Letter to the Editor

Leukocytosis-Induced Artifactual Hypoglycemia

To the Editor;

In vitro utilization of glucose by normal and leukeemic leukocytes has been previously described [1–3]. This phenomenon presents clinically as artifactual, asymptomatic, hypoglycemia. Despite few reports, some endocrine textbooks [4] do not include this possibility in the differential diagnosis of hypoglycemia. In this communication, multiple episodes of asymptomatic, artifactual hypoglycemia (AH) are described in a patient with polycythemia vera (PV) and leukocytosis.

Case: An 85 year old man was hospitalized for management of a four week history of progressive functional decline. Relevant medical history included PV, diagnosed in 1976, compensated congestive heart failure and endobronchial lymphoma. His medications included digoxin, quinidine, hydroxyurea, enalapril and omeprazol. Physical examination was unremarkable. Laboratory data on admission revealed a serum glucose of 44 mg/dl, a hematocrit of 42.8%, a RBC (Red Blood Cell Count) of \(4.99 \times 10^{12}/L\), a WBC (White Blood Cell Count) of \(33.2 \times 10^9/L\) and a total platelet count of \(748 \times 10^9/L\). The rest of his chemistries were normal. Repeat serum glucose level, within a few hours, was 42 mg/dl. The patient denied symptoms of hypoglycemia at any time. The Endocrine service was consulted for evaluation of hypoglycemia. The patient was asymptomatic at the times the two samples were drawn. A systematic review of laboratory data over the preceding six months was performed. Serum glucose levels, measured in tubes without additives, correlated (Pearson’s correlation coefficient) negatively with WBC \((r = -0.61, p<0.001; \text{Fig. } 1A)\) and RBC \((r = -0.42, p = 0.026; \text{Fig. } 1B)\) counts determined in simultaneously drawn samples. AH was suspected.

To confirm the diagnosis, three venous blood samples were drawn simultaneously for glucose determination. A bedside glucometer was used to assess one sample while two others were drawn in separate tubes and processed simultaneously in the laboratory, within one hour. One tube was without additives while the other contained 7.5 mg of sodium fluoride and 6.0 mg of potassium oxalate, a known inhibitor of aerobic glycolysis. Glucose concentrations in the 3 samples were 80 mg/dl, 42 mg/dl and 78 mg/dl, respectively.

Artifactual hypoglycemia has been reported to occur in PV and is caused by in vitro autoglycolysis due to both RBC and WBC-induced enhanced glycolysis [2, 3]. Serum glucose concentrations can drop significantly within 2 hours after sample collection, and longer intervals of time are associated with greater reduction in glucose levels. Delays in serum separation result in artifactual decrease in glucose concentrations, even in patients with normal WBC counts (0.17 mmol of glucose/L/h) [5]. The process can be minimized when samples are kept cold. Although RBC can metabolize glucose in vitro, WBC effects are more profound. Lack of symptoms should raise suspicion for the diagnosis which can be confirmed by glucose measurements in capillary blood or in venous blood collected in tubes pre-filled with inhibitors of glycolysis (e.g., NaF).

AH is often not listed or emphasized in textbooks or reviews on hypoglycemia [4]. Although it is true that symptomatic hypoglycemia can occur in patients with leukocytosis, leukemia or polycythemia [1–3], AH should be considered before initiating extensive work-up for reported low serum glucose levels.
References


