence of the two diseases is an intriguing discovery. There is no documentation of the co-occurrence. Methods: The possibility of coexisting of the two lethal illnesses, monkeypox and COVID-19, is an intriguing scientific subject. Using bioinformatic pathophysiological pathway analysis, the authors investigated the pathophysiological pathways of COVID-19 and monkeypox. Results: The most common pathway was identified. An interleukin-1 receptor antagonist-like protein has been identified as a common pathway between the pathogenic processes of monkeypox and COVID-19. Conclusion: The findings could explain why severe COVID-19 and monkeypox do not coexist.

Keywords: Monkeypox, COVID-19, interleukin, receptor, antagonist

Introduction

In modern clinical medicine, novel zoonotic infections are a major source of worry [1]. A serious public health issue has been created by the spread of monkey pox throughout Europe [2]. A unusual form of the pox called “monkey pox” has likely resurfaced due to zoonosis [1, 3-6]. A serious public health problem has been created by the spread of monkey pox throughout Europe, North America, and Asia [2, 7-12]. It is most probable because of zoonosis that monkey pox, a rare type of the virus, has returned. It is being thought about if it might spread from person to person. The medical community is concerned as the number of cases recorded in various nations rises, and careful planning is needed to get ready for a possibly massive outbreak. We must act quickly and decisively to move forward.

The western half of Africa, including Nigeria, has traditionally been the endemic location for monkeypox infection. Monkeypox has been present in this area for a very long time. For several years, this region has been affected by the COVID-19 pandemic. The outbreak state still exists. The co-occurrence of the two diseases is a fascinating discovery. There is no record of the co-occurrence. A fascinating research question is whether there is any pathobiological mechanism that can explain the possible coexistence of two deadly diseases, monkeypox and COVID-19. The authors explored the pathophysiological pathways of COVID-19 and monkeypox using bioinformatics pathophysiological pathway analysis. The most typical path was investigated.

Materials and methods

Study design

The current study is a clinical bioinformatics investigation that uses the pathway analysis technique. The study retrospectively analyzed the publicly available data using an in silico bioinformatics approach. The study does not deal

with any human, animal, or clinical samples. It requires no sampling and the inclusion/exclusion criteria are not applicable. This technique has been used in previous pathophysiological pathway analysis research [13] to understand the pathophysiological process of virus infection. Direct database mining using standard international databases, PubMed and SCOPUS, yielded knowledge on biological processes involving monkeypox and COVID-19. The data mining or literature search was first done in order to find the publications reporting the biological processes involving monkeypox and COVID-19. All related publications were included, and an exclusion was set for any report without complete data or not in English.

This study used the same bioinformatics protocol as the previous paper [4]. The data for this in silico medical informatics study was extracted from multinational databases. First, standard databases were examined for published data on the pathophysiological actions of monkeypox and COVID-19. PubMed (www.pubmed.com) and Scopus (www.scopus.com) were used as international databases. "Monkeypox" and "COVID-19" were significant words. The key terms "monkeypox", "COVID-19" and "pathway" were used to find publications for further investigation. Reports on biological processes involving monkeypox and COVID-19 were included for further analysis, and any reports with incomplete data or not in English were excluded.

Details of pathogenic processes were gathered from all derived papers. The pathological pathways reported in recruited papers were gathered and analyzed for further interrelationships.

Bioinformatic pathway analysis

A common pathophysiological pathway was first determined for interrelationship analysis. The technique is based on bioinformatics analysis, which identifies verbatim word-for-word matches between stated pathological or pharmacological processes in the literature. The technique enumerated the detected biological processes, including monkeypox and COVID-19 pathophysiological processes, and a common pathway was searched using a conventional procedure as stated in the referencing literature [14]. In summary, the pathophysiological activities of monkeypox and COVID-19 were evaluated in order to discover shared biological pathways. The common cross processes of both illnesses were related to a single node. The identified common node was utilized to construct the final interrelationship network by adding connecting paths to the discovered common node.

The main observation indicator in the present bioinformatics analysis is the identified common node. The common node in bioinformatics studies is the specific biological process that is shared by two or more pathways of pathophysiological or pharmacological interest. To locate the common node, all pathways of pathophysiological or pharmacological interest were listed in stepwise processes and the common process was sought. After the final construction of the common pathway with common node connectivity, the network pathway diagram demonstrating the association between pathophysiological processes and dengue was derived. The conclusion was based on the final network pathway diagram generated by the above-mentioned in silico network research.

Statistical analysis

This is a bioinformatics pathway analysis, and there is no sampling. It is not a quantitative study, and there is no statistical analysis.

Ethical approval

This report is a retrospective bioinformatics study and does not deal with human or animal subjects. It does not require ethical approval. Due to the lack of patients in this investigation, informed consent is not required.

Results

Data mining for bioinformatics pathway analysis

According to database searching (updated on July 26, 2022), there are at least 6,558 and 19 reports on biological processes involving monkeypox and COVID-19, respectively. After the exclusion of reports with incomplete data and not in English, there are 5,656 and 16 for further bioinformatics study. Detailed pathways presented in all included reports were collected and used for further identification of common pathways.

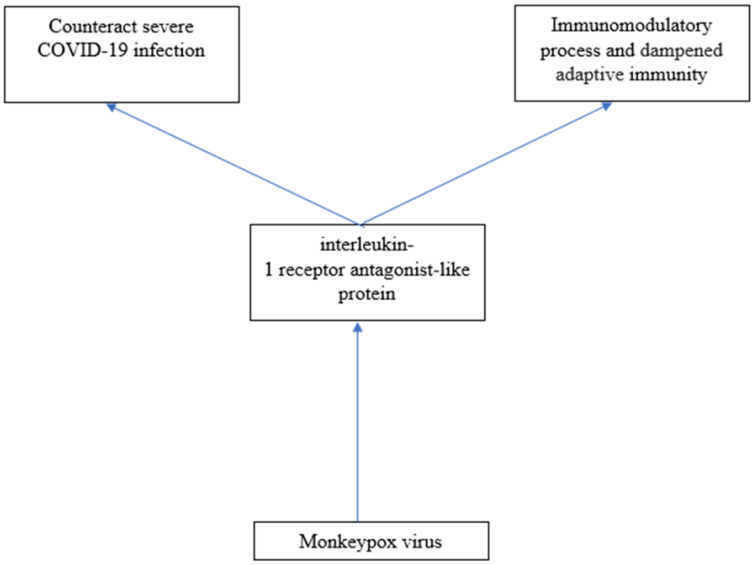

Figure 1. Interrelationship network showing the interrelationship between pathophysiological process of monkeypox and COVID-19 at the interleukin-1 receptor antagonist-like protein.

Bioinformatic pathway identification

According to the findings, the mechanism of interleukin-1 receptor antagonist-like protein, according to the findings, is a common link between the pathophysiological processes of monkeypox and COVID-19 [15, 16]. **Figure 1** depicts the final interrelationship network derived from further interrelationship network analysis. Considering the derived network, the interleukin-1 receptor antagonist-like protein induced by the monkeypox virus can play a role in the pathogenesis of the monkeypox infection and it can also counteract the severe COVID-19 at the same time. Therefore, there is an identified counteracting mechanism.

Discussion

The pathophysiology of a medical disease can be evaluated using bioinformatics, clinical pathological/pharmacological network analysis. The method is based on informatics analysis, which includes locating pathways, identifying common nodes, rearrangement, and finally the creation of an interrelationship network. This is the usual clinical informatics analysis that has been employed in previous studies [13, 14, 17, 18]. The technique is useful because it can rule out problems caused by confounding factors that cannot be totally eliminated in simple in vitro or in vitro experiments. Furthermore, in the case of a highly unusual, novel, or difficult to test situation, the bioinformatics technique can provide essential information needed for early management of a new emergent problem that necessitates an immediate response.

The authors performed a preliminary inquiry in this short preliminary study to explore the common pathophysiological mechanism that could explain the probability of co-occurrence between COVID-19 and monkeypox. Both the studied medical problems are current public health emergencies that require urgent public health containment. According to the current research, a single node connects the pathophysiological processes of monkeypox and COVID-19. Several pathogenic proteins are generated during monkeypox infection. The virus's interleukin-1 receptor antagonist-like protein has been identified [15]. The proteins aid in viral multiplication in the peripheral blood and lungs, resulting in the generation of a powerful and long-lasting adaptive immune response against the virus. On the other hand, an interleukin-1 receptor antagonist-like protein induces quick resolution of COVID-19 [16]. The protein has the potential to rapidly cure massive inflammatory effusions seen in severe COVID-19 [16]. Based on the discovered shared link, it may indicate that there is still a potential for the two diseases to coexist. However, the interleukin-1 receptor antagonist-like protein pathway may result in a milder COVID-19 infection. As a result, detecting the severe COVID-19 among cases of monkeypox is unlikely.

The COVID-19 epidemic is still clinically significant at the moment. The emergence of monkeypox is a new added challenge that necessitates investigation into both diseases. An intriguing problem is that, despite the fact that COVID-19 is highly frequent and there have already been thousands of cases of monkeypox, there have been no reports of co-exis-

tence. Concurrence is an intriguing problem that is still being researched scientifically [19-21]. The current article is a bioinformatics study that uses publicly available data to uncover the common pathway between the two diseases. The technique is standard and can adjust for confounding factors in in vivo and in vitro experiments. According to the authors' view, it can demonstrate the importance of recognizing the possibility of confluence between the two hazardous infectious diseases. If co-existence occurs, diagnosis may be difficult or delayed since there is a pattern of decreased clinical severity depending on if co-existence occurs, identification may be difficult or delayed since there is a pattern of decreased clinical severity based on the established pathway.

The results might be limited since this work is a pathway analysis using bioinformatic techniques. It is a retrospective study and does not involve human or animal subjects. The generalization of the results to the actual in vivo situation might be limited. Further research using in vitro or in vivo study models may provide additional evidence to support the current finding.

Conclusion

Interleukin-1 receptor antagonist-like protein has been discovered as a shared route between monkeypox and COVID-19 pathogenic processes. This could explain why there is no comorbidity between monkeypox and severe COVID-19.

Disclosure of conflict of interest

None.

Address correspondence to: Rujittika Mungmunpuntipantip, Private Academic Consultant, 111 Bangkok 112 Bangkok 103300, Bangkok, Thailand. Tel: 6623288238822; Fax: 6623288238822; E-mail: rujitika@gmail.com

References

[1] Wiwanitkit S and Wiwanitkit V. Atypical zoonotic pox: acute merging illness that can be easily forgotten. J Acute Dis 2018; 7: 88-9.

[2] Mungmunpuntipantip V and Wiwanitkit V. Re-emerging monkeypox: an old disease to be monitored. BMJ Rapid Response Accessible online at https://www.bmj.com/content/377/bmj.o1239/rr-1 Accessed on 21 May 2022.

[3] Hraib M, Jouni S, Albitar MM, Alaidi S and Alshehabi Z. The outbreak of monkeypox 2022: an overview. Ann Med Surg (Lond) 20224; 79: 104069.

[4] Deshmukh P, Vora A, Tiwaskar M and Joshi S. Monkeypox: what do we know so far? A short narrative review of literature. J Assoc Physicians India 2022; 70: 11-12.

[5] Jamil H, Tariq W, Tahir MJ, Mahfooz RS, Asghar MS and Ahmed A. Human monkeypox expansion from the endemic to non-endemic regions: control measures. Ann Med Surg (Lond) 2022; 79: 104048.

[6] Joob B and Wiwanitkit V. Monkeypox: Revisit of the old threat and emerging imported cases. Med J DY Patil Vidyapeeth 2022; 15: 457-9.

[7] Vivancos R, Anderson C, Blomquist P, Balasegaram S, Bell A, Bishop L, Brown CS, Chow Y, Edeghere O, Florence I, Logan S, Manley P, Crowe W, McAuley A, Shankar AG, Mora-Peris B, Paranthaman K, Prochazka M, Ryan C, Simons D, Vipond R, Byers C, Watkins NA; UKHSA Monkeypox Incident Management team, Welfare W, Whittaker E, Dewsnap C, Wilson A, Young Y, Chand M, Riley S and Hopkins S; Monkeypox Incident Management Team. Community transmission of monkeypox in the United Kingdom, April to May 2022. Euro Surveill 2022; 27: 2200422.

[8] Mauldin MR, McCollum AM, Nakazawa YJ, Mandra A, Whitehouse ER, Davidson W, Zhao H, Gao J, Li Y, Doty J, Yinka-Ogunleye A, Akinpelu A, Aruna O, Naidoo D, Lewandowski K, Afrough B, Graham V, Aarons E, Hewson R, Vipond R, Dunning J, Chand M, Brown C, Cohen-Gihon I, Erez N, Shifman O, Israeli O, Sharon M, Schwartz E, Beth-Din A, Zvi A, Mak TM, Ng YK, Cui L, Lin RTP, Olson VA, Brooks T, Paran N, Ihekweazu C and Reynolds MG. Exportation of monkeypox virus from the African continent. J Infect Dis 2022; 225: 1367-1376.

[9] Wallau GL, Maciel-de-Freitas R and Schmidt-Chanasit J. An unfolding monkeypox outbreak in Europe and beyond. Mil Med Res 2022; 9: 31.

[10] Kumar N, Acharya A, Gendelman HE and Byrareddy SN. The 2022 outbreak and the pathobiology of the monkeypox virus. J Autoimmun 2022; 131: 102855.

[11] Adler H, Gould S, Hine P, Snell LB, Wong W, Houlihan CF, Osborne JC, Rampling T, Beadsworth MB, Duncan CJ, Dunning J, Fletcher TE, Hunter ER, Jacobs M, Khoo SH, Newsholme W, Porter D, Porter RJ, Ratcliffe L, Schmid ML, Semple MG, Tunbridge AJ, Wingfield T and Price NM; NHS England High Consequence Infectious Diseases (Airborne) Network. Clinical features and management of human monkeypox: a retrospective observational study in the UK. Lancet Infect Dis 2022; 22: 1153-1162.

[12] Kluge H and Ammon A. Monkeypox in Europe and beyond - tackling a neglected disease together. Euro Surveill 2022; 27: 2200482.
[13] Yasri S and Wiwanitkit V. Usefulness of ginseng in management of dengue: a bioinformatics pathway interrelationship analysis. Int J Physiol Pathophysiol Pharmacol 2022; 14: 114-117.
[14] Sriwijitalai W and Wiwanitkit V. Effect of ginseng against tuberculosis: a pathway interrelationship analysis. Biomed Biotechnol Res J 2019; 3: 120-125.
[15] Estep RD, Messaoudi I, O'Connor MA, Li H, Sprague J, Barron A, Engelmann F, Yen B, Powers MF, Jones JM, Robinson BA, Orzechowska BU, Manoharan M, Legasse A, Planer S, Wilk J, Axthelm MK and Wong SW. Deletion of the monkeypox virus inhibitor of complement enzymes locus impacts the adaptive immune response to monkeypox virus in a nonhuman primate model of infection. J Virol 2011; 85: 9527-9542.
[16] Perna F, Verecchia E, Pinnacchio G, Gerardino L, Brucato A and Manna R. Rapid resolution of severe pericardial effusion using anakinra in a patient with COVID-19 vaccine-related acute pericarditis relapse: a case report. Heart J Case Rep 2022; 6: ytac123.
[17] Yasri S and Wiwanitkit V. Protein tyrosine phosphatase, opisthorchiasis and dengue: a proteomics interrelationship. J Vector Borne Dis 2018; 55: 245.
[18] Wiwanitkit V. Cancer immunomics and application of 'omics' for cancer management. Expert Rev Clin Immunol 2007; 3: 807-812.
[19] Pfaff F, Hoffmann D and Beer M. Monkeypox genomic surveillance will challenge lessons learned from SARS-CoV-2. Lancet 2022; 400: 22-23.
[20] Zhu F, Li L and Che D. Monkeypox virus under COVID-19: caution for sexual transmission - correspondence. Int J Surg 2022; 104: 106768.
[21] Bhattacharya M, Dhama K and Chakraborty C. Recently spreading human monkeypox virus infection and its transmission during COVID-19 pandemic period: a travelers' prospective. Travel Med Infect Dis 2022; 49: 102398.