Inflammation and Cell Signaling 2023; 10: e1239. doi: 10.14800/ics.1239; © 2023 by Lu Zhang, *et al*.
http://www.smartscitech.com/index.php/ics

CASE REPORT

A case of the application of Paxlovid for a patient infected by the SARS-CoV-2 Omicron variant

Lu Zhang[1], Mei Wang[2], Xianwei Ye[1,2,#]

[1] *Department of Respiratory and Critical Care Medicine, Guizhou Provincial People's Hospital, State Key Laboratory of Diagnosis and Treatment of Lung Immune Diseases, Guiyang, Guizhou 550002, China*
[2] *Department of Respiratory and Critical Care Medicine, People's Hospital of Wudang District, Guiyang, Guizhou 550018, China*

[#] Correspondence: Xianwei Ye
E-mail: yxw1205@163.com
Received: December 25, 2022
Published: March 17, 2023

Coronavirus disease 2019 (COVID-19) is a new acute respiratory infectious disease with high infectivity. To date, > 500 million cases of COVID-19 have been confirmed worldwide (World Health Organization). The Omicron variant has affected nearly every country worldwide due to its high infectivity and immune evasion, which has caused widespread anxiety. However, most of the existing treatments do not effectively reduce the risk of progression to more severe disease, or the existing treatments are too costly or not suitable for extensive use. Paxlovid is a novel oral antiviral drug that has proven effective against symptomatic COVID-19 infection by reducing the risk of progression to severe disease, hospitalization, and mortality.

Keywords: Paxlovid; COVID-19; Omicron

Abbreviations: COVID-19, coronavirus disease 2019; SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus 2;T, temperature; P, pulse; R, respiratory rate; CRP, C-reactive protein; IL-6, Interleukin-6; HRCT, high-resolution computed tomography; PaO_2, partial pressure of oxygen; FIO_2, fraction of inspiration O_2.

To cite this article: Lu Zhang, *et al*. A case of the application of Paxlovid for a patient infected by the SARS-CoV-2 Omicron variant. Inflamm Cell Signal 2023; 7: e1239. doi: 10.14800/ics.1239.

Introduction

Coronavirus disease 2019 (COVID-19) is a new acute respiratory infectious disease with high infectivity. To date, > 500 million cases of COVID-19 have been confirmed worldwide (World Health Organization) [1]. COVID-19 has already led to a major global health event. SARS-CoV-2, the virus that causes COVID-19, has mutated over time. The SARS-CoV-2 Omicron variant, first discovered in South Africa, has given rise to a new wave of COVID-19 infections. The Omicron variant has affected nearly every country worldwide due to its high infectivity and immune evasion, which has caused widespread anxiety [1,2]. Several antiviral drugs, monoclonal antibodies, and immunomodulatory drugs have been recommended as treatments against SARS-CoV-2 infection [3-5]; however, most of the existing treatments do not effectively reduce the risk of progression to more severe disease, or the existing treatments are too costly or not suitable for extensive use. Herein, we present a patient with a severe SARS-CoV-2 Omicron variant infection who received Paxlovid treatment.

Case Report

A 65-year-old female patient was admitted to the hospital at 21:38 on 13 September, 2022 due to fever for 1 week and SARS-CoV-2 nucleic acid positivity for 1 day. She had a history of hypertension for > 40 years, with a maximal blood pressure of 200/100 mmHg. She took amlodipine

besylate tablets (5 mg po QD) and valsartan (80 mg po QD) regularly before the onset of COVID-19 symptoms and was normotensive. She had a history of surgery for an ectopic pregnancy at another hospital > 30 years ago. She underwent a blood transfusion during surgery (details unknown). She had a history of diabetes for >10 years and regularly took metformin hydrochloride (0.5 BID) before COVID-19 onset, which maintained euglycaemia. The patient also had a history of cerebral infarction (details unknown). She had not received the COVID-19 vaccine prior to hospitalization. A physical examination at the time of admission revealed the following: T, 38.4℃; P, 101 beats/min; R, 20 breaths/min; SPO_2, 93% (no supplemental oxygen); BP, 126/80 mmHg; height, 172 cm; weight, 90 kg; and BMI, 30.51 kg/m^2. The thorax was symmetric without deformities. Breathing was rhythmic and regular. There were no chest wall varicosities. The bilateral respiratory motion was normal. Three depression signs were negative. Auscultation of the heart and lungs was not performed. The abdomen was flat and soft without an intestinal pattern or peristaltic waves. There was no tenderness, rebound, or muscle resistance in the entire abdomen. The liver and spleen were not palpable. Murphy's sign was negative. There was no tenderness over the liver.

Routine blood testing on 13 September 2022 revealed the following: white blood cell count, 13.57×10^9/L; neutrophil count, 11.23×10^9/L; neutrophil percentage, 82.80%; lymphocyte count, 1.36×10^9/L; erythrocyte sedimentation rate, 120 mm/h; and fasting blood glucose, 8.5 mmol/L. The patient's liver and kidney function, electrolytes, myocardial enzyme panel, markers of myocardial injury, NT-proBNP level, blood lactic acid level, and blood lipid levels were all normal. Blood gas analysis (no supplemental oxygen) showed the following: pH, 7.481; PCO_2, 28.9 mmHg; PO_2, 54 mmHg; HCO_3-, 21.1 mmol/L; base excess, -1.09 mmol/L; and oxygenation index, 248.3 mmHg. A chest CT scan on 13 September (Fig. 4a) revealed the following: 1. bilateral pulmonary infection (viral pneumonia) and 2. bilateral minimal pleural effusion. A nasopharyngeal swab for COVID-19 performed on 12 September 2022 was positive, with a Ct value of 25.3 and ORF1ab of 26.1. The following diagnoses were made based on a consultation with a national-level expert group upon admission: 1. COVID-19 infection (severe); 2. Grade 3 primary hypertension (very high risk); 3. Type 2 diabetes; 4. Sequelae of cerebral infacrtion; and 5.Obesity.

The following treatments were initiated after admission: (1) continuous prone position ventilation with oxygen therapy; (2) antiviral therapy (nirmatrelvir/ritonavir [3 pills po BID]); (3) an intravenous drip infusion of dexamethasone (10 mg QD) to relieve the pulmonary inflammatory response; (4) adjustment of hypoglycaemic therapy (metformin hydrochloride tablets [0.5 g po ac TID]); (5) prophylactic anticoagulation (subcutaneous administration of low-molecular weight heparin calcium injections [4000 u QD]); and (6) traditional Chinese medicine treatment. The patient had a fever and a temperature of 38.4℃ on the first day of admission. Concurrent symptoms included cough, expectoration, chest tightness, and polypnea after intense exercise. Re-examination by chest CT scan on Day 5 of hospitalization revealed that the pulmonary lesions had been absorbed (Fig. 4b). The patient had received antiviral therapy with Paxlovid for 5 days. Re-examination by routine blood testing revealed the following: white blood cell count, 10.32×10^9/L; neutrophil count, 7.08×10^9/L; neutrophil percentage, 68.6%; lymphocyte count, 2.47×10^9/L; lymphocyte percentage, 23.9%; C-reactive protein, 47.18 mg/L; interleukin-6 (IL-6), 9.73 pg/mL; erythrocyte sedimentation rate, 50 mm/h; and oxygenation index, 331 mmHg. Members of the State Council's Joint Prevention and Control Mechanism Comprehensive Team made ward rounds. The patient no longer had fevers, and her cough and chest tightness had improved. In addition, re-examination by chest CT scan indicated that the pulmonary lesions had resolved. Therefore, this patient was downgraded to a nonsevere form of COVID-19. On Day 9 of hospitalization, the patient no longer had fevers, and her fatigue and anorexia had improved. The C-reactive protein and IL-6 levels had decreased, and the fasting blood glucose level had improved. Re-examination by chest CT scan indicated absorption of the previous pulmonary lesions. The routine blood test results, C-reactive protein and IL-6 levels, and erythrocyte sedimentation rate were all within the normal ranges. The chest CT scan changes are shown in Figure 4c. Nasopharyngeal swabs for COVID-19 were negative on Days 15 and 16. The clinical symptoms had resolved. The patient was discharged to home when the discharge criteria for COVID-19 were met.

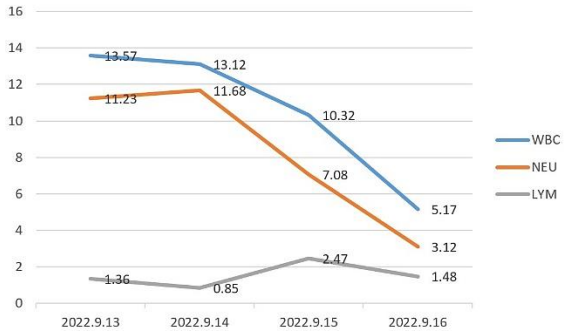

Figure 1. Routine blood tests. On Day 5 after treatment revealed a white blood cell count of 7.17×10^9/L, a neutrophil count of 3.12×10^9/L, and a lymphocyte count of 1.48×10^9/L.

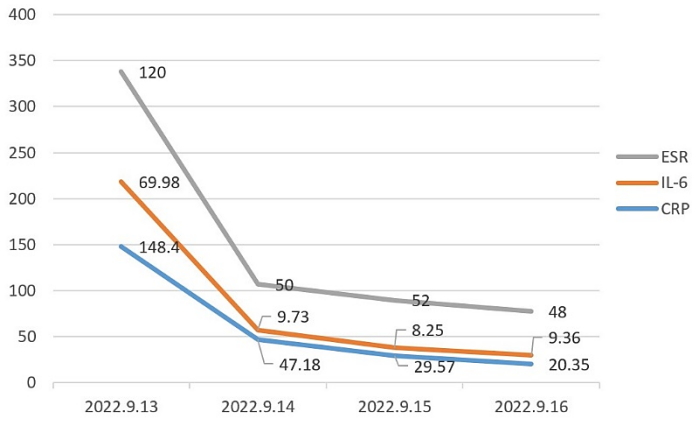

Figure 2. Erythrocyte sedimentation rate, IL-6 and CRP levels. On Day 1 of admission, an ESR of 120 mm/h, an IL-6 level of 69.98 pg/mL, and a CRP level of 148.4 mg/L were found. However, on Day 5 after treatment revealed an ESR of 48 mm/h, IL-6 level of 9.36 pg/mL, and a CRP level of 20.35 mg/L.

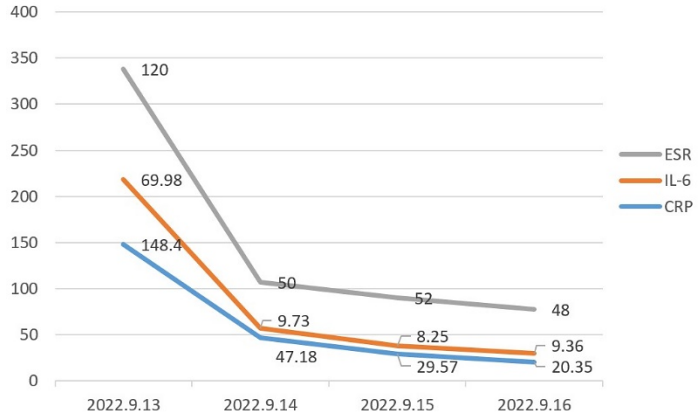

Figure 3. Fasting blood glucose. The fasting blood glucose level of the patient was 8.5 mmol/L on Day 1 of admission; the highest level it reached on Day 2 after admission was 23.7 mmol/L. After treatment, on Day 14 after admission, the fasting blood glucose level remained controlled within the normal range.

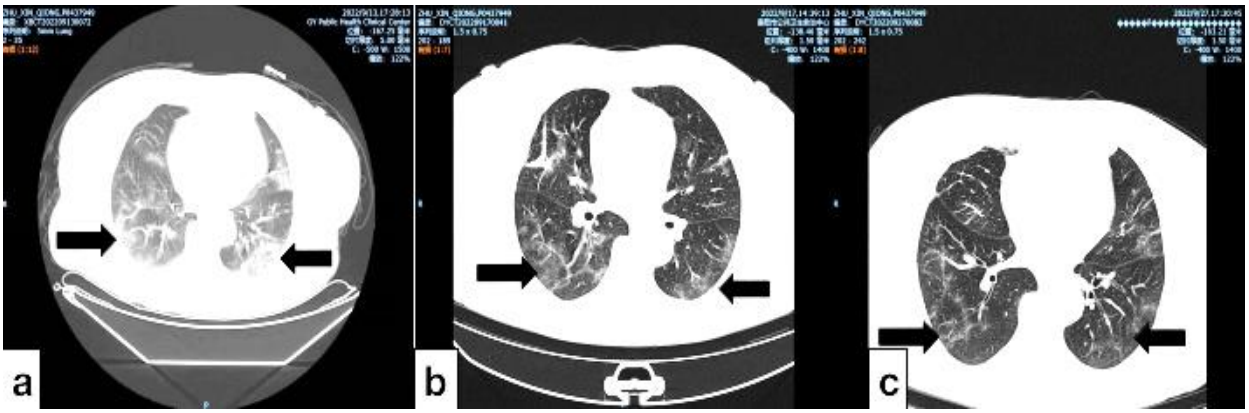

Figure 4. A high-resolution computed tomography (HRCT). (a) There were multiple patchy opacities mixed with ground glass opacities in the subpleural lung regions bilaterally on Day 1 of admission, some of which adhered to the adjacent pleural. (b) The multiple patchy opacities mixed with ground glass opacities in the subpleural lung regions bilaterally were absorbed on Day 4, with some lesions presenting as cord-like changes. (c) The multiple patchy opacities mixed with ground glass opacities in the subpleural lung regions bilaterally were significantly reduced on Day 15, and the boundaries became more distinct.

Discussion

COVID-19 currently remains a global emergency, with > 500 million confirmed cases and > 6 million deaths reported to the WHO. Vaccination is one of the most powerful weapons to prevent COVID-19 infection. It has been reported[6,7] that the third vaccination booster is associated with a reduced risk of pneumonia in adults aged > 60 years and a reduced risk of developing novel coronavirus pneumonia, even in cases of infection with the Omicron variant. The patient referenced in this paper had never received a COVID-19 vaccine. This patient (September 2022) was infected by the Omicron BA.2.76 variant of SARS-CoV-2 during a local epidemic of COVID-19 in Guiyang. This variant, first reported on 15 January 2022, is mainly found in India, the United States, and the UK. Compared with other Omicron variants, the BA.2.76 variant is more infectious, spreads more rapidly, and has a higher viral load. The Omicron BA.2.76 variant can spread for one generation in < 2 days. The Omicron BA.2.76 variant is more difficult to control than other variants. Paxlovid is a novel oral antiviral drug that has proven effective against symptomatic COVID-19 infection by reducing the risk of progression to severe disease, hospitalization, and mortality[6].

Paxlovid is a nirmatrelvir tablet copackaged with a ritonavir tablet. It is a novel oral drug developed by Pfizer to treat COVID-19. Each pill consists of 150 mg of nirmatrelvir and 100 mg of ritonavir. Nirmatrelvir, the core antiviral ingredient, inhibits the coronavirus 3CL protease. Ritonavir slows down the breakdown of nirmatrelvir to help the drug remain in the body for a longer period at a higher concentration. A phase 2-3 trial in patients who had not yet received a COVID-19 vaccine showed [6] that Paxlovid took effect 3 days after the patient developed symptoms, and the effect persisted for 5 days. The abovementioned study assessed COVID-19-related hospitalization or death due to any reason, the viral load, and safety from Days 8-16. The administration of Paxlovid to treat symptomatic COVID-19 infection reduced the risk of developing severe COVID-19 by 89% compared with placebo, and there were no apparent safety hazards.

The patient described in the present study was an elderly female who had various underlying diseases, including hypertension, diabetes, and obesity. In addition, this patient had never received a COVID-19 vaccine. The disease progressed rapidly after hospitalization. The patient presented with intermittent fevers from Day 1 of hospitalization. There were also symptoms of decreased appetite, polypnea after exercise, continuous increase in inflammatory indicators (e.g., C-reactive protein and IL-6), a significant increase in pulmonary lesions, and decreased oxygenation. Considering the presence of several risk factors for progression to severe COVID-19, Paxlovid was the preferred treatment option for this patient. The patient's symptoms dramatically improved 5 days after receiving a full course of Paxlovid treatment. There was a dramatic increase in the COVID-19 Ct value. The pulmonary lesions were not aggravated based on the chest CT scan and showed signs of absorption compared to the admission CT scan.

Studies have demonstrated that a combination of various complications (e.g., diabetes, hypertension, cardiovascular diseases, chronic lung diseases, and cancers), old age, and obesity are all independent risk factors for progression to severe COVID-19 and predict a poor prognosis[8]. One study, including 1122 American patients with COVID-19, showed that the mortality rate in patients with diabetes increased fourfold compared with that in patients without diabetes[9]. A meta-analysis including 33 studies with 16,003 COVID-19 patients showed that the risk of progressing to severe COVID-19 or death increased twofold in patients with diabetes[10]. Another study indicated that fasting blood glucose was closely related to the risk of mortality in COVID-19 patients[11]. In addition, a high fasting blood glucose level upon admission was associated with a poor prognosis in COVID-19 patients[12-13]. At present, the mechanism of interaction between diabetes or hyperglycaemia and COVID-19 is not fully understood. One possible reason may be that diabetes is usually complicated by immune dysfunction, which increases the risk of secondary infections. Prolonged hyperglycaemia can result in an increase in glycation end products and inhibit the production of γ-interferon by T-lymphocytes, thereby affecting viral elimination [14]. Our patient was classified as having severe COVID-19 based on consideration of the presence of concurrent diabetes, a poorly controlled fasting blood glucose level, postadmission symptoms, the oxygenation index, and pulmonary imaging findings. As expected, Paxlovid treatment reduced the risk of progression to severe disease and death.

A rise in the fasting blood glucose level is an independent risk factor for COVID-19 patients, and when combined with diabetes, progression to the critical type of COVID-19. According to other studies [6.15], in an era dominated by Omicron variants, Paxlovid dramatically reduces the risk of severe COVID-19 or COVID-19-related death, especially in elderly patients. Our study confirmed that the COVID-19 vaccine remains the most powerful weapon to prevent progression and death related to COVID-19.

Acknowledgement

This study was supported by grants from National Natural Science Foundation of China (No. 81760013), the Non-profit Central Research Institute Fund of Chinese Academy of Medical Sciences 2019PT320003.

Ethics Approval

Ethical approval was granted from the ethics committee of Guizhou Provincial People's Hospital.

Patient Consent for Publication

A written informed consent was obtained from the patient for publication of the information about them that appears within this case report.

Conflicting Interests

The authors declare that they have no conflict of interests.

References

1. WORLD HEALTH ORGANIZATION. Classification of omicron (B.1.1.529): SARS-CoV-2 variant of concern[EB/OL].[2021-11-26].https://www.who.int/news/item/26-11-2021-classification-of-omicron-(b.1.1.529)-sars-cov-2-variant- of-concern.
2. Kim MK, Lee B, Choi YY, et al. Clinical Characteristics of 40 Patients Infected With the SARS-CoV-2 Omicron Variant in Korea. J Korean Med Sci. 2022;37(3):e31.

3. Drożdżal S, Rosik J, Lechowicz K, et al. An update on drugs with therapeutic potential for SARS-CoV-2 (COVID-19) treatment. Drug Resist Updat. 2021;59:100794.
4. Parums DV. Editorial: Current Status of Oral Antiviral Drug Treatments for SARS-CoV-2 Infection in Non-Hospitalized Patients. Med Sci Monit. 2022;28:e935952.
5. Weinreich DM, Sivapalasingam S, Norton T, et al. REGN-COV2, a Neutralizing Antibody Cocktail, in Outpatients with Covid-19. N Engl J Med. 2021;384(3):238-251.
6. Hammond J, Leister-Tebbe H, Gardner A, et al. Oral Nirmatrelvir for High-Risk, Nonhospitalized Adults with Covid-19. N Engl J Med. 2022;386(15):1397-1408.
7. Li M, Liu Q, Wu D, et al. Association of COVID-19 Vaccination and Clinical Severity of Patients Infected with Delta or Omicron Variants - China, May 21, 2021-February 28, 2022. China CDC Wkly. 2022;4(14):293-297.
8. Zhang Y, Cui Y, Shen M, et al. Association of diabetes mellitus with disease severity and prognosis in COVID-19: A retrospective cohort study. Diabetes Res Clin Pract. 2020;165:108227.
9. Bode B, Garrett V, Messler J, et al. Glycemic Characteristics and Clinical Outcomes of COVID-19 Patients Hospitalized in the United States [published correction appears in J Diabetes Sci Technol. 2020 Jun 10;:1932296820932678]. J Diabetes Sci Technol. 2020;14(4):813-821.
10. Kumar A, Arora A, Sharma P, et al. Is diabetes mellitus associated with mortality and severity of COVID-19? A meta-analysis. Diabetes Metab Syndr. 2020;14(4):535-545.
11. Rao Kondapally Seshasai S, Kaptoge S, Thompson A, et al. Diabetes mellitus, fasting glucose, and risk of cause-specific death [published correction appears in N Engl J Med. 2011 Mar 31;364(13):1281]. N Engl J Med. 2011;364(9):829-841.
12. Lee MH, Wong C, Ng CH, Yuen DCW, Lim AYL, Khoo CM. Effects of hyperglycaemia on complications of COVID-19: A meta-analysis of observational studies. Diabetes Obes Metab. 2021;23(1):287-289.
13. Singh AK, Singh R. At-admission hyperglycemia is consistently associated with poor prognosis and early intervention can improve outcomes in patients with COVID-19. Diabetes Metab Syndr. 2020;14(6):1641-1644.
14. Chee YJ, Tan SK, Yeoh E. Dissecting the interaction between COVID-19 and diabetes mellitus. J Diabetes Investig. 2020;11(5):1104-1114.
15. Najjar-Debbiny R, Gronich N, Weber G, et al. Effectiveness of Paxlovid in Reducing Severe COVID-19 and Mortality in High Risk Patients. Clin Infect Dis. 2022;ciac443.