



Morphological changes of lymphocytes in peripheral blood smears of patients with COVID-19

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Clinical laboratory has played an important role in the diagnosis, treatment and prognosis of coronavirus disease 2019 (COVID-19) patients. A notable laboratory finding was that the absolute value of lymphocyte in most confirmed cases was reduced, which suggests that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) might mainly act on lymphocytes (1). Previous published studies mainly focused on epidemiological, radiological, and clinical characteristics of COVID-19 patients. Little attention has been paid to the morphological changes of peripheral white blood cell. Hence, this pilot study was to investigate whether SARS-CoV-2 infection causes morphological changes in peripheral lymphocytes.

A total of 23 most recently hospitalized patients from 25 February to 01 March, including 12 females, were enrolled in this study, with age ranging from 31 to 83 years old. All of the 23 inpatients denied histories of leukemia (*Table 1*). According to Novel Coronavirus Pneumonia Prevention and Control Program (5th edition) published by the National Health Commission of China, COVID-19 patients were categorized into four types: mild type, moderate type, severe type and critical type (2). The disease categories were as follows: 18 mild cases, 3 severe case and 2 critical case. All the blood samples were obtained on the admission day of each patient. Morphological changes, compared with normal lymphocyte, in peripheral lymphocytes were defined as atypical lymphocyte. Blood five differential counts were determined by Mindray automated hematology analyzer. Lymphocyte population analysis was performed via flow cytometry. Peripheral blood smears, obtained by use of

the wedge-pull smear technique and stained by means of Wright-Giemsa method, were visually examined by two independent experienced clinical technicians by use of light microscopy. In order to calculate the atypical lymphocytes ratios, 200 white blood cells were counted.

Our results showed that the highest percentage of atypical lymphocytes was just 4%, while the second highest in our cohort was 2%. The rest were all around 1% (*Table 1*). This was much lower than that of another similar study, whose results demonstrated that highest percentage of atypical lymphocytes was up to 13.5% (6.90%±4.30%) (3). Most of the atypical lymphocytes observed in our cohort was just irregular shaped lymphocytes with excessive cytoplasm but normal nucleus (*Figure S1*). Plasmacytoid lymphocytes were also observed but with a low percentage, which was in agreement with other studies (4,5).

The atypical lymphocyte can be found in small numbers in normal human blood (6) and in increased numbers in a variety of clinical settings, especially infectious mononucleosis and many viral as well as non-viral illnesses, because atypical lymphocytes are generally lymphocytes that have been activated to respond to a viral infection or sometimes a bacterial or parasitic infection. From the results of some sporadic researches with very limited number of enrolled participants, it can be concluded that SARS-CoV-2 infection is a new aetiology for atypical lymphocytes, however, is the presence of atypical lymphocytes, especially plasmacytoid lymphocytes, a laboratory feature of SARS-CoV-2 infection still needs to be validated by future studies with larger populations.

Table 1 Detailed information of the 23 patients with COVID-19

ID no.	Age years	Gender	Disease type	WBC, K/uL	Absolute lymphocyte, K/uL	% Atypical lymphocyte	Lymphocyte populations analysis			Co-morbidities	
							CD8+ T cells	CD4+ T cells	B cells		
1	62	F	Mild	2.7	0.92	0.5	235	356	67	46	T2DM; HBV Infection; Cognitive Dysfunction
2	62	M	Mild	52	1.36	0.3	447	727	110	128	Hypertension
3	31	M	Mild	4.7	1.69	2	517	486	139	281	None
4	33	M	Mild	96	3.01	0.8	551	670	351	476	None
5	50	F	Mild	5.9	2.12	1	392	1,167	167	233	Arthritis
6	41	F	Mild	6.6	1.28	0.7	364	459	159	208	None
7	82	F	Critical	16.9	1.48	4	300	629	52	258	Anemia; Hypertension; CHD
8	83	F	Critical	7.3	1.94	1	339	1,062	167	195	Hypertension
9	78	F	Mild	6.5	1.49	0.5	299	553	306	195	Hypertension; CHD; Cataract
10	73	M	Severe	4.8	1.08	0.8	202	307	289	137	Prostatic Cancer
11	58	F	Severe	4.3	0.95	1.2	186	423	175	101	None
12	36	F	Mild	9.1	2.33	0.7	763	897	112	280	None
13	57	F	Mild	3.8	1.98	1	368	942	322	313	Nephrolylits
14	57	M	Mild	10.6	0.99	0.8	162	438	183	87	None
15	21	M	Mild	8.5	1.02	0	349	486	177	160	None
16	62	F	Mild	4.1	1.21	0.4	290	509	70	264	None
17	33	M	Mild	3.6	0.74	0	174	194	184	81	None
18	65	F	Mild	3.5	0.77	0.3	114	275	225	104	None
19	58	M	Mild	4.6	1.27	0.6	337	571	288	131	Hypertension; COPD; Hepatic Cyst
20	34	M	Mild	2.9	0.98	1	208	482	65	73	None
21	57	M	Mild	3.6	1.49	0.8	255	370	434	150	CHD
22	64	F	Mild	4.9	1.52	0.3	NA	NA	NA	NA	CHD;T2DM
23	71	M	Severe	44	0.74	0.5	NA	NA	NA	NA	Hypertension; Parkinson; Cerebral Infarction

T2DM, type 2 diabetes mellitus; HBV, hepatitis B virus; CHD, coronary heart disease; COPD, chronic obstructive pneumonia disease; NA, not available; NK, natural killer.

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