

A severe COVID-19 patient with diabetes mellitus getting dexamethasone with depression disorders: a case report



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ABSTRACT

Background: Coronavirus disease 2019 (COVID-19) is caused by a novel coronavirus, known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The SARS-CoV-2 coronavirus requires host cells to replicate, leading to rapid and uncontrollable viral replication and could end in increased production of pro-inflammatory cytokines. This case study aims to evaluate a severe COVID-19 patient with diabetes mellitus getting dexamethasone with depression disorders.

Case Presentation: A-56 years old Javanese female who lives in Sidoarjo was admitted to the emergency room of Dr. Soetomo Public Regional Hospital, Surabaya due to shortness of breath from the patient's anamnesis. The shortness of breath was getting worse in the last 3 days before being admitted to the hospital. The patient had a fever in the previous 3 days before being admitted to the hospital. She also had a cough with phlegm for 1 week before being admitted to the hospital. The patient's condition is oxygen saturation at 93% with a simple mask 6-8 lpm (oxygen saturation at 72% in free air. Her medical history revealed that she had suffered from diabetes since approximately 8 years ago and routinely took 5 mg of glibenclamide once a day. She also had high blood pressure from 5 years ago and routinely took 10 mg of amlodipine once a day. Treatment for this patient in severe condition requires comprehensive management such as symptomatic therapy, oxygenation, and adequate nutritional therapy. In addition, the patient received dexamethasone and antidepressant drugs such as fluoxetine 10 mg.

Conclusion: The oxygenation therapy, symptomatic, antiviral, supportive, and adequate nutritional treatment can improve the clinical outcome regarding a severe COVID-19 patient with diabetes mellitus getting dexamethasone with depression disorders.

Keywords: COVID-19, Diabetes Mellitus, Dexamethasone, Depression Disorders.

Cite This Article: Ammar., Rusli, M. 2022. A severe COVID-19 patient with diabetes mellitus getting dexamethasone with depression disorders: a case report. *Bali Medical Journal* 11(1): 67-72. DOI: 10.15562/bmj.v11i1.2962

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Received: 2021-11-26

Accepted: 2022-01-30

Published: 2022-01-21

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by a novel coronavirus, which is currently known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).¹ This disease is rapidly spreading globally and causing Severe Acute Respiratory Syndrome (SARS). On March 11th 2020, WHO declared a global pandemic a serious public health problem.¹

Globally, as of March 26th 2020, the COVID-19 pandemic had 462,801 confirmed cases and caused 20,839 deaths. Regarding COVID-19, as of March 26th 2020, there had been reports in 192 countries with 462,801 confirmed cases and 20,839 deaths.¹ As of March 25th 2020, 790 confirmed cases had been reported in Indonesia from 24 provinces. The data from WHO revealed that on November

25th 2020, there were 60,272,757 confirmed cases and 1,418,260 deaths reported.²

The SARS-CoV-2 coronavirus requires host cells to replicate. The virus attachment and entry are mediated by an S-protein that binds to a receptor on host cells, specifically the angiotensin-converting enzyme 2 (ACE-2). This enzyme can be found in the oral and nasal mucosa, nasopharynx, lungs, digestive system, nervous system, pulmonary alveolar epithelial cells, esophageal epithelial cells, small intestine enterocytes, and colonocytes.³ This virus can reduce the antiviral IFN response, leading to rapid and uncontrollable viral replication and could end in increased production of pro-inflammatory cytokines. As a result of occurring immune system disorders and inflammations, its patient can fall into a severe or critical condition.³

Treatment for COVID-19 patients in severe conditions requires comprehensive management such as symptomatic therapy, oxygen, and adequate nutritional therapy. Some experts recommend administering dexamethasone to severe COVID-19 patients to reduce mortality. To this date, there is no specific management recommendation for COVID-19 patients, including antivirals or vaccines.⁴

The following is a case report of a patient with severe COVID-19 condition and comorbid diabetes mellitus getting dexamethasone therapy with depression disorders.

CASE REPORTS

A 56 years old Javanese female who lives in Sidoarjo was admitted to the emergency room of Dr. Soetomo Public Regional

Hospital, Surabaya due to shortness of breath from the patient's anamnesis for 6 days prior. The shortness of breath was getting worse in the last 3 days before being admitted to the hospital. The shortness of breath was not affected by activity or supine position. She had a fever in the previous 3 days before being admitted to the hospital. She also had a cough with phlegm for 1 week before being admitted to the hospital. The phlegm was yellow and showed no blood. She experienced

bowel movements with liquid consistency for 2 days before her admission to the hospital. She defecated with liquid consistency about 5-7 times in 1 day and got loperamide medicine at home. She experienced a decrease in appetite for about the last 1 month. She felt anxious two months before because it occurred to her husband, who had been treated in an isolation room at Dr. Soetomo Public Regional Hospital 2 months ago and died about 5 weeks ago due to the COVID-19

disease. She had difficulty sleeping from 1 month ago. She was able to eat and take care of herself, but she was constantly worried, thinking about the death of her husband because of the COVID-19 disease. Her medical history revealed that she had suffered from diabetes since approximately 8 years ago and routinely took 5 mg of glibenclamide once a day. She also had high blood pressure from 5 years ago and routinely took 10 mg of amlodipine once a day. Her family medical

Table 1. Physical and laboratory examination of the patient

Parameters	Day 1 (23-6-2020)	Day 7 (29-6-2020)	Day 20 (12-7-2020)
GCS	4-5-6	4-5-6	4-5-6
Blood Pressure	150/90 mmHg	140/90 mmHg	130/90 mmHg
Heart Rate	106 x/minute	94 x/minute	92 x/minute
Respiratory Rate	34 x/minute	32 x/minute	22 x/minute
Oxygen Saturation	72 % Free air (93 % with O2 6-8 lpm)	70 % Free air (91 % with O2 6-8 lpm)	95 % Free air
Temperature	38.3°C	37.0°C	36.0°C
Lung Examination	Bronchovesicular +/+	Bronchovesicular +/+	Vesicular +/+
Hemoglobin	15.2 g/dl	14.1 g/dl	14.5 g/dl
WBC	6,440 /uL	9,400 /uL	7,900 /uL
Neutrophil	85,4 %	76.4%	66.9 %
Lymphocyte	11,6 %	17,6 %	27.1 %
Platelet	158,000 /uL	238,000 /uL	298,000 /uL
Random Glucose	339 mg/dl	179 mg/dl	109 mg/dl
HbA1C	12.8%	-	-
BUN	7 mg/dl	9 mg/dl	11 mg/dl
Creatinine Serum	0.82 mg/dl	0.60 mg/dl	0.69 mg/dl
SGOT (AST)	83 U/L	145 U/L	63 U/L
SGPT (ALT)	62 U/L	125 U/L	38 U/L
Sodium (Na)	137 mmol/L	140 mmol/L	144 mmol/L
Potassium (K)	4.2 mmol/L	4.0 mmol/L	4.8 mmol/L
Chloride (Cl)	96 mmol/L	99 mmol/L	97 mmol/L
Albumin	2.2 mg/dl	2.8 mg/dl	3.1 mg/dl
HbsAg	Non-reactive	-	-
Anti HCV	Non-reactive	-	-
PT	11.8 seconds	12.8 seconds	12.5 seconds
APTT	28.5 seconds	29.5 seconds	29.3 seconds
D-Dimer	9,180 ng/ml	2,960 ng/ml	930 ng/ml
Fibrinogen	755.5 mg/dl	495.5 mg/dl	425.5 mg/dl
CRP	24.7 mg/L	19.6 mg/L	14.4 mg/L
Procalcitonin	0.75 ng/ml	0.15 ng/ml	0.05 ng/ml
Blood Gas Analysis	PO2 61 mmHg	PO2 67 mmHg	PO2 78
Urinalysis	PF Ratio 127 Glucose 2 +	PF Ratio 105 -	PF Ratio 390 -
PCR Swab	Positive	Positive	Negative
Chest X-Ray	Infiltrate in both lungs	Infiltrate in both lungs	Improvement (minimal infiltrate)

history revealed that her husband suffered from COVID-19 and died in the isolation room. A history of previous nutritional needs was found, showing decreased appetite that she had the habit of eating only one to two times a day, in small portions. There was no medical history of allergy.

A physical examination showed that her general condition was weak and *compos mentis* with GCS 4-5-6. She had 160 cm height, 75 kg weight, body mass index (BMI) at 29.3 kg/m², blood pressure at 150/90 mmHg, the pulse at 106 beats/minute, respiratory rate at 34 times/minute, axillary temperature at 38.3°C, oxygen saturation at 93% with a simple mask 6-8 lpm (oxygen saturation at 72% in free air). On her auscultation, bronchovesicular breathing sounds were noted; no additional breathing sounds or additional heart sounds were recorded. Further psychiatric examination revealed fluent relevant verbal contact, normal time-space orientation, slightly reduced willpower, mood-affective anxiety and fear, coherent realistic perception of worry, and psychomotor within normal limits.

Consultation with the psychiatry department revealed adjustment disorders with mixed reactions of depression and anxiety. The psychiatry department provided supportive psychotherapy management and education on relaxation therapy, along with psycho-pharma of 10 mg fluoxetine in the morning and 5 mg clobazam at night.

Based on the patient's anamnesis, physical examinations, and investigations, she was diagnosed with confirmed severe COVID-19 pneumonia, unregulated type 2 diabetes mellitus, hypoalbuminemia, non-specific reactive hepatitis, coagulopathy and adjustment disorder with mixed reactions of depression and anxiety. She received diet therapy of B1 1900 kcal/day, simple mask oxygenation 8 lpm, infusion triofusin 2:1 aminofluid in 24 hours intravenously, 500 mg paracetamol tablets every 8 hours orally when fever, 50 mg ranitidine injection every 12 hours intravenously, 10 mg amlodipine tablets every 24 hours orally, subcutaneous insulin act rapid injection 3x10 units, subcutaneous insulin Lantus injection 18 units every night, infusion

of 20% albumin 100 ml in 4 hours intravenously, 2 albumin capsules every 8 hours orally, 1 multivitamin tablet (Vit C 500 mg and Zinc 20 mg) every 24 hours orally, 600 mg n-acetylcysteine capsules every 8 hours orally, 0.6 ml Lovenox subcutaneous injection every 12 hours, administering 6 mg dexamethasone for 7 days, 2 tablets of lopivia (lopinavir-ritonavir) every 12 hours orally for 7 days. Evaluation of pre-prandial blood sugar showed that the pre-prandial blood sugar in the morning was 268, the pre-prandial blood sugar in the afternoon was 319, and the pre-prandial blood sugar at night was 277—recommendation of administering subcutaneous act rapid injection 3x12 units and subcutaneous Lantus injection of 1x24 units at night. Dosage adjustments could be made if the patient was receiving dexamethasone.

On day 7 of treatment, the complaints of shortness of breath were still noted accompanied by cough with phlegm, complaints of fever have decreased, general condition was weak and awareness was *compos mentis*. The results of urine sensitivity culture examination showed no germ growth, and also, the results of blood and sputum sensitivity culture examination showed no germ growth. The nasopharyngeal PCR swab was positive on June 29, 2020. The chest X-ray showed in both lungs (almost the same impressions as before) (Table 1).

On day 20 of treatment, no complaints from the patient were found, and awareness *compos mentis* with GCS 4-5-6. The Nasopharyngeal PCR swab result was negative on July 12, 2020. The results of the chest photo examination on July 12th 2020 showed an impression of improvement from previous days. A summary of the physical and laboratory examination of the patient is depicted in Table 1.

The patient was scheduled to be discharged from the hospital on day 24 of treatment with no patient complaints. Treatment for hospital discharge included 600 mg n-acetylcysteine capsules every 8 hours orally, subcutaneous act rapid injection 3x6 units, subcutaneous Lantus injection 12 units every night, 2 albumin capsules every 8 hours orally, 10 mg amlodipine every 24 hours orally, 1 multivitamin tablet (Vit C 500 mg and

Zinc 20 mg) every 24 hours orally, and 20 mg rivaroxaban every 24 hours orally, 10 mg fluoxetine in the morning and 5 mg clobazam at night. The patient was directed to perform control to COVID clinic and internal medicine clinic for laboratory evaluation, radiology chest x-ray evaluation and physical examination evaluation. Laboratory evaluation includes fasting glucose plasma, liver function test (SGOT and SGPT), renal function test (BUN and creatinine serum), lipid profile, uric acid, D-Dimer, and complete blood count. The patient is evaluated at the internal medicine clinic regarding blood sugar control and possible complications after COVID.

DISCUSSION

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by a novel coronavirus, which is currently known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This disease is rapidly spreading globally and causing the severe acute respiratory syndrome. On March 11th 2020, it was declared a global pandemic by WHO. Initially, the disease was named as 2019 novel coronavirus (2019-nCoV), then WHO announced a new name for the virus on February 11th 2020; Coronavirus Disease (COVID-19).^{1,5}

In December 2019, a mysterious case of viral pneumonia was first reported in Wuhan, Hubei Province, China. Initially, the transmission source of this case was linked to a fish market in Wuhan. From December 31st 2019 to January 3rd 2020, the number of cases increased rapidly to 44 reported cases. This virus can be transmitted from human to human and has spread widely in China and more than 190 other countries and territories.^{6,7} Globally, as of March 26th 2020, the COVID-19 pandemic had 462,801 confirmed cases and 20,839 deaths. Based on data from WHO, by November 25th 2020, there were reports of 60,272,757 confirmed cases and 1,418,260 deaths.²

Coronavirus is the agent causing COVID-19 which has now become a global pandemic. There are 6 types of coronaviruses identified in humans (HCoVs), including HCoV-NL63, HCoV-229E, HCoV-OC43, HCoV-HKU1, SARS-CoV, and MERS-CoV. SARS-CoV and

MERS-CoV can cause severe respiratory syndrome in humans, while the other 4 only cause mild upper respiratory problems.⁸ SARS-CoV-2 is an enveloped virus with a positive-sense single-chain RNA genome belonging to the Betacoronavirus lineage. The virus spreads with the human acting as the main transmission source, leading to faster transmission.⁷

The existing data reveal that patients with comorbid diabetes mellitus and hypertension, male gender, active smokers are risk factors for SARS-CoV-2 infection. In patients with hypertension, diabetes mellitus, and smokers, it is suspected that there is an increase in ACE-2 receptors.⁸ Another risk factor is close contact, including staying in one house with someone with COVID-19 and having a history of travel to infected areas. Being in one environment but not in close contact within a two-meter radius is considered a low-risk factor. Medical personnel is also populations at high risk of contracting the virus.^{8,9}

The clinical manifestations of COVID-19 have a broad spectrum, starting from asymptomatic, mild or moderate symptoms, and severe symptoms. About 80% of cases are classified as mild or moderate. 13.9% are classified as severe, and 6.1% of patients are classified as critical. Mild symptoms can be defined as acute upper respiratory tract infection with no complication, accompanied by fever, weakness, cough (with or without sputum), anorexia, fatigue, sore throat, nasal congestion, or headache. These patients do not need oxygen supplementation. In some cases, the patients may have complaints of diarrhea and vomiting. Severe COVID-19 patients with pneumonia are characterized by fever, respiratory rate >30 times/minute, severe respiratory distress, or oxygen saturation <90% in free air.⁵ Patients who fall in critical condition may experience acute respiratory distress syndrome characterized by rapid worsening of respiratory symptoms, bilateral opacification on radiological imaging, oxygenation with a P/F ratio of 201-300 at a light category, 101-200 at a moderate category, and <100 mmHg at a severe category of acute respiratory distress syndrome.⁵

In this case, the patient had shortness of breath for 6 days before she was admitted to the hospital and felt her condition was getting worse within 3 days before being admitted to the hospital. The patient also had complaints of fever in the last 3 days and diarrhea during the previous 2 days before being admitted to the hospital. For the past month, the patient had decreased appetite and 93% oxygen saturation with a simple mask of 6-8 lpm (72% oxygen saturation in free air).

Most patients infected with SARS-CoV-2 show respiratory symptoms such as fever, coughing, sneezing, and shortness of breath. The disease course begins with an incubation period of about 3-14 days (averaging 5 days). In this early phase, the leukocytes and lymphocytes are still within the normal limit or slightly decreased, with the patient being asymptomatic. The virus spreads through the bloodstream in the next phase, especially in tissues that express ACE2, such as the lungs, digestive tracts, heart, and nervous system.¹⁰ The symptoms are generally mild in this phase. The next phase occurs about seven days after the initial symptoms appear; the patient is still feverish, experiencing shortness of breath, showing worse lung lesions, and decreased lymphocytes. There are increased markers of inflammation and hypercoagulation. If it is not treated, the next phase will result in uncontrollable inflammation and cytokine overflow, resulting in respiratory distress and sepsis.¹⁰

In this case, the laboratory examination performed at admission obtained data of 85.4% neutrophils, 11.6 lymphocytes, D-dimer 9,180 ng/ml, fibrinogen 755.5 mg/dL, CRP at 24.7 mg/L, procalcitonin 0.75 ng/mL, blood gas analysis pH 7.44 PCO₂ 32 PO₂ 61 with a simple mask 8 lpm HCO₃ 21.3 BE -3.8 SaO₂ 93% P/F ratio of 127.

The diagnostic approach is used on COVID-19 patients based on anamnesis, physical examination, and several supporting examinations. The existing supporting examinations include laboratory examination, radiological imaging, and virological examination.¹¹ Laboratory examinations such as routine hematology, type count, kidney function, liver function, electrolytes, blood gas

analysis, hemostasis physiology, and procalcitonin can be done as indicated.¹¹ Chest X-ray and Computed Tomography Scan (CT-Scan) are the main imaging modalities of choice. That way, some features can be found, such as infiltrate, peribronchial thickening, ground-glass opacification, focal consolidation, pleural effusion, and atelectasis. Chest X-ray is less sensitive than CT-Scan because, in about 40-50% of cases, there are no abnormalities found in chest X-ray. According to viral pneumonia, CT scans' main finding is ground-glass opacification with or without consolidation. The molecular tests recommended by WHO for all patients with suspected COVID-19 are real-time reverse transcription-polymerase chain reaction (rRT-PCR) and by sequencing. A sample is said to be confirmed positive for SARS-CoV-2 if the rRT-PCR is positive for at least two genomic targets (N, E, S, or RdRP) that are SARS-CoV-2% specific). WHO recommends taking specimens at the upper respiratory tract (nasopharyngeal or oropharyngeal swab) or lower respiratory tract (sputum, bronchoalveolar lavage, or endotracheal aspirate).¹² In this case, the chest X-ray showed infiltrates in both lungs and a positive PCR nasopharyngeal swab on June 24th 2020.

The management of severe COVID-19 patients has the same general principles as those with Acute Respiratory Distress Syndrome (ARDS).⁴ The average symptom onset to admission to intensive care is 9-10 days. The majority of risk factors include those over 60 years old, having comorbid diabetes mellitus, hypertension, heart disease, pregnant women, and neonates. Guidelines for treating severe COVID-19 patients include oxygen therapy, symptomatic therapy, conservative fluid therapy, administration of vasoactive agents for COVID-19 patients with shock, administration of broad-spectrum antibiotics as early as possible on suspected bacterial co-infection, administration of antivirals can be considered even though there is no convincing evidence regarding the effectiveness through clinical trials, administration of corticosteroids can be considered in patients suffering from severe or critical conditions, and adequate nutritional therapy.⁴

International experts and researchers have developed a guideline on administering dexamethasone and other corticosteroids for the treatment of COVID-19 patients based on evidence collected from seven clinical trials. WHO highly recommends corticosteroids such as dexamethasone, hydrocortisone, or prednisone to be given orally or intravenously in severe and critical patients. Duration of treatment is carried out once a day for 7-10 days with a daily dose of 6 mg dexamethasone, equivalent to 160 mg hydrocortisone, 40 mg prednisone, 32 mg methylprednisolone (8 mg every 6 hours). Several research results have shown that patients who use ventilators with dexamethasone administration have reduced mortality by about one-third.^{2,13} Patients who only need oxygen by giving dexamethasone have reduced mortality by almost a fifth.^{2,13} In this case, the patient was given oxygenation therapy with 8 lpm simple mask oxygen, symptomatic therapy such as 500 mg paracetamol and ranitidine injection. In addition, adequate nutrition and administration of 6 mg dexamethasone injection for 7 days were also provided.

Insulin therapy in diabetes mellitus patients with steroid use can be subcutaneous admission of insulin basal-bolus regimen with basal insulin and/or prandial insulin, which is the most suitable choice to reach target blood glucose. Premixed insulin can be given twice a day if basal insulin therapy does not control hyperglycemia. Insulin dose adjustments are made for blood glucose control if the steroid dose increases or decreases.¹⁴ The blood glucose target according to the JBDS (Joint British Diabetes Societies) 2014 is 108-180 mg/dL. The recommended initial dose of basal insulin is 10 IU (0.1-0.2 IU/kg/day), with the daily dose can be increased by 20% -40%.¹⁴

Meanwhile, the initial dose of prandial insulin is 4 IU (0.1 IU/kg/day) with a daily dose of up to 15%. Blood glucose monitoring and early intervention are necessary to prevent hyperglycemia and hypoglycemia. Insulin dose adjustments are made for blood glucose control if the steroid dose is reduced or increased. If the steroid dose is reduced by about 50%, the insulin dose can be reduced by 25% from the previous dose. Meanwhile, if the

steroid dose is increased by about 50%, the insulin dose can gradually increase up to 25%. Another option for insulin that can be used in people with diabetes mellitus who use a single dose of steroids every day is NPH with a dose of 0.4 IU/kg/day, which can be increased up to 20% in conditions of blood glucose that is still above 200 mg/dL.^{14,15} This patient received subcutaneous insulin act rapid injection of 3x12 units and subcutaneous Lantus injection of 1 x 24 units at night. Dosage adjustments were made afterward with 3x6 units of rapid act injection and 12 units of Lantus injection every night.

The main complications that can occur in COVID-19 patients include acute respiratory distress syndrome, acute kidney disorders, liver disorders, cardiac injury, pneumothorax, septic shock, disseminated intravascular coagulation, and pneumomediastinum.^{6,16} Several factors influence the prognosis of COVID-19 patients. The main predictors of mortality include diabetes mellitus, hypertension, cardiovascular disease, chronic obstructive pulmonary disease, old age, and male gender. According to research in China, the mortality rate for severe COVID-19 patients reaches 38%, with a median length of intensive care to death of around 7 days.¹⁷ In this case, the patient had moderate acute respiratory distress syndrome with a P/F ratio of 127 accompanied by liver problems with AST 83 U/L, SGPT 62 U/L. In addition, the patient also experienced coagulopathy with an increase in D-dimer of 9,180 and fibrinogen 755.5 mg/dL.

Mood disorders are characterized by disturbance in the regulation of mood, behavior, and affect; subdivided into (1) depressive disorders, (2) bipolar disorders (depression plus manic or hypomanic episodes), and (3) depression in association with medical illness or alcohol and substance abuse. Clinical features of major depression affect 15% of the general population at some point in life; 6-8 % of all outpatients in primary care settings satisfy diagnostic criteria. Diagnosis is made when five or more of the following symptoms have been present for 2 weeks: depressed mood, loss of interest or pleasure, change in appetite or weight, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue or loss

of energy, feeling of worthlessness or inappropriate guilt, decreased ability to concentrate, and recurrent thoughts of death or suicide. Therapy for depression can be given monoamine oxidase inhibitors (MAOIs) or Selective Serotonin Reuptake Inhibitors (SSRIs). SSRIs, like MAOIs, may reduce fasting plasma glucose, but they are easier to use and may also improve dietary and medication compliance.¹⁸ Another drug, such as tricyclic antidepressants (TCAs), can be used for depression therapy. However, TCAs can produce hyperglycemia and carbohydrate craving.¹⁸ In this case, this patient was given SSRIs drug such as fluoxetine 10 mg because the consideration was that the patient had diabetes mellitus.

CONCLUSION

The oxygenation therapy, symptomatic, antiviral, supportive, and adequate nutritional treatment can improve the clinical outcome regarding a severe COVID-19 patient with diabetes mellitus getting dexamethasone with depression disorders.

CONFLICT OF INTEREST

All authors declare there is no conflict of interest regarding the manuscript

ETHICS CONSIDERATION

This case study has followed the COPE and ICMJE protocols regarding the publication ethics procedure.

FUNDING

Self-funded.

AUTHOR CONTRIBUTION

AM and MR were involved in conceptualizing, designing and supervising the manuscript. AM conducted the study and analyzed the data. All authors prepare the manuscript and agree for this final version of the manuscript to be submitted to this journal.

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