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LETTER TO THE EDITOR

Re: Porphyria Cutanea Tarda in a Patient with Myelofibrosis

Dear Sir,

We read the novel article by Serrano-Ordóñez *et al*. describing an alcohol addicted 63-year-old male patient with porphyria cutanea *tarda* (PCT) related to myelofibrosis (MF) treated by hydroxyurea and blood transfusions, who then developed a generalised melanoderma besides blisters and erosions on the dorsum of the hands.[1] Laboratory tests detected anaemia, thrombocytopaenia, hyperferritinaemia, in addition to high blood and urine porphyrines. The Wood's light test showed the bright red-pink fluorescence and the skin biopsy detected subepidermal blisters with IgG deposition on the dermal-epidermal junctions. With control of initial anaemia, he underwent periodic phlebotomies with clinical success, and the authors emphasised the scarce association of PCT with idiopathic MF. Of note, this patient presented a myeloproliferative disease (primary MF) concomitant with a lifestyle risk factor (alcohol consumption) related to the mechanisms of porphyria.[1–6]

Hsu *et al*. stressed that in alcoholic liver disease the ethanol metabolism is decreased followed by higher DMT1 and ferroportin expression, which can propitiate an iron overload (IO);[2] therefore, the serum ferritin levels may be elevated in 63% of the patients. They cited MF, thalassaemia, myelodysplastic syndrome, sideroblastic or sickle cell anaemia, pyruvate kinase deficiency and chronic liver disease as secondary causes of IO. Modesto Dos Santos emphasised PCT as the most common porphyria, with decreased hepatic uroporphyrinogen decarboxylase, high uroporphyrinogen and heptacarboxilate levels, the relation uroporphyrin/coproporphyrin higher than 3:1 and photosensitivity.[3] He commented on the PCT types: I or sporadic and II or familial (20%), the recurrent manifestations due to skin exposition to the sunlight, the urine color red-to-brown on natural light changing to pink-to-orange on the Wood's lamp and the alcohol risk factor.[7] Piérard-Franchimont *et al*. reviewed a variety of common and less frequent cutaneous manifestations related to alcohol consumption, including stellar angioma, acne rosacea, melanoderma, rhinophyma, nevoid telangiectasia, palmar erythema, purpura, pruritus, xerosis, jaundice, Terry's nails, pellagra and PCT; in addition to the worsening psoriasis.[4] The authors highlighted the classification of PCT: type 1 (75–80% of cases) with a prevalence of 0.2 to 20 per 100,000 population, type 2, autosomal dominant familial, and type 3 without genetic change, but with enzymatic activity deficit; the fluorescent staining of urine on Wood's lamp and elevated serum levels of ferritin and hemosiderin.[4] Rapozzi *et al*. highlighted the increase of porphyria that may occur during the progression from mild to severe COVID-19 infection, showing a relationship between SARS-CoV-2 and the iron metabolism, as already known in other RNA virus infections.[5] They stressed the high production of haem and of free haemoglobin, in addition to a link of SARS-CoV-2 with the haem; the viral ope+ target haem on the 1-beta chain of the Hb.[5] As the haem may act as a molecule that regulates the transcription, cell signaling and ion flux, one should highlight that the RNA interference functions in the antiviral immunity.[5] San Juan *et al*. determined the total porphyrin content in the sera of a cohort of 134 confirmed COVID-19 patients (COVID-pos) in the acute phase of disease, and of a cohort of 60 PCR-negative patients (COVID-neg) with diagnosis of pneumonia; besides 54 serum samples of medical check-up collected in 2018 and 2019, before the pandemic.[6] The by-products uroporphyrin I (URO I) and coproporphyrin I (COP I) and the metabolite coproporphyrin III (COP III) were significantly elevated in the serum from COVID-pos. Normal levels of protoporphyrin IX suggested that SARS-CoV-2 do not directly compete with the haem group for the iron atom; additionally, the porphyrin accumulation in COVID-19 sera is lower than in the porphyria patients, due to the short duration of the viral infection.[6] The authors focused on the elevated levels of 2-hydroxybutyric acid that is mainly synthesised in the liver and released by the transsulphuration pathway and the elevated levels reflect an increase of oxidative stress in COVID-19 patients and impaired hepatic mitochondrial function, which is also consistent with the accumulation of porphyrins.[6]

PCT has been described in cases of haematological disorders, is often associated with high serum levels of iron and ferritin where cutaneous manifestations may be triggered by alcohol intake and infectious agents including SARS-CoV-2 virus. Case studies may enhance the suspicion index about less common clinical associations.

AUTHORS' CONTRIBUTION

VMS and TAMS drafted the manuscript. VMS and TAMS reviewed the literature and performed the critical revision of the manuscript. All authors approved the final version of the manuscript.

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