Successful recovery of a patient with multiple myeloma from severe coronavirus disease 2019 (COVID-19) pneumonia during the first chemotherapy cycle: A case report

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Abstract. A continuing outbreak of pneumonia associated with the 2019 novel coronavirus (2019-nCoV) was initially described in Wuhan, China in December 2019. Weak and elderly individuals, and those with chronic diseases such as hematological malignancies are prone to develop severe pneumonia. The humoral immunity of patients with multiple myeloma is prevalently low, and their inferior immunity further deteriorates during chemotherapy. For patients with onco-hematological malignancies infected with 2019-nCoV during the first chemotherapy cycle, the clinical treatment experience is lacking. The present study is a report of a 61-year-old patient newly diagnosed with multiple myeloma in the key 2019-nCoV outbreak area, who suffered severe 2019-nCoV pneumonia during the first chemotherapy cycle. The present case report demonstrated that a rapidly progressive and severe form of pneumonia was a specific clinical feature of COVID-19, especially in immunocompromised patients with cancer. The treatment strategy combining timely suspending chemotherapy, early intervention using intravenous immunoglobulin, interferon α inhalation and oral antiviral drugs was effective. Therefore, in the pandemic environment, it is strongly recommend that the risk of 2019-nCoV infection is assessed prior to chemotherapy.

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Introduction

A continuing outbreak of pneumonia associated with a novel coronavirus was initially described in Wuhan, China in December 2019 (1). On 11 February 2020, the International Committee on Taxonomy of Viruses named the new coronavirus 'severe acute respiratory syndrome-related coronavirus 2' or SARS-CoV-2, whilst the World Health Organization named the disease coronavirus disease 2019 or COVID-19 (1). The most common symptoms of COVID-19 are fever, dry cough and shortness of breath (2). However, some patients present other symptoms similar to influenza or no obvious symptom of disease onset (2). Patients who had serious underlying illness and elderly individuals, particularly those with hematological malignancies, are at a high risk of developing severe pneumonia (1). Multiple myeloma (MM) is the second most common hematological cancer accounts for ~1% of neoplastic diseases and 13% of hematologic cancers, which results from the accumulation of malignant plasma cells in the bone marrow (3). Developed countries are reported to have much higher MM incidence and prevalence compared with those in developing countries (4,5). Three high-incidence areas around the world are North America, Australia and Western Europe, with incidences ranging from 3 to 6 per 100,000 person-years, where the 5-year prevalence range from 7 to 14 per 100,000 population (4,5). The humoral immunity of patients with multiple myeloma is prevalently low, and their inferior immunity further deteriorates during chemotherapy (6). For immunocompromised patient with cancer infected with 2019-nCoV during the first chemotherapy cycle, the treatment experience is lacking. In the front line facing 2019-nCoV, the present study is the first report outlining the clinical features and the treatment process of a severe pneumonia in a 2019-nCoV-infected patient with multiple myeloma undergoing the first chemotherapy cycle.

Case Report

On 8 January 2020, a 61-year-old male, who suffered from chest pain for several months, was admitted to Wuhan Union Hospital without symptoms of fever or cough. The patient

denied having ever been to the Huanan Seafood Wholesale Market, which was the key spot of the 2019-nCoV outbreak and was a 10-min ride away from the hospital. The patient subsequently underwent bone marrow aspiration.

On 15 January 2020 (day 1), the patient was admitted to the Department of Hematology and was diagnosed with multiple myeloma IgG-κ (Durie-Salmon Stage II A) (7). The computed tomography (CT) of the chest was normal on day 1 (Fig. 1A). Considering the patient's status, chemotherapy, including bortezomib (1.3 mg/m^2, planned for days 2, 5, 9 and 12) and dexamethasone (40 mg, planned for days 2, 5, 9 and 12) was prescribed. The patient did not feel any notable discomfort after the therapy commenced on 16 January 2020.

On 21 January 2020 (day 7), the patient developed a fever of 38.5˚C. Chemotherapy (bortezomib and dexamethasone, day 8 and day 11, intravenous infusion) was suspended. Ceftazidime (2.4 g per time, twice daily for 3 days, intravenous infusion) was administered the following day. However, the patient suddenly exhibited dyspnea, and capillary oxygen saturation (SpO$_2$) was 80% while breathing ambient air on the night of 24 January 2020. After inhaling oxygen via a face mask at 10 l/min, the SpO$_2$ of the patient reached 95%. Intravenous immunoglobulin was administered, and the antibiotics were upgraded to Meropenem (0.1 g per time, three times a day for 5 days, intravenous infusion) combined with Teicoplanin (400 mg per time, once daily for 5 days, intravenous infusion), combining antiviral Ganciclovir (300 mg per time, twice daily for 5 days, intravenous infusion) and antifungal Voriconazole (0.2 g per time, twice daily for 5 days, intravenous infusion) therapy (Fig. 2). Although no fever (≥38˚C) was observed after 27 January 2020, the symptoms of cough and dyspnea were progressing.

On 28 January 2020 (day 14), the pharyngeal swab nucleic acid test of 2019-nCoV was determined positive by reverse transcription-quantitative PCR. Since the chest CT on 23 January 2020 revealed multiple ground glass opacities in both lungs (Fig. 1B), according to the diagnostic criteria of COVID-19 Diagnosis and Treatment Plan (Trial Fifth Edition) issued by the National Health Commission of China, the patient was diagnosed with severe COVID-19 pneumonia (8). The patient was transferred to the Department of Infection, and the antiviral and antifungal therapy were ceased on 29 January 2020; IFN-α inhalation (5 MU per time, twice daily) was administered (Fig. 2). However, symptoms such as cough and bloody sputum gradually progressed. The routine blood tests revealed a gradually decrease in lymphocytes (Table I). The chest CT on 31 January 2020 (day 17) demonstrated a progression of pneumonia (Fig. 1C).

On 1 February 2020 (day 18), the patient was transferred to the COVID-19 Isolation Ward, and the treatment was changed to arbidol (0.2 g per time, three times a day), oseltamivir (75 mg per time, twice daily), IFN-α inhalation (5 MU per time, twice daily), and moxifloxacin (0.4 g per time, once daily) (Fig. 2). The patient's condition improved gradually and slightly. The chest CT on 10 February (day 27) demonstrated a notable decrease in the lesions (Fig. 1D). Since the patient's fever had stopped for 2 weeks and the CT scan was indicating improvement, the present treatment strategy was considered to be correct. On 24 February 2020 (day 41), the patient's symptoms improved significantly, and the chest CT demonstrated
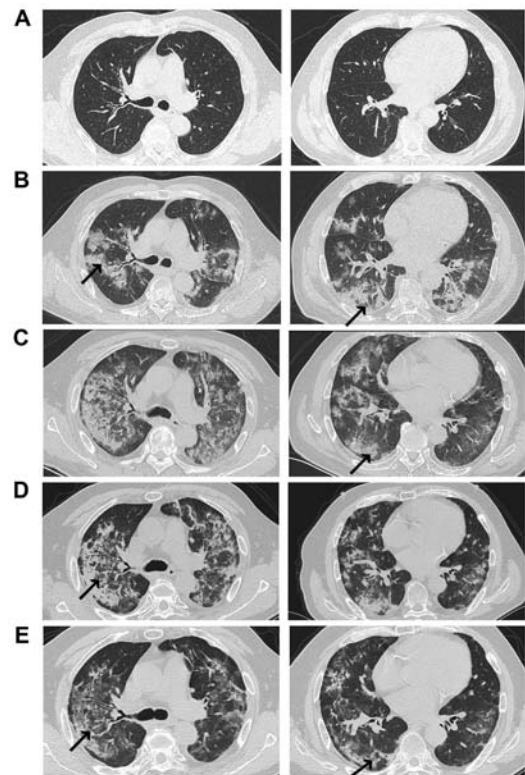

Figure 1. High-resolution computerized tomography of the lung. (A) Day 1 images demonstrate that the lung was normal. (B) Day 9 images demonstrate bilateral multiple ground glass opacities and mixed consolidations (arrow). (C) Day 17 images demonstrate that the range of lesions in both basal segments of the lower lobes was decreased (arrow), and the remaining lesions and consolidations were increased compared with Day 9. (D) Day 27 images demonstrate that the lesions in the middle lobe of the right lung were decreased compared with Day 17 (arrow). (E) Day 41 images demonstrate that the range and density of the lesions was decreased (arrow).

increased absorption in the lung lesions (Fig. 1E). The routine blood test revealed a gradual increase in lymphocyte count, and the patient exhibited significant improvement in dyspnea, cough and bloody sputum (Table I). On 28 February 2020 (day 45), the patient was provided with a nasal catheter for oxygen inhalation and remained in hospital for further improvement.

On 8 January 2020, the serum immunoglobulin test identified an IgG level of 68.8 g/l (reference range, 7.51-15.60 g/l) and IgA level of 0.44 g/l (reference range, 0.82-4.53 g/l). The chemotherapy was suspended on 23 January 2020, and antiviral drugs were administered from 25 January 2020. On 31 January 2020, the results of the serum immunoglobulin test demonstrated an IgG level of 56.2 g/l and an IgA level of 0.35 g/l. The level of IgG and IgA was lower compared with that prior to the antiviral treatment.

Discussion

The effective clinical recovery of the patient in the present study revealed that timely suspension of chemotherapy was necessary, and early treatment using intravenous immunoglobulin combined with aerosol inhalation of IFN-α and two oral antiviral drugs arbidol and oseltamivir was beneficial. The patient was administered both antibiotic and antiviral drugs

Table I. Clinical laboratory blood test results.

| Measure	Reference range	Day 1	Day 6	Day 9	Day 13	Day 17	Day 19	Day 24	Day 27	Day 31	Day 40
White cell count, cells x10^9/l	3.5-9.5	5.21	5.87	7.79	NA	6.56	6.33	7.17	6.54	NA	7.55
Hemoglobin, g/l	130-175	106	107	99	NA	93	91	81	82	NA	85
Platelet count, cells x10^9/l	125-350	227	141	163	NA	292	NA	390	394	NA	314
Neutrophils, %	40-75	66.0	86.2	87.2	NA	83.8	83.3	81.4	75.9	NA	72.4
Lymphocytes, %	20-50	26.5	12.3	11.8	NA	14.3	13.9	14.6	17.8	NA	17.2
Neutrophil count, cells x10^9/l	1.8-6.3	3.44	5.06	6.79	NA	5.50	5.27	5.84	4.96	NA	5.47
Lymphocyte count, cells x10^9/l	1.1-3.2	1.38	0.72	0.92	NA	0.94	0.88	1.04	1.17	NA	1.30
D-dimer, mg/l FE	<0.5	0.36	0.66	0.56	NA	NA	NA	0.36	NA	NA	NA
Fibrinogen, g/l	2.0-4.0	3.95	5.55	6.17	NA	NA	NA	6.25	NA	NA	4.95
Alanine aminotransferase, U/l	21-72	31	25	23	33	137	83	91	82	52	30
Albumin, g/l	35-50	33.5	25.6	24.7	25.0	26.2	20.6	16.8	20.7	25.8	30.1
Globulin, g/l	23-32	64.7	64.8	60.1	59.4	64.8	70.2	71.3	70.2	67.6	57.0
Creatinine, μmol/l	58.0-110.0	80.7	75.2	69.8	60.3	55.9	51.0	53.0	55.4	55.9	52.5
Creatine kinase, U/l	38-174	60	NA	NA	NA	27	NA	24	30	NA	47
Lactate dehydrogenase, U/l	109-245	135	NA	NA	336	326	NA	157	147	157	153
Procalcitonin, μg/l	<0.5	NA	NA	<0.13	0.31	<0.13	0.07	0.70	3.80	NA	0.40
C-reactive protein, mg/l	<8.00	NA	NA	120.00	139.00	49.40	108.78	101.99	46.06	10.41	23.57

NA, not available; FE, fibrinogen equivalent.
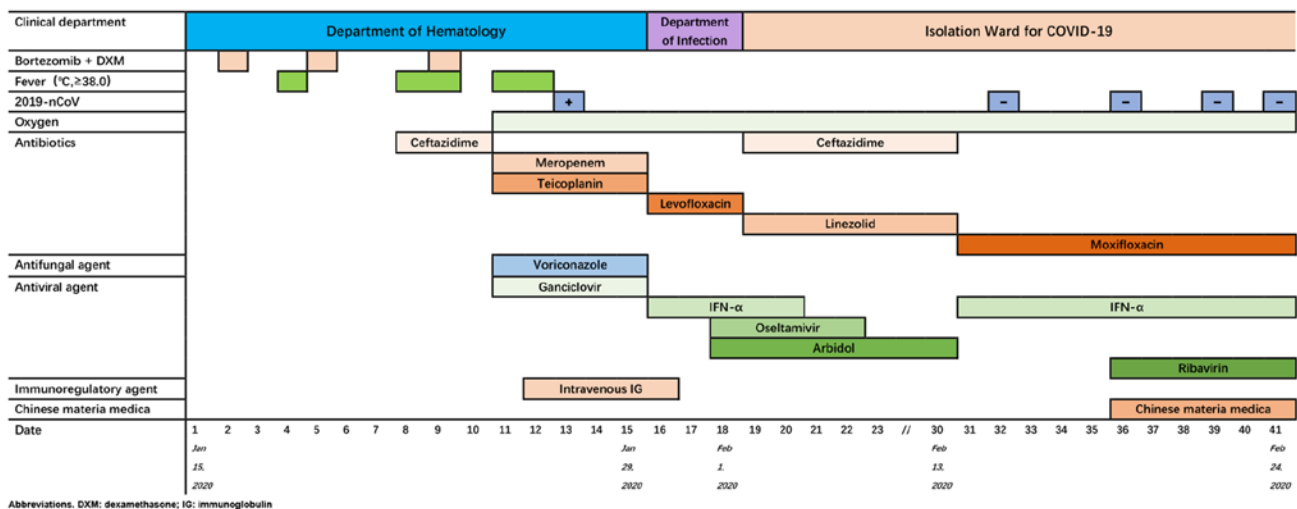
Figure 2. Clinical treatment process according to hospital days (days 1-41). DXM, dexamethasone; IG, immunoglobulin; IFN, interferon; 2019-nCoV, 2019 novel coronavirus.

in the initial phase of treatment for several reasons. Firstly, the respiratory defense mechanism can be severely damaged and the ability of the immune system to identify and clear the virus can be inhibited during influenza virus infection (9,10). Secondly, protein kinases produced by *Streptococcus pneumoniae* and *Staphylococcus aureus* promote the spread of influenza virus (11). Lastly, atypical pathogens may cause opportunistic infections due to the hypoimmunity of the patient.

Considering the time consistency of CT images and pulmonary symptoms, a previous study argued that the CT manifestations were lagging behind the clinical symp-

toms (12). In the present case, when the patient's 2019-nCoV nucleic acid tests were negative twice and his symptoms had notably improved, the chest CT image still indicated no significant improvement.

Of note, another patient (56-year old female) with multiple myeloma in complete remission in the same ward was not infected. Furthermore, the infected patient's close contacts (accompanying family members) were not infected. It was observed that immunocompromised patients were much more susceptible and, thus, it may be speculated that hypoimmunity is an important risk factor in 2019-nCoV infection and progression.

Zhang *et al* (13) previously showed that tocilizumab is effective in the treatment of COVID-19 in MM with obvious clinical recovery. Compared with data from the present study, the study by Zhang *et al* (13) indicated that excessive immune response and a strong cytokine storm are activated in severe COVID-19, rendering immunotherapy to be an appropriate treatment for COVID-19 patients with hematologic malignancies (14). Compared with a reported case of a patient with Middle East respiratory syndrome (MERS), who also had multiple myeloma (15), it was observed that the patient with COVID-19 recovered successfully using the current treatment strategy. One patient with multiple myeloma in remission (non-chemotherapy period) infected with MERS-CoV died after intensive antimicrobial treatment with meropenem, levofloxacin, vancomycin, caspofungin, aciclovir and oseltamivir (15). This case of MERS suggests that since the immune function of the MM patient was compromised, which represents a high risk for virus infection, the MM patient with MERS in remission died even after intensive antimicrobial treatment. It also appears that the lethality of 2019-nCoV is lower compared with that of MERS-CoV, which needs further investigation. However, no previous reports of severe acute respiratory syndrome infection in patients with multiple myeloma are currently available.

It has been reported that IFN-α treatment prolongs remission in patients with multiple myeloma; response rates of 20% were achieved when IFN-α (between 4.8 and 18.7 MU/week) was applied as single-agent treatment for multiple myeloma (16). For COVID-19 treatment in the present study, IFN-α was administered by aerosol inhalation (5 MU, twice daily). It is postulated that this treatment strategy may coincidentally and synergistically help to control multiple myeloma.

Of note, a single case in determining a treatment strategy for a diverse population has limitations. Owing to a lack of sufficient knowledge about the new infection, the management of COVID-19 in the hematological malignancy population remains unclear. According a previous report, comorbidities increase the risk of severe pneumonia in patients with COVID-19 (17), although history of hematological malignancies has not been reported as a risk factor. Despite the limitations of single-case observations, the presentation pattern and resolution of the disease using the described measures in the present case may serve to inform the treatment if such patients are encountered elsewhere. Further large-scale epidemiologic studies are needed to analyze the potential treatment strategies in patients with hematological malignancies infected with 2019-nCoV.

In conclusion, the present report describes for the first time the clinical features and treatment process of severe 2019-nCoV pneumonia in a patient with cancer undergoing the first chemotherapy cycle. The patient achieved a notable improvement. The present case highlights that a rapidly progressive and severe form of pneumonia is a specific clinical feature of COVID-19, particularly in immunocompromised patients. The treatment strategy in the present report, which included timely suspension of chemotherapy and early administration of intravenous immunoglobulin combined with IFN-α inhalation and oral antiviral drugs, was demonstrated to be effective. Therefore, in the pandemic environment, it is strongly recommended that the risk of 2019-nCoV infection is assessed prior to chemotherapy.

Availability of data and materials

The data generated and/or analyzed during the current study are not publicly available due to protection of patient privacy but are available from the corresponding author on reasonable request.

Authors' contributions

ZL and YC were major contributors in acquiring data and writing the manuscript. BY and HS helped with data collection and contributed to the critical revision of the manuscript for important content. BY and HS confirmed the authenticity of all the raw data and given constructive suggestions. HZ and WC designed the study and revised the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Written informed consent was obtained from the patient.

Patient consent for publication

The patient gave consent for the lung images to be published in this article.

Competing interests

The authors declare that they have no competing interests.

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