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Case Report

COVID-19 Case Report: Circulating blood cells morphology in convalescent patient

Nahla Tayyib[1,2] , Mabrouk A. Abo-Zaid[3], Ahmed H. Ismail[3], Soha S. Mohammed[4] and Ali H Amin*[,1, 5]

[1] Deanship of Scientific Research, Umm Al-Qura University, Makkah, Saudi Arabia
[2] Faculty of Nursing, Umm Al-Qura University, Makkah, Saudi Arabia
[3] Biology department, faculty of science, Jazan University, Jazan, Saudi Arabia
[4] Ministry of Health and Population, Cairo, Egypt.
[5] Zoology Department, faculty of science, Mansoura University, Mansoura, Egypt.

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***Corresponding author:**
Ali H Amin
E: ahamin@uqu.edu.sa

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ABSTRACT

Objective: Many studies have detailed the mechanisms of infection and quantitative peripheral blood findings reported in severe acute respiratory syndrome virus 2 (SARS-CoV-2) patients during the severity of infection since the start of the coronavirus disease 2019 (COVID-19) pandemic. Though, only a few studies have described blood morphologic abnormalities. We report peripheral blood cells morphologic changes in convalescent patient.

Design: We performed complete blood counts (CBC), and blood smear of 52-year-old patient who were COVID-19 positive test by (RT-PCR), from May 20, 2021, through June 15, 2021. The peripheral blood smears of a convalescent patient were collected the morphological structures of Leukocytes, red blood cells (RBCs) and platelets were examined and documented, after 3 weeks from infection with COVID-19 RT-PCR was negative to look for viral changes on blood cells morphology.

Results: On a complete blood count (CBC), the most common quantitative hematologic abnormalities were mild anemia with RBCs showed no abnormality followed by WBCs normal in count, and relative lymphopenia. Neutrophils showed the most substantial morphologic alterations with C-shaped bi-lobulated nuclei, coarse toxic granulations and cytoplasmic vacuolization. Activated neutrophil granulocytes with elongated cell membrane, pseudo Pelger–Huët anomaly-like nuclei, ring form nuclei and pyknotic nucleus. Lymphocytes were atypical reactive lymphocytes with cytoplasmic pseudopod formation. Plasmacytoid lymphocytes with an eccentric nucleus and deeply basophilic cytoplasm are frequently seen. Monocytes seen in active form with cytoplasmic vacuolization and cytoplasm contain granules, with pseudopod formation. Platelets were adequate in number with giant platelets are occasionally seen. Smudge cell is also seen. RBCs were normocytic; normochromic.

Conclusion: Our work identifies and characterizes significant morphologic abnormalities in recovered COVID-19 patients' peripheral blood cells. Understanding these morphologic changes, in addition to established hematologic parameters, can help follow with COVID-19 patient during recovery through serial CBC and peripheral smear examination. Serial complete blood count and blood film review may become an essential tool to help physicians allocate patients to risk categories based on morphological findings if these proposals are supported by large-scale investigations of convalescent patients.

1.INTRODUCTION

Coronavirus disease (COVID-19) caused by a virus named the severe acute respiratory syndrome virus 2 (SARS-CoV-2) spread all over the world, beginning from Wuhan, a city in China, in 2019. Infection by this virus was mainly accompanied with respiration disorders which may be converted to acute respiratory dysfunction syndrome (ARDS) (**Abo-Zaid et al., 2020**).The pathogenesis of COVID-19 has also been linked to immune system activation and subsequent immunological dysregulation. Involvement of the immune system is demonstrated by the presence of lymphopenia, especially in patients with severe disease (**Kaur et al., 2021**). Since the current outbreak of COVID-19 pandemic, several studies have determined a correlation with the disease severity and haematological anomalies a condition defined

by abnormally in counts of white blood cells and morphology. Until yet 480,170,572 confirmed cases of COVID-19, including 6,124,396 deaths, reported to WHO. As of 26 March 2022, a total of 11,054,362,790 vaccine doses have been administered (**WHO, 2022**).In this case study, we attempt to describe the morphology of circulating RBCs and WBCs in a convalescent patient, which may shed light on understanding and recovery from this viral infection.

2. CASE SUMMARY

A 52-year-old, previously healthy male developed flu symptoms with cough and fever. After few days, he presented to a government hospital. Clinical investigations showed worsening lung findings along with worsening respiratory symptoms. He was confirmed as a COVID-19 patient by a positive RT-PCR nasopharyngeal swab. Three weeks after receiving treatment (antibiotics (erythromycin) for three days, antipyretics, Zinc and Vitamin C), his complete blood count (CBC) showed a haemoglobin concentration (Hb %) of 13.4 g/dL and RBCs showed no abnormality, total white blood cells (WBCs) of 6.9 x 10^3/cmm with polymorph nuclear leucocytes of 5.037 x 10^3/cmm with relative lymphopenia (17%) of 1.173 x 10^3/cmm that looked to be in reactive form. Plasmacytoid cells with an irregular nucleus (eccentric) and highly basophilic cytoplasm were prominent among them. Monocytes appear in an active form with cytoplasmic vacuolization and cytoplasm containing granules (0.690 x 10^3/cmm) and a normal platelet count (170 x 10^3/cmm) with giant forms were occasionally seen. The patient was successfully treated and recorded a negative COVID-19 RT-PCR result.

To reach a good and specific result regarding the abnormal changes that occurred to cells as a result of infection by the virus, this needs to be studied on a large scale and in multiple stages, both during the COVID-19 infection and after recovery (**Singh et al., 2020**).

The microscopic examination for the case leukocytic morphology presented here are in agreement with other findings in cases during infection with SARS-CoV-2 (F**oldes et al., 2020; Singh et al., 2020**) and **Tummidi & Shankaralingappa** (**2021**). **Mitra et al. (2020)** reported that Lymphopenia was established with numerus smudge cells in addition to platelets count with giant platelets seen (**Salib et al., 2020**), while our results have been obtained after the patient recovered from the infection (three weeks) which indicates that the COVID-19 viral infection still shows anomalies for a period after recovery.

Anemia, leukopenia, particularly lymphopenia, and leukocytosis, including neutrophilia and monocytosis, are the most common laboratory abnormalities seen in COVID-19 patients. (**Zheng et al.; Tan et al. and Zhang et al., 2020**). In our case study, mild anemia was finding according to (**Pagana et al., 2019**), followed by normal neutrophil count, relative lymphopenia and monocytes normal in count. Several studies exist for the morphologic changes in peripheral blood cells of COVID-19 patients during the severity of infection. While; our study described RBCs and WBCs morphologic changes in peripheral blood smear of convalescent COVID-19 patients. The polymorphonuclear leukocytes (neutrophils) showed anomalous nuclear shapes such as C-shaped bi-lobulated nuclei, activated neutrophil granulocytes with elongated cell membrane. The pseudo Pelger–Huët anomaly-like nuclei was also identified (**Nazarullah et al.,2020**). Ring-nucleus neutrophils were frequently seen and pyknotic nucleus (apoptotic cells) these morphologic changes have been reported in other studies. However, to our knowledge, few authors have fully defined the morphologic abnormalities in cells of peripheral blood smear of convalescent COVID-19 patients (Fig.1).

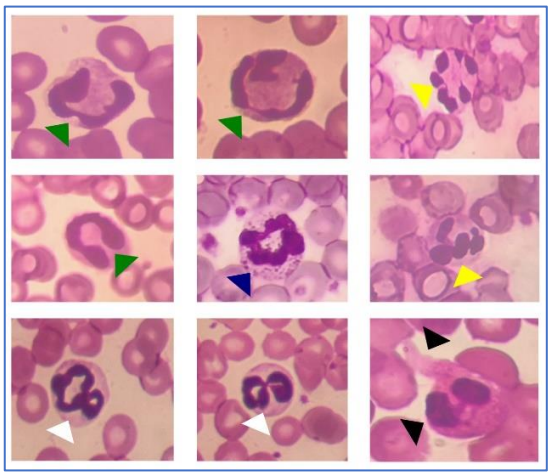

Figure 1:Review of the peripheral blood smear Giemsa Stain at (100x magnification) shows morphological anomalies. Neutrophils with C-shaped bi-lobulated nuclei (green arrow). Neutrophil with coarse toxic granulations and cytoplasmic vacuolization (blue arrow). Activated neutrophil granulocytes with elongated cell membrane and pseudo Pelger–Huët anomaly-like nuclei (black arrow). Neutrophil with ring nuclei (white arrow). Pyknotic nucleus (apoptotic cells) (yellow arrow).

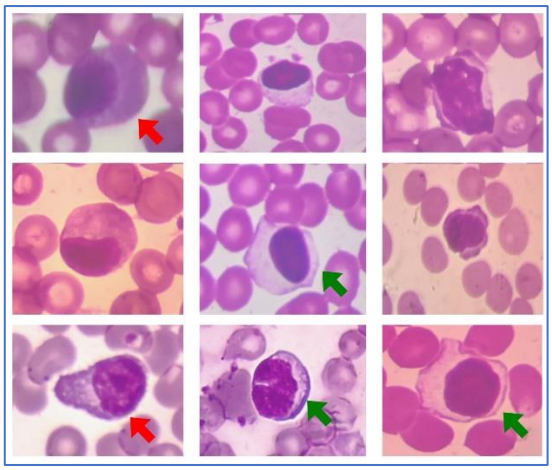

Figure 2: Blood film showing atypical reactive lymphocytes with cytoplasmic pseudopod formation (green arrow). Plasmacytoid lymphocytes with an eccentric nucleus and deeply basophilic cytoplasm are frequently seen (red arrow). (Giemsa Stain x 100 objective).

Kaur et al., (2021) and **Zini et al., (2020**) described similar alterations in neutrophils, lymphocytes, and platelets during the manifestation stage of infection in their study. This observation suggests the immune system still active to neutralize viral epitopes. The lymphocytes showed atypical reactive lymphocytes with cytoplasmic pseudopod formation and frequently encountered are plasmacytoid cells with an eccentric nucleus and strongly basophilic cytoplasm. Monocytes observed in active form with cytoplasmic vacuolization and cytoplasm contain granules, pseudopod formation, giant platelets are seen and smudge cells are frequently seen (Fig. 2 & Fig. 3).

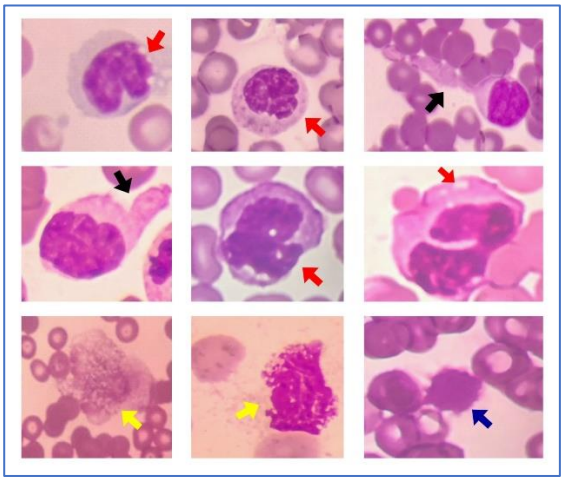

Figure 3: Peripheral blood films displaying monocytes in active form with cytoplasmic vacuolization and cytoplasm contain granules (red arrow). Monocytes with pseudopod formation (black arrow). Giant platelets are seen (blue arrow). Smudge cell is also seen (yellow arrow). (Giemsa Stain x100 objective).

Singh et al., (2020) described similar morphology in polymorphonuclear leukocytes, monocytes, and lymphocytes during COVID-19 infection in their case report. Also, activated monocytes and lymphocytes may indicate an improvement in the patient's clinical condition. Monocytes exhibit ACE-2 receptors and are directly impacted by COVID-19, according to Zhang et al. (2020), resulting in monocytosis and the appearance of large, atypical and cytoplasmic vacuolation monocytes in circulation. Smudge cells are frail remains of leukocytes, mainly lymphocytes, that are destroyed/smudged during the smear-making process (**Kaur et al., (2021**); suggest that due to viral stressed on these cells.

3. CONCLUSION

Finally, we present a review of morphologic alterations in the peripheral blood cells of a COVID-19 patient who is recovering. Despite the fact that this is only one case study, it represents a step toward better understanding COVID-19's hematological symptoms. These signs of morphologic deviations in blood smear could aid physicians in diagnosing COVID-19 in the absence of a negative COVID-19 RT-PCR test. Furthermore, some researchers have postulated a link between morphological alterations in CBC and the severity or recovery of infection. Serial CBC and blood smear review may become an essential tool to help physicians allocate patients to risk categories based on morphological findings if these proposals are supported by large-scale investigations of convalescent patients.

ETHICAL APPROVAL AND CONSENT TO PARTICIPATE

Blood samples were collected according to the ethical standards for donor approval required by the national regulatory bodies under supervision of a physician and after having signed informed consent for the use of the blood in this study. In addition, final approval No. (HAPO-02-K-012-2022-03-1018) from the biomedical research committee at Umm Al-Qura University, Makkah, Saudi Arabia

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CONFLICT OF INTEREST

The authors state there are no conflicts of interest.

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