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Article type : Letters

**Title:**

**COVID-19 in a patient with pre-existing acute lymphoblastic leukemia**

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This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/bjh.16799](https://doi.org/10.1111/bjh.16799)

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Accepted Article

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**Number of figure(s): 1**

**Number of table (s):1**

**Abbreviations**

COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; ALL, acute lymphoblastic leukemia; CT, computed tomography; PCR, polymerase chain reaction.

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Coronavirus disease 2019 (COVID-19) is a novel respiratory infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), newly discovered since December 2019(Chen et al, 2020; Guan et al, 2020; Lu et al, 2020). According to WHO situation report (<<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports>>) on 1 April, 2020, a total of 823626 cases and over 40000 death had been documented globally, rapidly evolving into a pandemic. As reported by previous studies, patients with pre-existing health conditions are more likely to progress to severe COVID-19 pneumonia(Guan et al, 2020; Huang et al, 2020; Yang et al, 2020; Zhao et al, 2020b). Here we report a COVID-19 case with pre-existing acute lymphoblastic leukemia(ALL).

A 62-year-old woman with previous history of ALL was admitted on 1 February, 2020 for 2-day of productive cough and fatigue. This patient was diagnosed with ALL in July 2016 and received chemotherapy and CAR-T therapy in a teaching hospital in Wuhan. On July 2019, result of bone marrow puncture confirmed a relapse of ALL. She went to Wuhan city on 17 December, 2019 for the first course of chemotherapy after relapse. On 17 January, 2020, she returned to her hometown after discharge from Wuhan hospital. She denied the exposure to any confirmed case of COVID-19 on that

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trip.

On 30 January (13 days after she returned from Wuhan), she suffered from productive cough and fatigue. No fever, breathless, chest pain, diarrhea or anosmia was reported. A computed tomography (CT) of the chest was performed on the same day, showing mild infusion in the right lung (Figure1a). The diagnosis of COVID-19 infection was confirmed on 31 January and 5 February by repeated real-time Polymerase Chain Reaction (PCR) test. She was admitted to an isolation wards on 1 February, and given lopinavir/ritonavir (200mg/50mg/capsule, 2 capsules each time, twice daily, orally) as recommended by the Chinese Guideline for the diagnosis and treatment of COVID-19 infections( National Health Commission of the People’s Republic of China, 2020). The laboratory tests showed normal white blood cell count, lymphocyte count, neutrophil count, platelet count, estimated glomerular filtration rate and liver enzymes on admission (Table1). During the first 2 weeks of hospitalization, the body temperature, PaO<sub>2</sub>/FiO<sub>2</sub> and white blood cell counts remained normal, while reductions in hemoglobin and platelet count were observed(Table1). On 14 February (day 16 of illness), she developed fever at the first time, with the daily maximum body temperature ranging from 38°C to 40°C. Hemocytopenia and elevated procalcitonin were detected (Table1). A repeated CT scan showed the slightly expansion of the lung lesions(Figure1c). Then she received antibiotic treatment with meropenem and teicoplanin, followed by linezolid and tigecycline, however, the temperature did not return to normal. Meanwhile, the white cell count dropped to the

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lowest level ( $1.65 \times 10^9/L$ ) on 17 February. Bone marrow puncture on 19 February revealed 90% of immature cells in bone marrow, suggesting a relapse of ALL. On 20 February, she developed severe shortness of breath, with an oxygen saturation of 98%, and PaO<sub>2</sub>/FiO<sub>2</sub> of 584 mmHg. N-terminal B-type natriuretic peptide was performed with a result of 14284.0 pg/ml. Echocardiogram found a reduced ventricular ejection fraction and a small amount of pericardial effusion, indicating cardiac asthma. She was then given strict fluid management and higher diuretic doses. In the following days, this patient's symptoms slightly improved. A repeat chest x-ray showed the improvement of the lung lesions(Figure 1d and e). Two consecutive COVID-19 tests on 24 February and 26 February were both negative. Yet the fever was still ongoing. On day 30 of illness, she was transferred to the hematology department for further treatment. However, this patient eventually deceased from cardiogenic shock on 1 March, 32 days after the onset of symptoms.

Due to the high infectivity of COVID-19, most people are vulnerable to this virus. Unexpectedly, patients with underlying hematologic malignancy are at higher risks for SARS-CoV-2 infection and disease progression(Huang et al, 2020; Liang et al, 2020). Patients with leukemia often have pulmonary infection, fever and hemocytopenia, which are similar as the symptoms of COVID-19. The similarity in the symptom may confuse the diagnosis.

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The reported case had pre-existing ALL and laboratory confirmed SARS-Cov-2 infection during COVID-19 outbreak in Wuhan city. The epidemiological history and repeated PCR tests confirmed the diagnosis of SARS-Cov-2 infection. However, the early symptoms of this patient were uncharacteristic of the typical presentations of COVID-19, which are dry cough, fever, lymphocytopenia, hypoxemia and the multiple small patches and interstitial change in CT( National Health Commission of the People's Republic of China, 2020; Zhao et al, 2020a). The first onset fever occurred 2 weeks after admission, with elevated C-reactive protein and procalcitonin level. The fever in this case did not happen at the onset of disease and never return to normal even after the virus test was negative, suggesting these clinical manifestations were more likely to be resulted from bacterial infection and the relapse of underlying ALL itself, rather than the COVID-19. The symptoms of COVID-19 were mild at the onset of disease in the patient, however the outcome of this patient was poor.

Although there is limited data on the relationship between the COVID-19 and leukemia, a report from China suggested that patients with malignancy had a higher risk of developing severe events as compared with patients without(Liang et al, 2020).

It is difficult to rule out the possibility that even mild COVID-19 might exacerbate the underlying hematologic diseases. There is no specific treatment for COVID-19 to now, while the management of ALL has been standardized, therefore the careful differential diagnosis of these two diseases is crucial at the time of COVID-19 pandemic.

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In conclusion, COVID-19 in patients with hematologic disease may have complex clinical manifestations. Careful differential diagnosis is important in the management of COVID-19 in this population.

### **Acknowledgements**

This study was financially supported by Fuzhou Science and Technology Plan Project (Social Development Project 2017-S-133-2).

### **Authors' contributions**

Yinlian Wu and Heng Lin contributed equally to the study. Yinlian Wu, Heng Lin, Qiang Xie, Qun Chen and Yanfang Huang were involved in design and data interpretation. Yinlian Wu wrote the manuscript. Yueyong Zhu and Lizhou Chen conducted critical revision of the manuscript. All authors reviewed and commented on the manuscript and approved the final version. Written informed consent to publication was obtained.

### **Competing interests**

The authors have no conflicts of interest related to this article.

### **Reference**

- Chen, Y., Liu, Q. & Guo, D. (2020) Emerging coronaviruses: Genome structure, replication, and pathogenesis. *Journal of Medical Virology*, 92(4), 418-423.
- Guan, W. J., Ni, Z. Y., Hu, Y., Liang, W. H., Ou, C. Q., He, J. X., Liu, L., Shan, H., Lei, C. L., Hui, D. S. C., Du, B., Li, L. J., Zeng, G., Yuen, K. Y., Chen, R. C., Tang, C. L., Wang, T., Chen, P. Y., Xiang, J., Li, S. Y., Wang, J. L., Liang, Z. J., Peng, Y. X., Wei, L., Liu, Y., Hu, Y. H., Peng, P., Wang, J. M.,

Liu, J. Y., Chen, Z., Li, G., Zheng, Z. J., Qiu, S. Q., Luo, J., Ye, C. J., Zhu, S. Y. & Zhong, N. S. (2020) Clinical Characteristics of Coronavirus Disease 2019 in China. *The New England Journal of Medicine*, 382(18), 1708-1720.

Huang, J., Lin, H., Wu, Y., Fang, Y., Kumar, R., Chen, G. & Lin, S. (2020) COVID-19 in posttransplant patients—report of 2 cases. *American Journal of Transplantation*. [Epub ahead of print]. Available from: <https://doi.org/10.1111/ajt.15896>.

Liang, W., Guan, W., Chen, R., Wang, W., Li, J., Xu, K., Li, C., Ai, Q., Lu, W., Liang, H., Li, S. & He, J. (2020) Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *The Lancet Oncology*, 21(3), 335-337.

Lu, H., Stratton, C. W. & Tang, Y.-W. (2020) Outbreak of pneumonia of unknown etiology in Wuhan, China: The mystery and the miracle. *Journal of Medical Virology*, 92(4), 401-402.

National Health Commission of the People's Republic of China. (2020) Guideline for the diagnosis and treatment of COVID-19 infections. Available from: [http://www.nhc.gov.cn/yzygj/zcwj2/new\\_zcwj.shtml](http://www.nhc.gov.cn/yzygj/zcwj2/new_zcwj.shtml).

World Health Organization. (2020) Coronavirus disease (COVID-2019) situation reports. Available from: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports>.

Yang, X., Yu, Y., Xu, J., Shu, H., Xia, J., Liu, H., Wu, Y., Zhang, L., Yu, Z., Fang, M., Yu, T., Wang, Y., Pan, S., Zou, X., Yuan, S. & Shang, Y. (2020) Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *The Lancet Respiratory Medicine*. [Epub ahead of print]. Available from: [https://doi.org/10.1016/S2213-2600\(20\)30079-5](https://doi.org/10.1016/S2213-2600(20)30079-5).

Zhao, Q., Meng, M., Kumar, R., Wu, Y., Huang, J., Deng, Y., Weng, Z. & Yang, L. (2020a) Lymphopenia is associated with severe coronavirus disease 2019(COVID-19) infections: A systemic review and meta-analysis. *International Journal of Infectious Diseases*. [Epub ahead of print]. Available from: <https://doi.org/doi:10.1016/j.ijid.2020.04.086>

Zhao, Q., Meng, M., Kumar, R., Wu, Y., Huang, J., Lian, N., Deng, Y. & Lin, S. (2020b) The impact of COPD and smoking history on the severity of Covid-19: A systemic review and meta-analysis. *Journal of Medical Virology*. [Epub ahead of print]. Available from: <https://doi.org/10.1002/jmv.25889>.

## Figure Legends

Figure 1. Radiological characteristics of the chest.(a) Day 1, mild infusion in the right lung in CT;(b) Day 6, mild infusion in the right lung in CT, without obviously deterioration; (c) Day 17, expansion of the lung lesions in CT; (d) Day 22, patchy high-density shadow in both lungs in X-rays; (e) Day 29, substantial improvement with a reduction of pulmonary exudative lesions in X-rays.

Table1. The most relevant clinical findings and drug use for treatment.



Table1. The most relevant clinical findings and drug use for treatment

Date	2/1	2/3	2/6	2/9	2/11	2/14	2/15	2/17	2/19	2/21	2/22	2/25	2/27	2/28
Day of hospitalation	1	3	6	9	11	14	15	17	19	21	22	25	27	28
Day of illness	3	5	8	11	13	16	17	19	21	23	24	27	29	30
Tmax(°C)	36.7	36.9	36.9	36.5	37	39	39	39.5	39.8	37.5	38.5	39	38.5	38.8
WBC( $\times 10^9/L$ )	6.03	5.25	7.01	6.38	5.7	3.02	2.59	1.65	2.03	1.92	2.12	1.89	2.48	1.92
NEUT( $\times 10^9/L$ )	4.32	2.36	3.25	3.15	3.05	1.46	1.34	0.92	1.35	1.46	1.57	1.24	1.61	1.11
LYM( $\times 10^9/L$ )	1.64	2.18	3.58	3.03	2.39	1.52	1.2	0.7	0.66	0.43	0.52	0.63	0.83	0.79
HB(g/L)	94	74	72	65	62	53	62	51	63	78	72	73	69	74
PLT( $\times 10^9/L$ )	140	95	101	77	64	32	36	47	45	31	25	31	30	27
CRP(mg/L)	119.2	98.97	228.3	211.04	254.63	248.3	265.33	261.81	273.91	259.33	234.96	154.01	192.42	141.68
PCT(ng/ml)	0.171	0.198	0.185	0.161	0.195	-	1.28	1.59	-	1.02	0.446	0.21	0.253	-
NT-proBNP(pg/ml)	1615	342.4	580.4	937.9	-	4554	2676	7257	19364	4651	4438	1685	1004	2525
PO2(mmHg)	145.1	123.9	122.8	138.5	127.4	120.6	182.5	202.6	127.3	-	105	-	107.4	-
PCO2(mmHg)	23.9	30.4	37.4	41.5	32.6	31.8	31.2	29.4	39	-	34.4	-	30	-
CREA(umol/L)	65	66	54	44	42	40	36	32	28	26	29	31	40	-
LDH(U/L)	1317	906	910	1625	2145	1721	1846	1088	1250	1122	1028	891	891	-
ALT(U/L)	20	20	21	20	18	16	21	28	26	21	24	16	18	-
AST(U/L)	45	29	26	29	29	24	25	30	32	23	20	20	28	-
lopinavir/ritonavir										arbidol hydrochloride				
							meropenem and teicoplanin		meropenem and linezolid		meropenem and tigecycline			
								immunoglobulin(5g daily)		immunoglobulin(15g daily)				
										methylprednisolone (40mg daily)				

Tmax, maximum temperature; WBC, white blood cell; NEUT, neutrophil; LYM, lymphocyte; HB, haemoglobin; PLT, platelet; CRP, C-reactive protein; PCT, procalcitonin; NT-proBNP, N-terminal B-type natriuretic peptide; PO2, partial pressure of oxygen; PCO2, partial pressure of carbon dioxide; CREA, creatinine; LDH, lactic dehydrogenase; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

