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The 2019 Novel Coronavirus Disease (COVID-19) causing Severe ARDS: Serial Computed Tomography Findings

Yeni Corona Virüs Hastalığı (COVİD-19) Ağır ARDS'ye Neden Oluyor: Bilgisayarlı Tomografi Bulguları Serisi

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Abstract

Since mid-December 2019, a novel coronavirus (COVID-19) has spread to many countries around the world, and the number of critically ill patients with COVID-19 is increasing as the number infections increase. The optimum treatment and prognosis of the disease is still unknown. Here, we present the clinical course and serial computed tomography of a critically ill Korean patient with COVID-19. The progression of COVID-19 infection is fast and aggressive, and no treatment protocol has yet been established. Additional clinical data are required to determine whether or not corticosteroid use is clinically beneficial.

Key words: *Coronavirus, viral load, corticosteroids, pneumonia.*

Özet

Yeni korona virüs (Covid-19) 2019 Aralık ortalarından beri dünyada pek çok ülkede yayılmakta ve COVID-19'lu ağır hasta sayısı, enfeksiyon sayısı arttıkça artmaktadır. Hastalığın optimum tedavisi ve prognozu halen bilinmemektedir. Burada, COVİD-19'lu Kore'li bir ağır hastanın klinik seyri ve seri bilgisayarlı tomografi bulgularını sunduk. COVİD-19 enfeksiyonunun progresyonu hızlı ve agresif olup henüz tedavi protokolü oluşturulmamıştır. Kortikosteroid kullanımının klinik yararı olup olmadığını belirlemek için ilave klinik verilere ihtiyaç vardır.

Anahtar Sözcükler: *Korona virüs, virüs yükü, kortikosteroid, pnömoni.*

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Since mid-December 2019, a novel coronavirus (COVID-19) has spread to many countries around the world. On March 11, 2020, the World Health Organization declared a pandemic, identifying COVID-19 as a public health emergency of international concern (1).

In the second week of March 2020, the number of confirmed cases in Korea passed the 8,000 mark, although accurate counting was a difficult task being experienced worldwide. The numbers of patients who are being cured and discharged is increasing over time, although the number of patients classified as critically ill with COVID-19 that require ventilator or extra-corporeal membrane oxygenator support is also gradually increasing. While data on the epidemiology and clinical manifestations of the disease is accumulating, clinical data on critically ill patients is lacking. The clinical course changes in computed tomography (CT) findings and cycle threshold (Ct) values, which means that the cycle number at which the fluorescent signal of the reaction crosses the threshold can help to confirm the characteristics of the disease and support the creation of a treatment plan for the patients. To offer an overview of the clinical features of COVID-19 infection, we present a case of a patient in Korea.

CASE

A 78-year-old man with no remarkable past or family medical history presented with chills, myalgia, cough and sputum on February 28, 2020. The symptoms and clinical course of the patient are presented in Figure 1.

Upper respiratory tract (URT) and lower respiratory tract (LRT) specimens were collected from the patient. Nasopharyngeal and oropharyngeal swabs were collected for URT, and sputum was used for the LRT specimen (2). Quantitative real-time polymerase chain reaction amplification was carried out using the AllplexTM 2019-nCoV assay (Seegen, Seoul, Korea) (3). Ct values were checked for the RNA-dependent RNA polymerase gene (R gene) and E gene.

The patient was found to be COVID-19 positive (Ct value: upper R gene, 19.86; upper E gene, 17.1; lower R gene, 21.92; lower E gene, 18.59) upon examination by the public health center, and the patient was hospitalized in a community hospital in Busan, Korea. On day 2, a chest radiography revealed mild haziness in the left lower lobe, and a chest CT revealed ground-glass opacities in the left lower lobe (Figure 2). Shows the serial changes in chest CT and radiography. The patient was started on lopinavir/ritonavir (Kaletra, AbbVie); 2 tablets (lopinavir 200 mg/ritonavir 50 mg) were given orally bid. On day 4, fever and sputum persisted and loose stool started. Chest radiography findings worsened, and the patient had a fever of 39.0°. Accordingly, the ceftriaxone antibiotic was started on day 5, and piperacillin/tazobactam and levofloxacin were started on day 6. The patient showed no improvement.

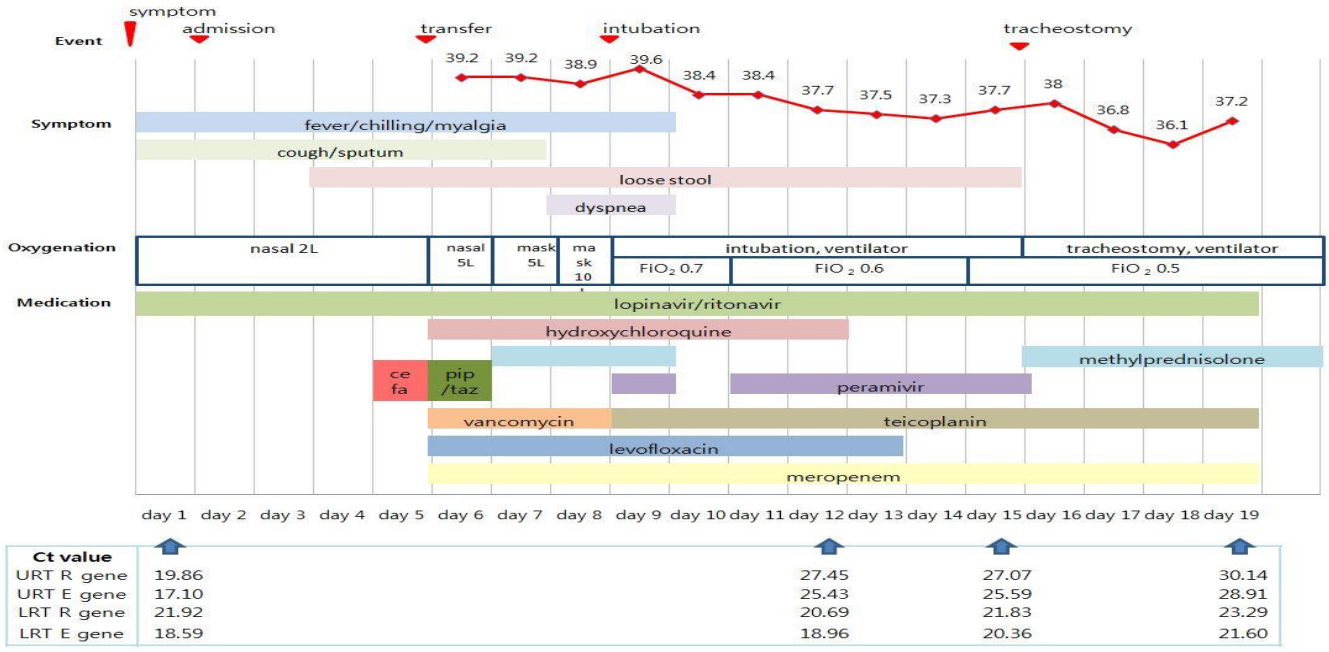

Figure 1: *Clinical course of the patient. Ct values: cycle threshold value; URT: upper respiratory tract; LRT: lower respiratory tract; cefa: cephalosporin; pip/taz: piperacillin/tazobactam; FiO2: fraction of inspired oxygen*

On day 6, the patient was transferred to the hospital in Busan, Korea. Upon presentation, he had no dyspnea, but required oxygen supplementation via a nasal cannula (2L/min). Vital signs: blood pressure, 148/88 mmHg; pulse rate, 85 beats/min; respiratory rate, 13 breaths/min; and body temperature, 38.3°C. Laboratory tests revealed a white blood cell count (WBC) of 5,290/μL, lactate dehydrogenase (LDH) of 570 U/dL, and high sensitivity C-reactive protein (Hs-CRP) of 14.8 mg/dL. Table 1 shows the detailed blood test results. A follow-up chest CT showed an increase in the extent of the multifocal peribronchial ground grass opacity in bilateral lungs and mild pleural effusion. A sustained dose of lopinavir/ritonavir was given and hydroxychloroquine and antibiotics (meropenem 1g tid, vancomycin 1g bid, levofloxacin 750 mg qd) were administered. Despite the use of acetaminophen and non-steroidal anti-inflammatory drugs (NSAIDs), the high fever persisted. Although the test for influenza was negative, peramivir was injected clinically. The patient had no underlying disease, although a chest CT showed underlying pulmonary fibrosis. Methylprednisolone (0.5 mg/kg) was administered from day 7 to day 9.

Subsequently, the patient's dyspnea worsened and an intubation was performed on day 9. A follow-up COVID-19 test was positive on day 12 and Ct values were: upper E gene, 25.43; R gene, 7.45; lower E gene, 18.96; R gene, 20.69.

Serial laboratory tests and a chest radiography were performed. The chest radiography revealed diffuse consolidation in bilateral lungs. On day 15, a follow-up chest CT showed diffuse ground-grass opacity, consolidation in the bilateral lungs and increased interstitial thickening. The COVID-19 test was still positive (Ct values: upper R gene, 27.07; upper E gene, 25.95; lower R gene, 21.83; lower E gene, 20.36).

A tracheostomy was performed and injections of methylprednisolone (1 mg/kg) were started on day 16. After starting methylprednisolone, the patient's oxygen demand decreased and his chest radiography findings improved. (Figure 3) The clinical situation was improved through the use of a higher dose of corticosteroid; however, on day 21 the methylprednisolone was stopped due to gastrointestinal bleeding. Close monitoring and optimum supportive care were continued, with measurements of the Ct value.

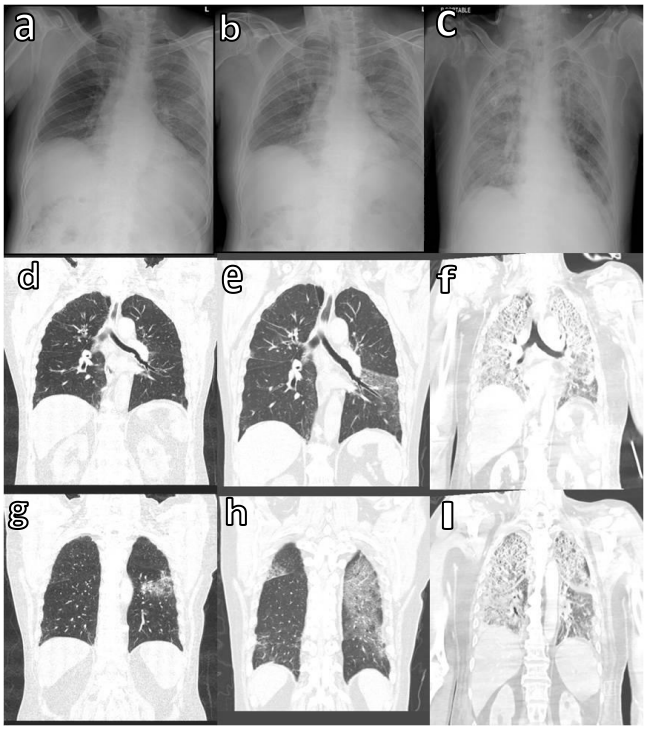

Figure 2: *Radiologic findings of the patient. Chest radiography on day 2 (A), chest radiography on day 6 (B), Chest radiography on day 15 (C), chest computed tomography on day 2 (D and G), computed tomography on day 6 (E and H), chest computed tomography on 15 (F and I)*

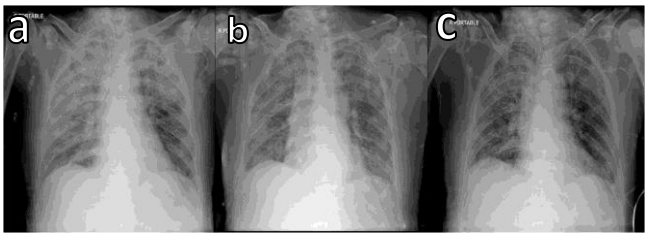

Figure 3: *Chest radiography after methylprednisolone administration. Chest radiography on day 16 (A), chest radiography on day 18 (B), chest radiography on 20 (C)*

DISCUSSION

As the number of COVID-19 infections increase worldwide, the number of critically ill patients with COVID-19 is also increasing. COVID-19 infection is particularly risky for older patients and those with underlying diseases (4). The patient in the present study was otherwise healthy, with no specific past history, aside from the 78 years of age. At the time of the first diagnosis, CT showed mild pneumonia, while the peribronchial pneumonic consolidation gradually increased on follow-up CT. Pneumonia progressed rapidly in a short period.

The progression of pneumonia was apparent on a serial chest radiography, although it was difficult to determine the exact degree, and so a follow-up chest CT was performed, showing far more severe lesions than the chest radiography.

Table 1: Laboratory test results of the patient

Variables	Day 2	Day 6	Day 8	Day 10	Day 12	Day 15	Day 17	Day 19
WBC, /μL	5400	5290	4560	11860	7870	8790	5520	5500
Segment neutrophil, %	66.0	84.9	91.1	96.5	80.0	78.0	74.0	81.0
Lymphocyte, %	2.4	7.5	6.1	1.8	4.0	4.0	7.0	5.0
Eosinophil, %	0.1	0.0	0.0	0.0	0.0	1.0	0.0	0.0
Hemoglobin, g/dL	15.0	13.3	14.3	12.6	14.0	12.3	9.8	10.5
Platelets, ×103/μL	147	104	100	125	79	96	96	117
BUN, mg/dL	16.5	20.8	19.8	29.2	38.6	39.1	62.3	73.9
Creatinine, mg/dL	0.99	0.89	0.78	0.92	0.77	0.68	1.51	1.1
Total bilirubin, mg/dL	0.67	0.77	1.14	1.79	2.79	2.81	2.19	6.00
AST, U/L	19	34	49	34	33	52	32	56
ALT, U/L	20	20	29	27	26	28	25	46
LDH, U/dL	207	570		865	852	885	441	535
Sodium, mEq/L	135.0	125.1	134.2	132.3	136.0	138.0	139.5	142.1
Potassium, mEq/L	4.50	4.17	4.48	4.78	4.27	4.30	4.01	3.96
Chloride, mEq/L	101.0	98.9	104.0	104.5	102.0	102.6	102.6	104.7
Total protein, g/dL	6.8	6.2	5.9	5.4	5.1	5.2	5.4	5.9
Albumin, g/dL	4.1	3.3	3.5	2.8	2.7	2.2	2.2	2.9
Hs-CRP, mg/dl	7.43	14.80	18.30	21.54	20.69	23.76	21.60	4.48
Pro-calcitonin, ng/mL		0.392		0.378				
PT, sec	11.4	13.8	17.5	12.8	13.5	14.0	14.1	14.1
PT INR	1.04	1.04	1.41	0.94	1.01	1.06	1.07	1.07
Troponin i	14				370	151	107	72

WBC: white blood cell; BUN: blood urea nitrogen; AST: aspartate aminotransferase; ALT: alanine aminotransferase; LDH: lactate dehydrogenase; Hs-CRP: high sensitivity C-reactive protein; PT: prothrombin time; INR: international normalized ratio

Another unusual finding was that the patient's oxygen demand was not as large as would be expected based on the chest CT images. On day 6, upon his presentation to our hospital, the patient had no complaints of dyspnea, and oxygen saturation was 92~98% with nasal oxygenation of 2L. On day 15, chest CT showed damage to the entire lung because of the pneumonia, but the fraction of inspired oxygen on ventilator was 0.5~0.6.

In reports concerning the laboratory tests in early stages of the disease, lymphocytopenia appears to be a negative prognostic factor (4). Furthermore, highly elevated LDH and CRP levels are associated with disease severity (5), and the patient in the present study showed similar characteristics (Table 1).

Similar to the influenza virus, the amount of COVID-19 output was large in the early phase, and it was confirmed that the virus output of symptomatic and asymptomatic people was similar (6,7). In this case, comparing the Ct values at the time of the first CT (day 2) and at the time of the last CT (day 15) revealed pneumonia to be more severe in the CT performed later, although the viral load decreased. It was thus considered that the viral load was not related to the patient's lung condition or the severity of the infection.

In Korea currently, lopinavir/ritonavir and hydroxychloroquine are being administered for the treatment of COVID-19 (6), with antibiotics administered together with both drugs, considering the possibility of bacterial pneumonia. However, it is questionable whether lopinavir/ritonavir and hydroxychloroquine are helpful. While they may help lower the concentrations of the virus, they have not prevented the rapid clinical progression. These results are in part consistent with the randomized controlled trials in China comparing the lopinavir/ritonavir group with a standard care group (8). Despite the medication, the patient's fever persisted and the pneumonia

progressed. After peramivir was administered for approximately 6 days, the fever improved.

Although, intravenous glucocorticosteroids were commonly used in patients with severe Middle East respiratory syndrome or severe acute respiratory syndrome, their effects remain controversial, and their efficacy for the treatment of COVID-19 is as yet undetermined (9). Injecting methylprednisolone (0.5 mg/kg) on days 7–9 resulted in no significant changes, while clinical improvement was noted after injecting methylprednisolone (1 mg/kg) on day 15. It is not known exactly what it was that affected the clinical course, but these results may derive from the dose of methylprednisolone or the timing of the disease progression. More data on methylprednisolone will be needed in the future.

CONCLUSION

Severe COVID-19 infection proceeds rapidly, according to the clinical finding and chest CT findings, although no effective drug has yet been identified. In such situations, the use of glucocorticosteroids may be clinically useful. The number of patients continues to increase worldwide, while data on the treatment and prognosis of the disease are still insufficient. Further research is warranted in the future.

CONFLICTS OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

Concept - S.J., J.Y.L., J.K.; Planning and Design - S.J., J.Y.L., J.K.; Supervision - S.J., J.Y.L.1, J.K.; Funding -; Materials -; Data Collection and/or Processing - S.J.; Analysis and/or Interpretation - S.J., J.K.; Literature Review - J.K.; Writing - S.J.; Critical Review - J.K., J.Y.L

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