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Artifactual Hypoglycaemia During Treatment with Filgrastim (rHu-met-G-CSF)

J.J. Illarramendi, A. Iruin and I. Mitxelena

Services of Oncology and Pharmacy, Hospital de Navarre, E-31008, Pamplona, Spain

NON-GLYCOSILATED RECOMBINANT-methionyl human granulocyte colony-stimulating factor (filgrastim) is a glycoprotein produced through recombinant DNA technology. The main indication of this protein in medical oncology is to enhance neutrophil recovery after various chemotherapy regimens. Filgrastim has shown an excellent safety profile in trials and in widespread clinical practice [1]. Metabolic disturbances associated with this drug have been described as asymptomatic, mild or moderate elevations of lactate dehydrogenase, alkaline phosphatase, uric acid and gamma-glutamyl transpeptidase [2]. We report a case of severe artifactual hypoglycaemia secondary to filgrastim-induced hyperleucocytosis.

A 65-year-old man was diagnosed in June 1996 with gastric adenocarcinoma, UICC clinical stage pT4N3M1. He started therapy with etoposide, folinic acid and 5-fluorouracil [3]. A few days after the third cycle he needed admission to the Vascular Surgery ward because of severe arterial ischaemia in his left arm. During admission, early neutropenic fever developed, and supportive therapy was instituted with filgrastim (300 mcg/day), ceftazidime and amikacin. Filgrastim therapy was maintained for 9 days in this patient, before a new referral to the Oncology Service. At that moment, blood analysis revealed a severe hyperleucocytosis (white blood cell count, WBC: 101 000/mm^3) and hypoglycaemia (1.39 mmol/l, 25 mg/dl). However, the patient did not manifest any significant symptom of hypoglycaemia. He maintained previous nutritional habits and was not taking any drug with potential hypoglycaemic effects. Immediate bedside glucose determination from a finger drop was normal and a bedside glucose profile during the day did not reveal any disturbance. A diagnosis of factitious or artifactual hypoglycaemia was made. Filgrastim was withdrawn, and leucocyte counts normalised after several days.

Hyperleucocytosis is a recognised cause of artifactual hypoglycaemia and this phenomenon has been described in several settings, as in leukaemia, polycythaemia vera and leukaemoid reactions [4]. The explanation of this finding is *in vitro* glucose depletion by augmented and stimulated leucocytes and the magnitude of the artifact is dependent upon temperature, duration of time that the cells and plasma are left in contact and the presence of an antiglycolytic inhibitor. There is one previously reported case of severe artifactual hypoglycaemia associated with G-CSF therapy and 2 additional cancer patients with less severe decreases in blood glucose [5]. In the severe case, a 5-h delay of the sample in reaching the laboratory was considered an important associated factor. Delay in our patient was less than 1 hour, but probably the existence of severe hyperleucocytosis and associated sepsis were more determinant in depleting glucose levels.

Although factitious hypoglycaemia secondary to G-CSF stimulation of leucocytes is not a major event *per se*, we suggest that it must be recognised by the clinician in order to avoid inappropriate reporting of adverse effects, performance of unnecessary evaluations and inadequate monitoring of treated patients with previous hyperglycaemia.

Correspondence to J.J. Illarramendi.
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