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CASE IMAGE

Heinz bodies in COVID-19

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Oxidative stress has emerged as a substantial feature of COVID-19 pathophysiology, which may alter blood cells, red blood cells (RBCs) especially, as reported by different observations presenting oxidative-stress related morphological alterations (bite cells, mushroom-shaped cells…).[1–3] To assess whether RBCs may present preformed or induced intracellular inclusions such as Heinz bodies, indicative of oxidative damages (as evidenced in G6PD deficiency or some haemoglobinopathies), blood films from 15 unselected patients with COVID-19 hospitalized in intensive care units were carefully reviewed after 20 min, 4 h and 24 h of incubation with Brilliant Cresyl Blue at 37°C. Regarding patients (seven females/eight males, median age 60 years, without history of RBCs disorder), the median delays between the positive nasopharyngeal swab and (1) ICU admission, (2) blood withdrawal were 6 and 10 days, respectively. Furthermore, 10/15 presented acute hypoxemic respiratory failure (AHRF) requiring high-flow nasal canula oxygen ($N = 5$), intubation and mechanical ventilation ($N = 3$), or extracorporeal membrane oxygenation ($N = 2$) at the time of the observation. Regarding COVID-19 specific medications, 13/15 patients had corticosteroïds at the time of blood sampling, among which seven patients received Tocilizumab and one patient received Baricitinib; none of the fifteen patients received antiviral therapy, four had Cefotaxime (associated with Rovamycin in two patients), one had

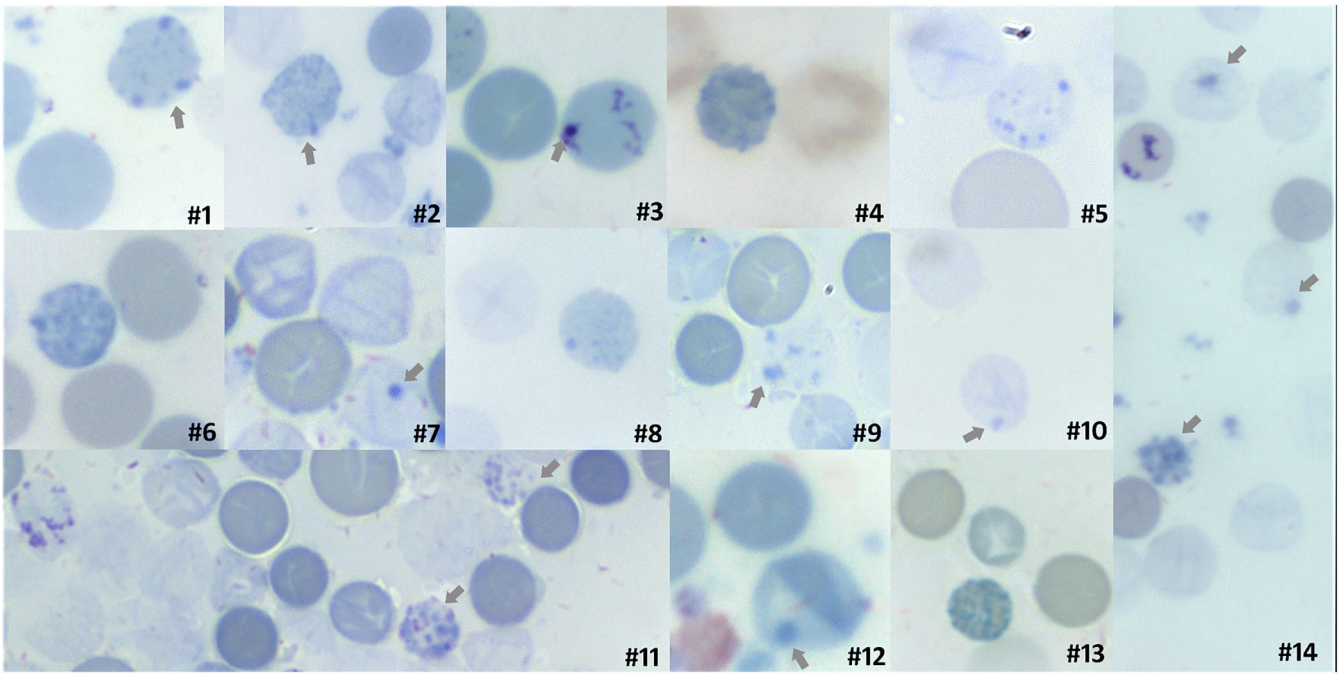

FIGURE 1 Heinz Bodies evidenced in 14 patients (grey arrows); each thumbnail corresponds to a single patient; original magnification ×100

Levofloxacin+Amoxicillin/Clavulanic acid; one received Ivermectin (for deworming).

Median blood count data were RBC = 4.1 x 10^{12}/L, haemoglobin = 123 g/L, MCV = 94 fL, MCHC = 321 g/L, leukocytes = 8.7 x 10^{9}/L, platelets = 230 x 10^{9}/L. Of note, May-Grünwald Giemsa stained-blood films showed few amounts of mushroom-shaped in the majority of patients. After Brilliant Cresyl Blue stain, no inclusion was observed after 20 min, indicating there was no preformed Heinz Bodies in RBCs. However, after 24 h of incubation (and for few patients as early as 4 h), inclusions within RBCs were evidenced in all patients but 1 (Figure 1; each thumbnail corresponds to a single patient, #1-14; original magnificationx100). Interestingly, inclusions display different appearances among patients: single (e.g., #3-7-12) or multiple refractile (e.g., #1-11-14) bodies, and even multiple greenish-blue "golf ball" inclusion bodies (e.g., #4-6-13); interestingly, RBCs ghosts, sporadically still presenting intracellular inclusions, were observed in few patients (e.g., #7-9-14). In anyway, such inclusions, which are not evidenced in health subjects under similar conditions, may be observed in case of alpha-thalassemia or unstable haemoglobin, and in the present context, are indicative of oxidative injury leading to denaturation and precipitation of haemoglobin. It is noteworthy that some patients did not present AHRF indicating that the presence of these inclusions is not restricted to high intensity oxygen therapy.

In the end, these observations further support the substantial impact of SARS-CoV2 infection in generating these RBCs abnormalities.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data available on request due to privacy/ethical restrictions.

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