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Letter to the Editor

Glucose-6-phosphate dehydrogenase deficiency associated hemolysis in COVID-19 patients treated with hydroxychloroquine/chloroquine: New case reports coming out



Afra TP et al comment our recent report entitled: "acute hemolysis by hydroxychloroquine (HCQ) was observed in G6PD-deficient patient with severe COVID-19 related lung injury" [1,2]. Afra et al. underlight "confounding factors and inconsistencies" in our conclusion, linking acute drop in Hb in COVID-19 patient with suspected G6PD and HCO treatment. We respectfully disagree with comments from Afra et al. Our case report was the first one of a series, linking G6PD deficiency with HCO/CO treatment for COVID19 infection such as Kuiper ME et al. or Beauverd Y et al. or Maillart et al. [3-5]. In our case, we observed an acute drop of Hb values associated with the appearance of hemoglobinuria and abnormalities in red cell morphology at the blood smear within 48 h after patient hospital admission and the introduction of HCQ treatment. Our patient was transfused and HCQ was withdrawn with stabilization of Hb values. Thus, this was not a spontaneous recovery of Hb values as suspected by Afra et al. (see Fig. 1 in De Franceschi L et al 2020) [2]. In addition, hemoglobinuria is a hallmark of intravascular hemolysis, which characterizes drug induced acute hemolysis in G6PD patients [6]. Otherwise, drug induced hemolytic anemia in patients with healthy red cells is general an extravascular hemolysis without hemoglobinuria.

Italy is an endemic area for G6PD deficiency [6]. Our patient was suspected for G6PD deficiency based on previous hemolytic events recorded in patient history. To fully answer the question raised by Afra et al., we have evaluated G6PD activity in our patients at 8 weeks after hospital discharge. As expected we found G6PD deficiency with normal complete blood count analysis and normal reticulocyte count (43.500 retics/uL).

Collectively our results and the post-recovery determination of G6PD support the link between acute hemolysis and HCQ/CQ treatment in COVID-19 patients.

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Disclosures

The authors have nothing to disclose.

Declaration of Competing Interest

The authors declare that they have no known competing financial

interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

- Afra T.P.R.V.N.V., Muhammed Razmi T., Bishurul Hafi N.A.. Linking hydroxychloroquine to hemolysis in a "suspected" glucose 6 phosphate dehydrogenase deficient patient with COVID-19 infection-a critical appraisal. Eur J Intern Med 2020; doi:10.1016/j.ejim.2020.07.001.
- [2] De Franceschi L, Costa E, Dima F, Morandi M, Olivieri O. Acute hemolysis by hydroxycloroquine was observed in G6PD-deficient patient with severe COVD-19 related lung injury. Eur J Intern Med 2020;77:136–7.
- [3] Kuipers MT, van Zwieten R, Heijmans J, Rutten CE, de Heer K, Kater AP, et al. Glucose-6-phosphate dehydrogenase deficiency-associated hemolysis and methemoglobinemia in a COVID-19 patient treated with chloroquine. Am J Hematol 2020;95:E194–E6.
- [4] Beauverd Y, Adam Y, Assouline B, Samii K. COVID-19 infection and treatment with hydroxychloroquine cause severe haemolysis crisis in a patient with glucose-6phosphate dehydrogenase deficiency. Eur J Haematol 2020:1–3.
- [5] Maillart E, Leemans S, Van Noten H, Vandergraesen T, Mahadeb B, Salaouatchi MT, et al. A case report of serious haemolysis in a glucose-6-phosphate dehydrogenase-deficient COVID-19 patient receiving hydroxychloroquine. Infect Dis 2020;52:659–61.
- [6] Cappellini MD, Fiorelli G. Glucose-6-phosphate dehydrogenase deficiency. Lancet 2008;371:64-74.

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