The Role of Chest Radiograph, Procalcitonin and Moxifloxacin in Diagnosis and Management of Breast Cancer Patients with COVID-19

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ABSTRAK

Pandemi global coronavirus disease 2019 (COVID-19) saat ini telah menimbulkan hambatan besar dalam pelayanan kesehatan secara global. Penyakit ini disebabkan oleh coronavirus tipe beta baru, yang dikenal sebagai Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), dapat menyebabkan sindrom disfungsi multiorgan sistemik dan kemudian menyebabkan kematian karena berlimpahnya reseptor angiotensin-converting enzyme 2 di berbagai organ. Pasien onkologi bahkan memiliki prognosis yang lebih buruk, berkaitan dengan kerentanan infeksi yang lebih besar karena berada dalam kondisi imunosupresi akibat keganasan dan terapi antikanker. Masalah ini membuat perawatan yang memadai dan tepat sangat dibutuhkan. Beberapa obat telah diketahui memberikan respons yang baik pada pasien COVID-19 melalui uji acak terkontrol. Pada artikel ini, kami melaporkan kasus seorang wanita berusia 49 tahun yang terkonfirmasi COVID-19 melalui manifestasi klinis, profil radiologi, kadar prokalsitonin yang tinggi, dan tes polymerase chain reaction (PCR) yang positif. Pasien juga memiliki riwayat kanker payudara dan tiroid dan telah menjalani berbagai modalitas terapi seperti kemoterapi, operasi tiroid, dan operasi payudara. Pasien sedang menjalani terapi hormon dan mengalami progresivitas penyakit setelah mencapai remisi lengkap berdasarkan pencitraan PET-CT 4 bulan sebelumnya. Pasien dirawat dengan berbagai antibiotik tetapi menunjukkan peningkatan klinis yang signifikan setelah pemberian moxifloxacin.

Kata kunci: *COVID-19, SARS-CoV-2, kanker payudara, foto toraks, Moxifloxacin, Prokalsitonin.*

ABSTRACT

Global widespread of current coronavirus disease 2019 (COVID-19) pandemic has emerged huge predicament to healthcare systems globally. This disease caused by a new beta-type coronavirus, known as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), may lead to systemic multiorgan dysfunction syndrome and subsequently cause death due to abundant angiotensin converting enzyme 2 as its functional receptors throughout body. Oncology patients even have a worse prognosis with greater infection susceptibility because they are in a state of suppression of the systemic immune system due to malignancy and anticancer therapy. This problem makes adequate and appropriate treatment urgently needed. Through randomized clinical

trials, various drugs were known to have good responses in COVID-19 patients. Here, we reported a-49-year-old-woman that was confirmed for COVID-19 by clinical manifestation, radiology profile, high procalcitonin concentration, and positive polymerase chain reaction (PCR) test. The patient also had breast and thyroid cancers history and had undergone various therapeutic modalities such as chemotherapy, thyroid surgery, and breast surgery. She was undergoing hormone therapy but experiencing disease progression after achieving complete remission based on PET-CT scan 4 months before. The patient was treated with various antibiotics but showed a significant clinical improvement by administering moxifloxacin.

Keywords: *COVID-19, SARS-CoV-2, breast cancer, chest radiograph, Moxifloxacin, Procalcitonin.*

INTRODUCTION

In the recent months people worldwide have been facing together, a pandemic situation due to a new beta-type coronavirus, known as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).[1] Rapid viral transmission and high mortality count in various countries such as China, USA, Japan, and Spain encouraged WHO to declare Coronavirus Disease 2019 (COVID-19) as an international public health emergency and then stated as a pandemic. COVID-19 causes deaths more likely because of multiorgan dysfunction syndrome rather than respiratory failure due to the distribution of functional receptors of SARS-CoV-2, angiotensin converting enzyme 2, in various organs throughout the body.[2] Oncology patients are individuals with greater infection susceptibility than individuals without cancer because they are in a state of suppression of the systemic immune system due to malignancy and anticancer therapy such as chemotherapy or surgery. Thus, cancer patients are at a higher risk of being infected with SARS-CoV-2 and have a worse prognosis.[3,4]

Data from the National Clinical Research Center for Respiratory Disease in collaboration with the National Health Commission of the People's Republic of China until 31 January 2020 analyzed 2007 cases from 575 hospitals with an exclusion of 417 cases because the data was incomplete. The data found 18 patients (1%; 95% CI 0.61-1.65) of 1590 COVID-19 cases had a history of cancer.4 Lung cancer was the most cancer found (5 out of 16 patients, 28%). Four (25%) of 16 patients (therapeutic status of 2 out of 18 patients were unknown) received chemotherapy or surgery in the past month and 12 patients (75%) were cancer survivors who had routinely controlled after primary tumor resection.[4]

Most importantly, patients with cancer had a higher risk of experiencing severe events (which is defined as the percentage of patients treated in intensive care who need invasive ventilation or death) compared to patients without cancer (7 (39%) of 18 patients vs 124 (8%) out of 1572 patients; Fisher exact = 0.0003).[4] This report will show a case of a patient with multiple cancers, which is breast cancer and thyroid cancer, that have undergone various therapeutic modalities, have recently undergone chemotherapy, thyroid surgery, and breast surgery. She was undergoing hormone therapy but experiencing disease progression after achieving complete remission based on PET-CT scan 4 months before.[4]

CASE ILLUSTRATION

A 49-years-old female patient came with complaints of worsening cough and shortness of breath since a week before. Two days before the patient began to have fever. The patient had been coughing since 2 months ago. Physical examination showed fully alert awareness, blood pressure of 110/70 mmHg, heart rate of 98 times/minute, respiratory rate of 24 times/minute, body temperature of 38.5^0C, and weakened vesicular sound on the left lung auscultation. Her laboratory showed a prolonged erythrocyte sedimentation rate/ESR (60 mm/hour, normal <20 mm/hour), elevated lactate dehydrogenase/LDH (515 U/L, normal <400 U/L), and elevated procalcitonin (1.17). Her renal laboratory showed ureum of 55 mg/dL (normal 15-40 mg/dL), creatinine of 1.5 mg/dL (normal 0.6-1.1 mg/dL) and eGFR of 41 uL/min. Her liver function test

revealed an increase in SGOT (58 U/L, normal <31 U/L), SGPT (54 U/L, normal <31 U/L), Gamma GT (73 U/L, normal 32 U/L), and direct bilirubin (0.26 mg/dL, normal < 0.20 mg/dL). Other laboratory values were normal. The chest radiograph revealed right lung consolidation, possibly pneumonia or pulmonary metastases, and left pleural effusion (**Figure 1**).

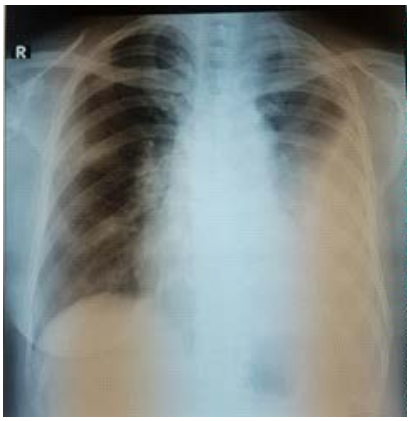

Figure 1. Chest radiograph on 11/3/2020.

The patient was diagnosed with a left breast cancer with positive estrogen and progesterone receptors and negative Cerb-2 since 6 years ago. The patient had already undergone cryotherapy, followed by chemotherapy for 6 cycles and was then declared cancer-free. In the past 3 years, the patient was stated relapsed. One year later, PET CT scan revealed metastases in the bones and lungs, also an increased uptake of FDG in the thyroid which turned out to be thyroid papillary cancer on FNAB. The patient afterward underwent thyroid and left breast surgery, received levothyroxine 100 mcg/day, exemestane 25 mg/day, leuprolide 3M, and ibandronate 6 mg/4 weeks, also underwent thyroid ablation for 12 weeks postoperatively. In 7 months ago, she was stated in complete remission based on her PET CT.

On the first day of admission, the patient received 5x4.5 g of piperacillin-tazobactam, inhalation of salbutamol, bromhexine, and normal saline per 8 hours, nutritional infusion and pleural puncture. On the second day of admission, she complained of worsen dyspnea and fluctuating fever, so that the prior antibiotics were replaced with 3x1 g of meropenem and 1x500 mg i.v. of levofloxacin. The patient was also given methylprednisolone 1x62.5 mg. The next day, dyspnea worsened so that the patient must get 10 LPM of oxygen in NRM. Chest radiograph was performed with worsening findings compared to prior radiograph. Antibiotics were then replaced again with 1x400 mg i.v. of moxifloxacin and 2x1920 mg of cotrimoxazole forte per day (**Figure 2**).

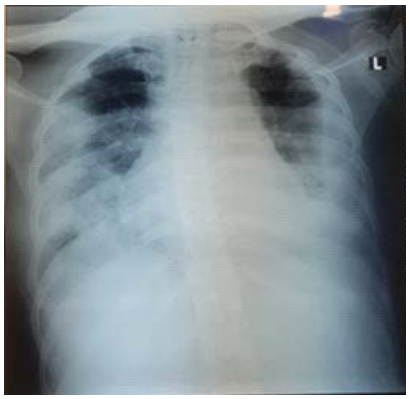

Figure 2. Chest radiograph on 17/3/2020.

SARS-CoV-2 PCR revealed a positive result on the fourth day. Pulmonary doctor suggested for giving 2x75mg of oseltamivir (5-10 days), 1x500 mg of azithromycin (5-7 days), 1x250 mg of levofloxacin (7 days), 2x500mg of levofloxacin (5 days), and high dose vitamin C (14 days), while corticosteroids needed to be stopped. Meanwhile, pleural fluid cytology results were positive for adenocarcinoma.

The patient started to show improvement of all her symptoms, even before the administration of oseltamivir. On the seventh day of admission, her chest radiograph revealed an improvement in right lung infiltrate while her left lung was relatively stqa (**Figure 3**). Based on this chest radiograph, oseltamivir was not given.

On the twelfth day of admission, the patient returned coughing and dyspnea so that chest radiograph was reperformed. The result showed reduced right lung infiltrate, but with homogeneous consolidation of the entire left hemithorax (**Figure 4**).

Based on this result, pleural puncture was reperformed. Dyspnea started to disappear afterward. The patient's clinical condition

improved afterward, she no more complained of fever, cough, nor shortness of breath. On the 15th and 22nd day of admission, patients were given oseltamivir and azithromycin. SARS-COV-2 PCR was then performed on 4/4/2020. SARS-COV-2 Antibody Rapid Test was performed on 6/4/2020 and revealed positive for IgG SARS-COV-2. On 14/4/2020, the results of the SAR-Co-V2 PCR examination came out with a negative result.

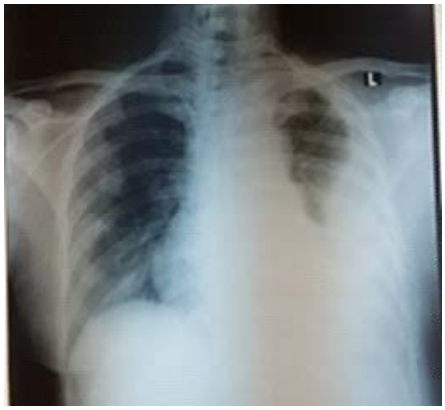

Figure 3. Chest radiograph on 21/3/2020.

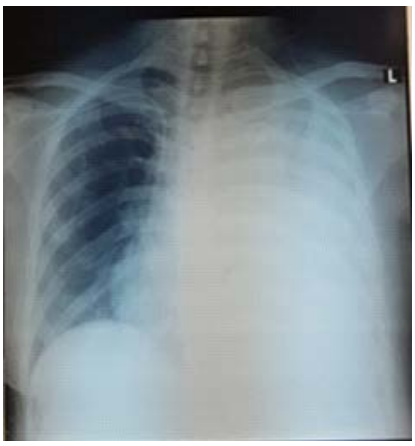

Figure 4. Chest radiograph on 26/3/2020.

DISCUSSION

In this case, a 49-year-old woman who had been diagnosed with breast cancer 6 years ago, had just 10 months ago undergone thyroid cancer surgery and left breast surgery. The patient has been declared achieving complete remission based on PET-CT Scan in December 2019 and is receiving hormone therapy for breast cancer and thyroid cancer. On admission day, the patients showed symptoms and signs related to lung infection, including fever since 2 days before and coughing for a week. These signs are the most common signs found in lung infection that causes current pandemic, COVID-19.

Shortness of breath in patients infected with SARS-CoV-2 tends to occur in moderate cases.[5] Our patient had experienced shortness of breath for 2 months. Shortness of breath that lasted long before current coughing and fever may be caused by pleural effusion due to metastases of her breast cancer. This was proven by improvement of breath after left pleural puncture on the first day of admission. However, on the third day of admission, the patient experienced severe shortness of breath and required 10 liters of oxygen per minute of non rebreathing mask (NRBM) to achieve oxygen saturation >95%. On that day, her chest radiograph showed worsening infiltration of the right lung and left lung, bilateral pleural effusion especially in the left, and bilateral pleuropneumonia, while pulmonary metastases may not be excluded. This figure might be difficult to ascertain SARS-COV-2 infection, but fortunately the following day a positive SARS-COV-2 result was obtained.

Chest X-ray features can also be a guide to determine the suspected occurrence of SARS-COV2 infection, although it is less sensitive when compared to Computed Tomography (CT). The most common radiological features are pulmonary consolidation and ground glass opacities (GGO).[6] The density of ground glass that appears on CT can often correlate with images on chest radiographs that are extremely difficult to detect. Reticular opacification on the chest X-ray may be related to the GGO on CT. Blurry opacity on the chest X-ray can also give an image of GGO on CT. SARS-CoV2 and other viral pneumonia usually produce opacification in more than one lobe so that multifocal lung abnormalities on the chest radiograph can be a significant clue to SARS-CoV2 pneumonia. In the initial SARS-CoV-2 infection, COVID-19 researchers initially noted that pulmonary abnormalities in COVID-19 tended to be distributed in the lower lung and most often in the bilateral lung. One of the most

unique and specific things about COVID-19 pneumonia is the high frequency of peripheral lung involvement, often reflecting inflammatory processes such as organized pneumonia. Some researchers report this frequency (33%-86%) on chest CT. Such peripheral pulmonary opacities also tend to be multifocal, patchy or confluent, and can be easily identified on chest radiographs. Diffuse pulmonary opacification in SARS-CoV-2 infection has a similarity in chest X-ray pattern with other widespread lung infections or inflammatory processes including acute respiratory distress syndrome (ARDS). Pulmonary opacification in a short time can turn into diffuse coalescence or a consolidative pattern within 1-3 weeks of symptom onset, often peaks on days 6-12 after initial presentation. Pleural effusion was reported rarely on chest X-ray in patients with COVID-19 infection and if present, was most often identified late in the course of the disease. Cavitation and pneumothorax were also rarely found in COVID-19 patients but can occur. Large nodules have also been reported in the literature. Emphysema and pneumomediastinum after intubation of COVID-19 patients have also been reported in one case report.[7]

These findings seemed to exist on our patient's chest radiograph on 3/17/2020 which showed opacification in both lobes of the lung, some are multifocal in peripheral and lower field of the lung, while the rest are in the form of consolidation. The similar findings were also shown on chest radiograph on 11/3/2020, including opacification in the left lung and possibly also in the right lung, but it could not be seen due to massive left pleural effusion, mostly peripheral and multifocal. Changes in lung opacification from 11/3/2020 to 17/3/2020 seemed to fit into a study which stated that the peak of opacification occurred 6-12 days after the initial presentation.[8]

Unfortunately, GGO, which is considered specific in COVID-19, was not shown in our patient's chest X-ray. Indeed, GGO is not easy to show in chest radiographs. Chest CT examination in these patients may need to be done to find GGO which is often found in COVID-19 infection. The positive result of SARS-CoV2 PCR a day after worsening of symptoms and chest radiograph in this patient on the fourth day of admission, made chest CT examination no longer be indicated in this patient as the throat swab for SARS-CoV2 showed positive and the patient's condition, then continued to improve.

The above is also supported by recommendations from the American College of Radiology (ACR). This recommendation is based on various considerations. The Centers for Disease Control (CDC) does not currently recommend a chest X-ray or CT for diagnosing COVID-19. Only virus testing is a specific method for diagnosing. As a preliminary examination of the diagnosis of patients with suspected COVID-19, the CDC recommends taking and examining specimens in the upper airway (nasopharyngeal and oropharyngeal swabs) or from the lower airway when virus testing is available.[9]

When the patient complained of worsening dyspnea on the third day of admission, in addition to a chest X-ray, Procalcitonin (PCT) was also evaluated. The results of this examination showed PCT 1.17. According to a study, PCT level of less than 0.1 μg / L indicates no bacterial infection, thus the initiation or administration of antibiotics should be strongly discouraged; PCT level between 0.1 and 0.25 μg / L indicates that bacterial infection is not possible, and the initiation or administration of antibiotics must be prevented; PCT level between 0.26 and 0.5 μg / L indicates the possibility of bacterial infection, and the initiation or continuation of antibiotic therapy should be encouraged; whereas PCT level of greater than 0.5 μg / L strongly indicate bacterial infection and antibiotic treatment, and their continuation should be highly recommended.[10] Therefore, PCT value of this patient showed that she had a bacterial infection, but from the results of peripheral blood tests and an initial differential count it was more suitable for conditions of viral infection. Another alleged alternative is bacterial pneumonia in cancer patients who have undergone chemotherapy many times does not cause an increase in leukocytes because of a decrease in the immune response that occurs in these cancer patients. The presence of viral infections, especially COVID-19 is confirmed by the positive SARS-COV2 PCR results. The

possibility of COVID-19 and bacterial infections at the same time cannot be denied if referring to the available data so that the administration of antibiotics in these patients is still rational.

Management of this patient is of course challenging given the lack of definitive therapy for COVID-19. On the first day care the patient was given the antibiotic piperacillin tazobactam. On the second day, antibiotic treatment was replaced with meropenem and levofloxacin and intravenous methylprednisolone was also administered because the patient was still experiencing a fluctuating fever. On the third day antibiotic treatment was replaced again with intravenous moxifloxacin and cotrimoxazole at a dose of 1920 mg twice daily because the patient complained of worsening dyspnea and needed oxygen up to 10 liters per minute to get 95% oxygen saturation. On the fifth day, dyspnea was improving and fever disappeared. On the seventh day of treatment, the PCT improved to 0.06 ng / mL. The possibility of bacterial infection mixed with COVID-19 infection in these patients was evidenced by a decrease in PCT from 1.17 ng / mL to 0.06 ng / mL. Thus, a normal leukocyte count in this patient suggested that there might be a bacterial infection in an inadequate immune response condition due to cancer or a bacterial infection along with a viral infection.

Huijskens et al[11] rough their prospective study showed that cough, age, pneumonia severity index (PSI), and immunodeficiency could distinguish viral or bacterial or both infections. Cough was an independent symptom that could distinguish lung infections due to viruses or bacteria. If cough is found, then viral etiology is relatively more common (OR 5.536, 95% CI 2.130-14.390). The probability of finding pathogens were smaller with increasing age, but viral etiology was relatively more prevalent because age has less negative effect compared to non-viral etiology (OR closer to 1). According to the univariable multinomial logistic regression model, Pneumonia Severity Index (PSI) as a continuous variable was significantly related to etiology (P = 0.012). Any increase in PSI score points continuously led to a higher likelihood of finding the virus (OR 1.011, 95% CI 1.002-1.020) or mixed (OR 1.012, 95% CI 1.004-1.012) etiology. Immune deficiency associated with etiology was statistically significant (P = 0.028), regardless of other signs and symptoms. A relatively more diverse etiology was found in patients with immune deficiency (OR 2.323, 95% CI 1.006-5.363), while patients without immune deficiency showed a greater bacterial etiology component.[11] In our patient, presence of cough, presence of immunodeficiency (breast cancer), severity of symptoms (breast cancer), and high PSI score, that causes hypoxemia until saturation drops and requires oxygen of 10 liters per minute, reinforces the suspicion of viral and bacterial infection. This is evidenced by the positivity of SARS-CoV-2 PCR.

Atypical bacterial infections were also often found concomitant with SARS-CoV-2 infection. Rawson et al conducted a rapid study of COVID-19 patients about bacterial and fungal co-infections in COVID-19 cases. This study showed 68/806 (8%) COVID-19 patients had bacterial / fungal coinfection, while 89/815 (11%) non-COVID-19 coronavirus patients had these co-infections, some patients who came to the hospital with infections SARS-COV-2 had a clinical phenotype that was not different from atypical bacterial pneumonia.[12] The result showed that although the percentage of co-infection was low, the clinical phenotype of SARS-CoV2 was not different from atypical bacterial pneumonia. According to Rawson et al when the coverage of the SARS-CoV pre-test probability increased, the atypical empirical role needed to be considered. Therefore, the use of azithromycin, a macrolide group, which could include atypical bacteria that also have antiviral effects, in handling COVID-19 is a major therapy in handling COVID-19. Other choice of antibiotics for this atypical bacterial infections are the quinolone and tetracycline.[12]

The antibiotics choice related to this case was also seen in the patient. In this patient, after receiving piperacillin-tazobactam antibiotics and then replaced with meropenem, this patient still did not show any significant clinical improvement such as the remaining fever, and even increased shortness of breath. The patient was then administered moxifloxacin once daily 400 mg intravenously. Moxifloxacin

is a quinolone antibiotic and has the ability to overcome bacterial infections in pneumonia. This type of bacterial infection, administered with Moxifloxacin, is usually obtained from communities and resistant to penicillin and macrolide group antibiotics. Administering moxifloxacin rapidly overcame the fever and shortness of breath in this patient. One day after antibiotic injection this fever and shortness of breath completely disappeared. Apparently, atypical bacteria or bacteria that are resistant to penicillin or macrolide were bacteria that coexist with COVID-19 infection in this patient. The administration of moxifloxacin which has a sensitivity to atypical bacteria robustly improved clinical symptoms subsequently prevent worsening of COVID-19 which is even heavier. The theory that non-virulent pathogenic germs cause exacerbation of COVID-19 resulting in acute respiratory distress syndrome appeared on the fourth day of treatment when worsening symptoms of shortness of these patients but were resolved immediately after given moxifloxacin.

Moxifloxacin is a fourth-generation fluoroquinolone that has activity against microorganisms isolated in broad-spectrum community-acquired pneumonia, including multi-resistant pneumococci and pathogens such as *M. catarrhalis* and *H. influenzae* that are resistant to penicillin, macrolides, and tetracycline. Moxifloxacin also has activity against atypical pathogens including *L. pneumophila, C. pneumoniae*, and *M. pneumoniae*.[13] Moxifloxacin 400 mg once daily has been recommended based on research evidence with a prospective, randomized, double-blind, and meta-analysis clinical trial design in patients with community-based and hospital-based mild, moderate, and severe community-acquired pneumonia. Moxifloxacin is very well tolerated by patients because of the low incidence of side effects in clinical trials and post marketing.[13]

Besides moxifloxacin, this patient also received cotrimoxazole. Cotrimoxazole is the definitive therapy for Pneumocystis carinii pneumonia (PCP). PCP has symptoms similar to COVID-19 namely fever and shortness of breath. Hypoxemia is often found in COVID-19 patients. This happens because of interstitial pneumonia. Chest X-ray images and chest CT imaging also have similarities with COVID-19.[14] PCP often affects HIV patients and non-HIV patients who have decreased immunity such as cancer patients especially those undergoing chemotherapy, radiotherapy, long-term high-dose steroids. The clinical appearance of PCP in non-HIV patients is more severe than in HIV patients, especially in terms of length of stay, may require intensive care unit (ICU) care and require a mechanical ventilator. The mortality rate is also higher in patients who are non-HIV compared to HIV (34-39% vs 6-7%).[14] Breast cancer is a cancer that is often found to be infected with PCP especially those undergoing chemotherapy 19TT, 20 or mTOR inhibitor therapy (Everolimus) 18TT and mTOR inhibitors such as Everolimus 18TT. These patients were not patients who were receiving chemotherapy or mTOR inhibitors, but patients who had received Doxorubicin and Cyclophosphamide chemotherapy one and a half years ago, but had only undergone thyroid and breast surgery 10 months ago, and also were not currently experiencing lymphopenia or were receiving corticosteroid long. So in fact this patient does not have a risk factor for PCP as mentioned in some literature, but clinical and radiological features in this patient can also be found in PCP patients so that cotrimoxazole is appropriate for PCP cases (TMP-SMZ 5-25mg / kgBB every 8 hours or every 6 hours in severe cases for 21 days) 21 can be given. Therapeutic response can be assessed after 3-5 days of therapy or can be waited for up to 4-8 days of therapy.[14,15]

When the patient first experienced worsening shortness of breath on the fourth day of treatment, oseltamivir and hydroxychloroquine were given. However, due to improvement after administering moxifloxacin and cotrimoxazole, administration of oseltamivir and hydroxychloroquine was postponed. Later, after the 10th, 15th, and 22th day of treatment, new hydroxychloroquine, oseltamivir, and azithromycin were given respectively. These three drugs are recommended to patients who have been confirmed infected by SARS-CoV-2.[16] Nasal swab at 21st day of care with results at 31st day of treatment showed

negative results. On the 23rd day of treatment, a rapid test showed positive IgG SAR-CoV2. The effects of moxifloxacin and cotrimoxazol which improved complaints of shortness of breath and fever in patients before the administration of drugs that have been recommended for COVID-19 patients raise the question whether the complaints of fever and shortness of breath in these patients were really due to COVID-19 alone or due to secondary bacterial infection especially atypical bacteria or a combination of both? If the administration of moxifloxacin and cotrimoxazole had been able to overcome the complaints of fever and shortness of breath in this patient, then the possibility of atypical bacteria or Pneumocystis jiroveci infection was the dominant cause of pneumonia in this patient. However, the presence of SARS-CoV-2 virus in these patients could not be ignored because PCR test proved this. So, there was a possibility of SARS-CoV-2 infection in this patient together with atypical bacterial infection and / or Pneumocystis jiroveci. The successful administration of moxifloxacin and cotrimoxazole in managing symptoms in this patient might be a reference for COVID-19 patients with high procalcitonin and normal leukocytes. Further research needs to be done on patients with different characteristics.

The COVID-19 treatment administered to this patient gave satisfactory results because the patient finally experienced a PCR swab conversion from positive to negative after undergoing treatment for 18 days. This shows that not every patient with cancer especially breast cancer or breast and thyroid cancer will experience severe COVID-19 infection that requires intensive care and mechanical ventilator or death. According to the literature cancer patients infected with COVID-19 would experience severe symptoms and required mechanical ventilator or death if they received chemotherapy within 4 weeks before symptom onset (odds ratio [OR] 3.51 [95% CI 1.16–10.59]; p = 0.026) and male (OR 3.86 [95% CI 1.57–9.50]; p = 0.0033). This patient is a woman and was not receiving chemotherapy, but was undergoing hormonal therapy. Therefore, these patients only had mild or moderate symptoms and did not experience worsening symptoms or death in the treatment.[17]

CONCLUSION

COVID-19 infection in breast cancer patients can be found in mild and moderate symptoms without episode of severe events if they are not undergoing chemotherapy especially in the 4 weeks before symptoms and women. Antibiotics for atypical bacteria can benefit COVID-19 patients because of the possibility of a secondary bacterial infection in a viral infection or a joint infection between a viral and bacterial infection. The throat swab PCR is very important in establishing the diagnosis of COVID-19, so there is no need for chest CT scan to find GGO that is not highly specific for SARS-CoV2 infection.

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REFERENCES

1. Hamid S, Mir MY, Rohela GK. Novel coronavirus disease (COVID-19): a pandemic (epidemiology, pathogenesis and potential therapeutics). New Microbes New Infect. 2020;35:100679. Published 2020 Apr 14. Available from: https://www.sciencedirect.com/science/article/pii/S2052297520300317.
2. Verdecchia P, Cavallini C, Spanevello A, Angeli F. The pivotal link between ace2 deficiency and sars-cov-2 infection. Eur J Intern Med. 2020;76(April):14–20. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0953620520301515.
3. Fu L, Wang B, Yuan T, et al. Clinical characteristics of coronavirus disease 2019 (COVID-19) in China: A systematic review and meta-analysis. J Infect. 2020;80(6):656-65. Available from: https://www.sciencedirect.com/science/article/pii/S0163445320301705.
4. Liang W, Guan W, Chen R, et al. Cancer patients in sars-cov-2 infection: a nationwide analysis in china. Lancet Oncol. 2020;21(3):335-7. Available from: https://www.thelancet.com/pdfs/journals/lanonc/PIIS1470-2045(20)30096-6.pdf.
5. Yang J, Zheng Y, Gou X, et al. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. Int J Infect Dis. 2020;94:91-5. Available from: https://www.sciencedirect.com/science/article/pii/S1201971220301363.

6. Yang W, Sirajuddin A, Zhang X, et al. The role of imaging in 2019 novel coronavirus pneumonia (COVID-19). Eur Radiol. 2020;1-9. Available from:10.1007/s00330-020-06827-4.
7. Jacobi A, Chung M, Bernheim A, Eber C. Portable chest X-ray in coronavirus disease-19 (COVID-19): A pictorial review. Clin Imaging. 2020;64:35-42. Available from: 10.1016/j.clinimag.2020.04.001.
8. Yoon SH, Lee KH, Kim JY, et al. Chest radiographic and ct findings of the 2019 novel coronavirus disease (covid-19): analysis of nine patients treated in korea. Korean J Radiol. 2020;21(4):494-500. Available from:10.3348/kjr.2020.0132.
9. Slanetz PJ, Parikh U, Chapman T, Motuzas CL. Coronavirus disease 2019 (covid-19) and radiology education-strategies for survival. J Am Coll Radiol. 2020;17(6):743-745. Available from:10.1016/j.jacr.2020.03.034.
10. Muller F, Crain MC, Bregenzer T, et al. Procalcitonin levels predict bacteremia in patients with community-acquired pneumonia: a prospective cohort trial. Chest. 2010; 138(1):121-9. Available from: https://journal.chestnet.org/article/S0012-3692(10)60356-X/fulltext.
11. Huijskens EGW, Van Erkel AJM, Palmen FMH, Buiting AGM, Kluytmans JAJW, Rossen JWA. Viral and bacterial aetiology of community-acquired pneumonia in adults. Influenza Other Respi Viruses. 2013; 7(4):547-73. Available from: https://core.ac.uk/reader/232453612.
12. Rawson TM, Moore LSP, Zhu N, et al. Bacterial and fungal co-infection in individuals with coronavirus: a rapid review to support covid-19 antimicrobial prescribing. Clin Infect Dis. 2020;ciaa530. Available from:10.1093/cid/ciaa530.
13. Kuzman I, Bezlepko A, Kondova Topuzovska I, et al. Efficacy and safety of moxifloxacin in community acquired pneumonia: a prospective, multicenter, observational study (caprivi). BMC Pulm Med. 2014;14:105. Published 2014 Jun 30. Available from:10.1186/1471-2466-14-105.
14. Cooley L, Dendle C, Wolf J, et al. Consensus guidelines for diagnosis, prophylaxis and management of Pneumocystis jirovecii pneumonia in patients with haematological and solid malignancies, 2014. Intern Med J. 2014;44(12b):1350-63. Available from:10.1111/imj.12599.
15. Bollée G, Sarfati C, Thiéry G, et al. Clinical picture of pneumocystis jiroveci pneumonia in cancer patients. Chest. 2007;132(4):1305-1310. Available from:10.1378/chest.07-0223.
16. Wu R, Wang L, Kuo HD, et al. An update on current therapeutic drugs treating COVID-19. Curr Pharmacol Rep. 2020;1-15. Available from:10.1007/s40495-020-00216-7.
17. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020; 395(10229):1054-62. Available from:10.1016/S0140-6736(20)30566-3.