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COVID-19 in a patient with pre-existing acute lymphoblastic leukaemia

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.[1–3] According to a World Health Organization situation report on April 1, 2020,[4] a total of 823,626 cases and over 40,000 deaths had been documented globally, suggesting the situation was 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.[2,5–7] Here, we report a COVID-19 case with pre-existing acute lymphoblastic leukaemia (ALL).

A 62-year-old woman with previous history of ALL was admitted on February 1, 2020, for two days 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. In July 2019, results of bone marrow puncture confirmed a relapse of ALL. She went to Wuhan city on December 17, 2019, for the first course of chemotherapy after relapse. On January 17, 2020, she returned to her hometown after discharge from Wuhan hospital. She denied the exposure to any confirmed case of COVID-19 on that trip.

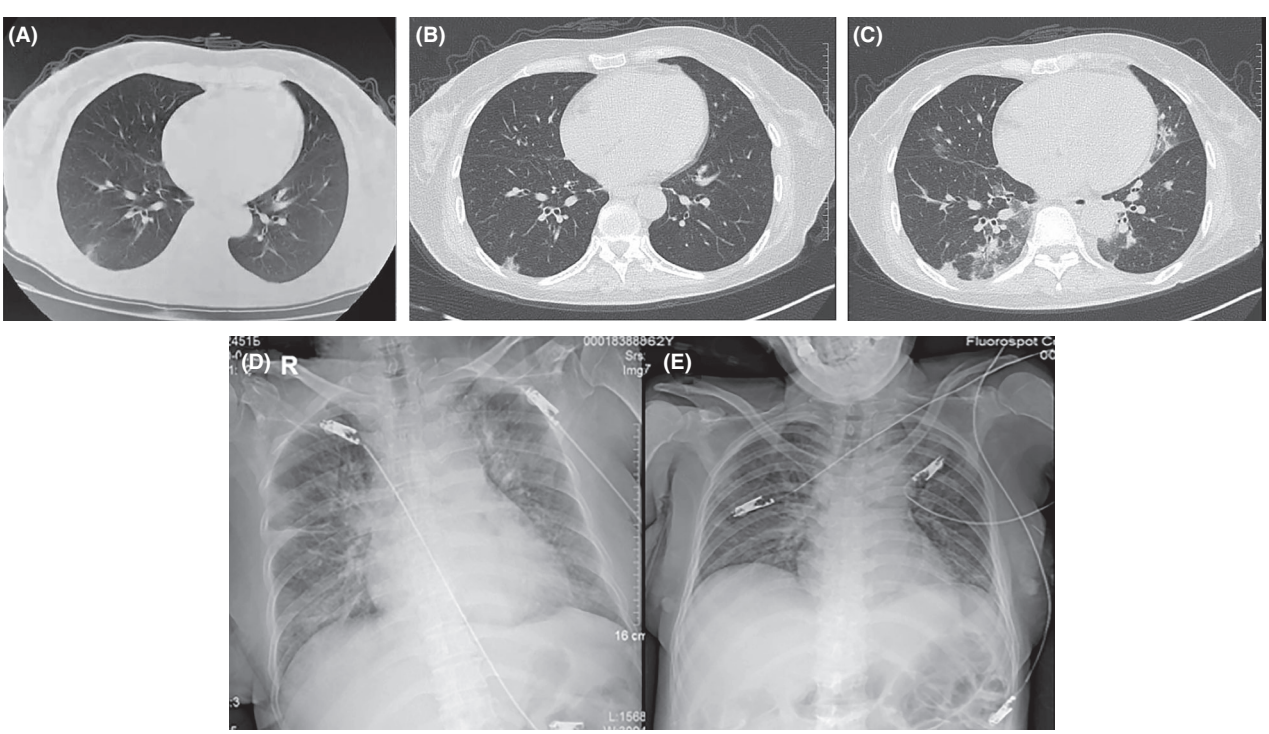

Fig 1. Radiological characteristics of the chest. (A) Day 1, mild infusion in the right lung in CT; (B) Day 6, mild infusion in the right lung in CT, without obvious deterioration; (C) Day 17, expansion of the lung lesions in CT; (D) Day 22, patchy high-density shadow in both lungs in X-rays; (E) Day 29, substantial improvement with a reduction of pulmonary exudative lesions in X-rays.

On January 30 (13 days after she returned from Wuhan), she suffered from productive cough and fatigue. No fever, breathlessness, 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 (Fig 1a). The diagnosis of COVID-19 infection was confirmed on January 31 and February 5 by repeated real-time Polymerase Chain Reaction (PCR) test. She was admitted to an isolation ward on February 1 and given lopinavir/ritonavir (200 mg/50 mg/capsule, two capsules each time, twice daily, orally) as recommended by the Chinese Guideline for the diagnosis and treatment of COVID-19 infections.[8] The laboratory tests showed normal white blood cell count, lymphocyte count, neutrophil count, platelet count, estimated glomerular filtration rate and liver enzymes on admission (Table I). During the first 2 weeks of hospitalisation, body temperature, PaO2/FiO2 and white blood cell counts remained normal, while reductions in haemoglobin and platelet count were observed (Table I). On February 14 (day 16 of illness), she developed fever for the first time, with the daily maximum body temperature ranging from 38°C to 40°C. Haemocytopenia and elevated procalcitonin were detected Table I. A repeated CT scan showed the slightly expansion of the lung lesions (Fig 1c). 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 lowest level ($1{\cdot}65 \times 10^9$/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 PaO2/FiO2 of 584 mmHg. N-terminal B-type natriuretic peptide was performed with a result of 14 284·0 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 (Fig 1d,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 haematology 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

Table I. 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 hospitalisation	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 (μmol/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.

underlying haematologic malignancy are at higher risks for SARS-CoV-2 infection and disease progression.[5,9] Patients with leukaemia often have pulmonary infection, fever and haemocytopenia, which are similar to the symptoms of COVID-19. The similarity in the symptoms may confuse the diagnosis.

The reported case had pre-existing ALL and laboratory confirmed SARS-Cov-2 infection during the 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.[8,10] The first onset of fever occurred 2 weeks after admission, with elevated C-reactive protein and procalcitonin levels. The fever in this case did not happen at the onset of disease and never returned to normal, even after the virus test was negative, suggesting these clinical manifestations were more likely resulted from bacterial infection and the relapse of underlying ALL itself rather than 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 COVID-19 and leukaemia, a report from China suggested that patients with malignancy had a higher risk of developing severe events compared to patients without.[9] It is difficult to rule out the possibility that even mild COVID-19 might exacerbate the underlying haematologic diseases. There is no specific treatment for COVID-19 as of now, while the management of ALL has been standardised; therefore, the careful differential diagnosis of these two diseases is crucial at the time of the COVID-19 pandemic.

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

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Conflict of interest

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

Authors' contributions

Y.W. and H.L. contributed equally to the study. Y.W, H.L., Q.X., Q.C. and Y.H. were involved in design and data interpretation. Y.W. wrote the manuscript. Y.Z. and L.C. 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.

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