Methaemoglobinaemia and haemolysis after rasburicase administration in a patient with G6PD deficiency

Ismael Boussaid, Johanna Mondesir, Nicolas Chapuis, Rudy Birsen

DESCRIPTION

A man in his 20s complained of progressively worsening dyspnoea. He reported no medical history. Clinically, there was an abolition of the left vesicular breath sounds and a superior vena cava syndrome. CT scan revealed a large mediastinal mass causing bronchial compression with left atelectasis (lower lobe and lingula). A transthoracic biopsy revealed a lymphoblastic lymphoma. We initiated a treatment with corticosteroids and rasburicase to prevent the high risk of tumour lysis syndrome. At the time of treatment initiation, his saturation was 96%, with no oxygen requirement. Three hours later, the patient presented a rapidly progressive drop in oxygen saturation to 85%, unimproved by the administration of oxygen. The clinical examination and the chest radiograph were unchanged. We performed an arterial blood gas which showed: pO2 68.5 mm Hg, pCO2 32.7 mm Hg and methaemoglobinaemia 3.7%. CT scan excluded atelectasis, pneumonia and pulmonary embolism. As the patient was a man from Southeast Asia, we suspected the occurrence of methaemoglobinaemia on administration of rasburicase in a context of glucose-6-phosphate dehydrogenase (G6PD) deficiency. The occurrence of blood smear abnormalities typical of G6PD deficiency and haemolysis requiring repeated blood transfusions subsequently reinforced this diagnosis (figure 1). All clinical and biological abnormalities resolved within a few days after rasburicase eviction, folate suplementation and repeated red blood cell (RBC) transfusion, allowing the start of chemotherapy. An enzymatic assay confirmed G6PD deficiency remotely from the episode by an enzyme assay.

G6PD deficiency is an X-linked disease, conferring a relative protection against malaria, which explains its geographical distribution (Africa, Mediterranean Rim and Asia). G6PD belongs to the pentose phosphate pathway, which is the only source of regeneration of reduced nicotinamide adenine dinucleotide phosphate (NADPH) in the RBC. Reduced NADPH is the coenzyme of NADPH methaemoglobin reductase, which allows the reduction of inactive methaemoglobin to haemoglobin in situations of oxidative attack. It is also the main coenzyme of glutathione reductase, which ensures the regeneration of reduced glutathione, and provides protection against oxidation of globin and various structural proteins of the RBC. In most patients, the G6PD deficiency is partial, and the residual activity is sufficient in basal state but does not allow the elimination of peroxides accumulated under the effect of oxidants, most often drugs. Methaemoglobin is
haemoglobin in which oxidised iron changes from the ferrous (Fe$^{2+}$) to the ferric (Fe$^{3+}$) state, making it unfit for oxygen transport.¹

Haemolytic anaemia or methaemoglobinaemia in patients with G6PD deficiency has been classically described with rasburicase.³ Indeed, it is a potent uricolytic agent that catalyses the enzymatic oxidation of uric acid to allantoin, a watersoluble substance that is easily excreted by the kidney in the urine. The enzymatic oxidation of uric acid leads to the stoichiometric formation of hydrogen peroxide. The increase in hydrogen peroxide beyond the usual level can be normalised by endogenous antioxidants. In the case of G6PD deficiency, the ability of the RBC to reform endogenous antioxidants is exceeded, explaining the occurrence of haemolysis and/or methaemoglobinaemia.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

REFERENCES


Learning points

► Haemolytic anaemia or methaemoglobinaemia in patients with G6PD deficiency have been classically described with rasburicase.
► A careful examination of the blood smear may allow the diagnosis of G6PD deficiency in the presence of characteristic abnormalities (hemighosts cells and Heinz body).