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CASE REPORT IN EMERGENCY MEDICINE

A case of silent myocardial ischemia associated with severe and prolonged hypoglycemia

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Abstract

The scientific literature on treatment options and complications following large insulin overdoses is limited to case reports and few retrospective, epidemiological reports providing limited clinical insights. The effect of hypoglycemia on the heart is uncertain. There are two main factors that are commonly associated with electrocardiographic changes during hypoglycemia, of which the first is linked to the rapid decrease in blood glucose levels, and the other to the decrease in potassium serum levels.

We report a case of severe and prolonged hypoglycemia due to deliberate misuse of long-acting insulin associated with transient electrocardiographic ischemic changes without symptoms of myocardial ischemia. We diagnosed and treated this patient as a case of silent cardiac ischemia.

Hypoglycemia is a common event in patients affected by insulin dependent diabetes mellitus. The emergency physicians should be aware of aspecific or ischemic ECG alterations associated with severe hypoglycemia. As shown in this case report, ECG monitoring is crucial for early detection of ischemic electrocardiographic changes suggestive of myocardial ischemia in diabetic patients.

KEY WORDS: Diabetes mellitus; hypoglycemia; insulin overdose; myocardial ischemia.

Riassunto

La letteratura scientifica relativa agli aspetti clinici e terapeutici in caso di sovradosaggio di insulina consiste principalmente di case report aneddotici e di alcuni studi epidemiologici retrospettivi. L'effetto dell'ipoglicemia sul cuore è ancora poco conosciuto. Le alterazioni elettrocardiografiche in corso di ipoglicemia sono associate a due fattori, di cui uno è correlato direttamente alla riduzione della glicemia e l'altro all'ipopotassiemia secondaria.

Riportiamo il caso di un paziente con grave e prolungata ipoglicemia, a causa di un abuso volontario di insulina ad azione prolungata, associata ad alterazioni elettrocardiografiche di tipo ischemico, transitorie e senza sintomi di ischemia miocardica. Questo è stato diagnosticato e trattato come un caso di ischemia miocardica silente. L'ipoglicemia è un evento comune anche nei pazienti affetti da diabete mellito insulino-dipendente. I medici di pronto soccorso devono essere consapevoli delle alterazioni elettrocardiografiche aspecifiche o ischemiche associate all'ipoglicemia severa. Come evidenziato in questo case report, il monitoraggio

elettrocardiografico è cruciale per il precoce riconoscimento delle modifiche elettrocardiograpfiche suggestive di ischemia miocardica nei pazienti diabetici.

TAKE-HOME MESSAGE: In case of severe and prolonged hypoglycemia, ECG monitoring is crucial for early detection of aspecific or ischemic electrocardiographic changes in diabetic patients.

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INTRODUCTION

Electrocardiographic (ECG) changes have been observed during insulin-induced hypoglycemia, including depression of the ST segment, flattening of the T wave and prolongation of the QT interval [1]; moreover, anecdotal cases of hypoglycemia-induced ischemic ECG changes have been also reported [2–7]. We report a case of severe and prolonged hypoglycemia due to

deliberate misuse of long-acting insulin associated with transient ECG ischemic changes in a patient without symptoms of myocardial ischemia.

CASE REPORT

A 55-year-old man referred to our emergency department following a low-impact car accident. He was found unconscious, with low capillary blood glucose level (7 mg/dl). A peripheral intravenous cannula was inserted and blood extracted followed by administration of 30 ml (9.9 g) of 33% dextrose solution. After infusion he was confused, yet he was able to report to be affected by diabetes in treatment with oral antidiabetic therapy. On arrival, ECG was normal (Figure 1).

After about 2 hours, despite continuous infusion of 10% dextrose, he fell again unconscious with a capillary blood glucose level as < 40 mg/dl. During treatment, the patient showed an epileptic seizure, which was treated with intravenous diazepam.

Arterial blood gas test showed the following parameters: pH 7.31; PaO2 56 mmHg; PaCO2 44 mmHg; HCO_3 22.2 mMol/L; Serum Lactate 6.4 mMol/L; Na 135 mMol/L; and K 2.3 mMol/L.

A naso-gastric aspiration showed the absence of any residual of tablets in his stomach.

The patient remained unconscious with low levels of capillary blood glucose despite dextrose infusion and, therefore, he was unable to provide further information about his medical history.

After 2 hours, the sister-in-law arrived, reporting that the patient was affected by a not well-defined psychiatric disorder and the previous evening he had threatened of harming himself, while leaving home. Despite administration of dextrose-containing fluids was continued for many hours, blood glucose levels did not come back completely normal.

After his awakening, in the following hours the patient admitted to having intook, the evening before, a whole long-acting basal insulin-pen (glargine 300 U) and one type of rapid-acting insulin-pen (lispro 300 U), for self-injurious purpose.

Dextrose infusion was continued with a subsequent slow improvement of the metabolic values (glucose, pH, potassium and lactate).

An ECG monitoring was performed, which showed an inversion of T wave in II, III, aVF, and V3-V6 (Figure 2). However, our patient reported no chest pain or other symptoms of myocardial ischemia during all medical observation.

Echocardiogram showed normal kinesis, as well as ejection fraction value and serial ultrasensitive T troponin measurements were found to be normal.

After about 30 hours from the arrival, an ECG monitoring showed the regression of the ischemic signs and the patient, who was diagnosed with silent cardiac ischemia, was discharged.

Figure 1. Normal ECG on arrival at emergency department

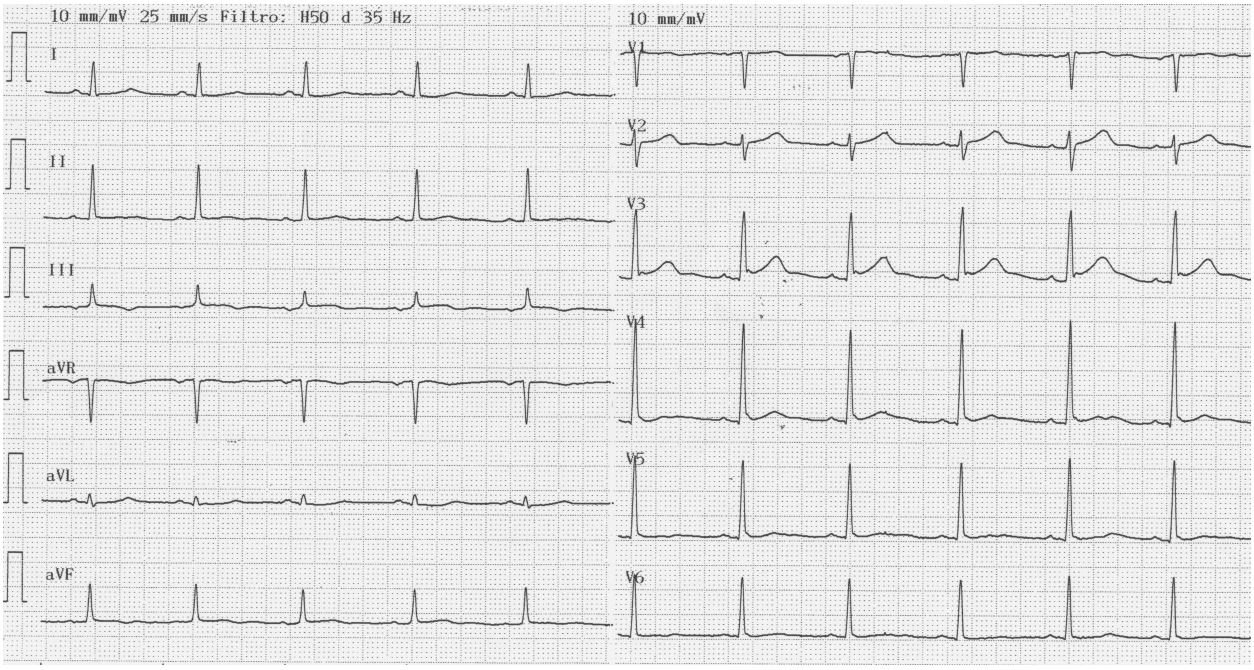
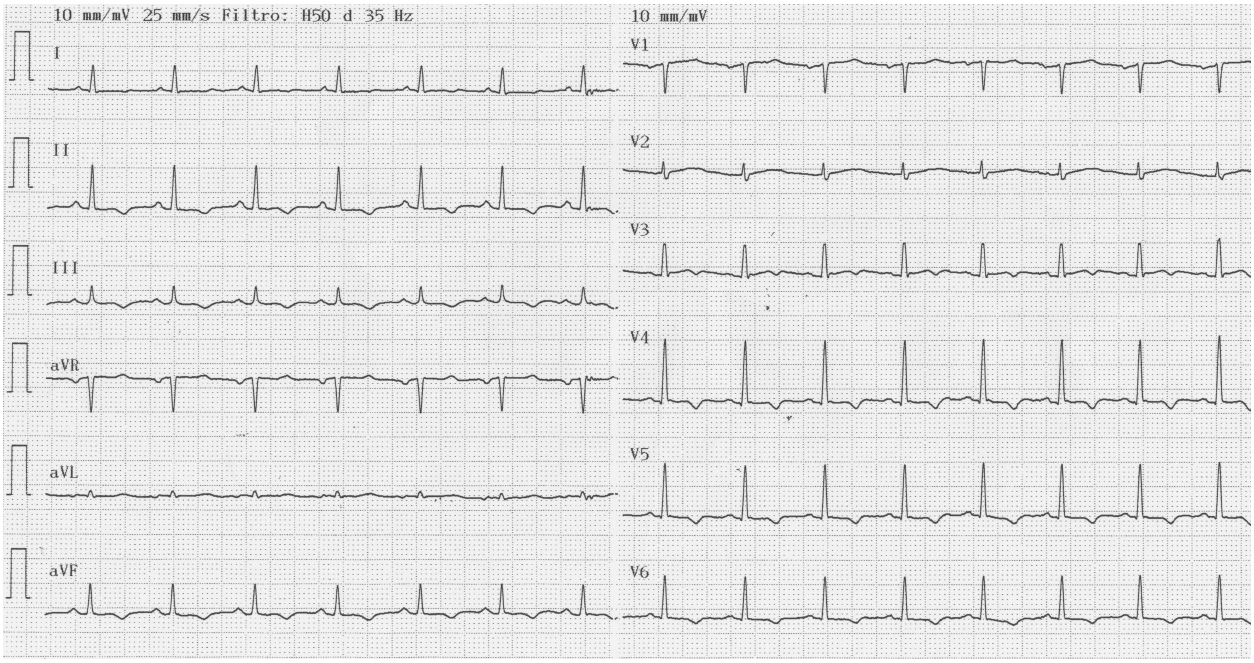


Figure 2. ECG showing an inversion of T wave in II, III, aVF, and V3-V6 about 6 hours after arrival at the emergency department.



DISCUSSION

The scientific literature concerning the consequences and treatment of large insulin overdoses mainly consists of case reports and a few retrospective, epidemiological evaluations with limited clinical information [2–8]. However, a systematic review on clinical course, complications and treatment of insulin overdose cases has been recently published [9].

Electrolyte disturbances, including hypokalemia and hypocalcemia, cardiac disturbances and organ toxicity, such as hepatotoxicity were also reported as a result of insulin overdoses [9].

Also, recent studies showed that mild-to-severe hypoglycemia was associated with increased frequency of cardiovascular events [10–12]. Moreover, Desouza and coll. [13] found that silent hypoglycemia was more likely to be associated with cardiac ischemic events than normoglycemia and hyperglycemia in diabetic patients.

Hypoglycemia is known to trigger counter-regulatory adrenosympathetic systems and thereby create cardiac electrical instability and electrophysiologic alterations [14]. Simultaneous ECG monitoring may highlight the following ECG changes in atrioventricular conduction, ventricular depolarization, and ventricular repolarization in response to hypoglycemia: P-R interval shortening; ST-segment depression; T-wave flattening; reduction of T-wave area; and QTc-interval prolongation [12].

There are two common causes of ECG changes during hypoglycemia: The first one has been associated with the reduction in blood glucose, whereas the other one was related to the decrease in serum potassium concentration.

Indeed, glucose plays a direct role, because hypoglycemia can alter the important balance between energy supply and demand; in addition, it is well-recognized that the administration on insulin, by an increased potassium influx, may result in hypokalemia-induced ECG changes [5], such as prolongation of the QT interval, decreased of amplitude of the T wave, flattening and broadening of the wave, or inversion of T wave in II, III, aVF, and V3-V6, as observed in our clinical case.

Furthermore, hypoglycemia induces the release of some counter-regulatory hormones such as catecholamine (epinephrine and, to a lesser extent, norepinephrine), glucagon, cortisol, and growth hormone (15). Both catecholamine release and increased myocardial work and oxygen

consumption have been shown to occur in patients affected by hypoglycemia, especially in case of rapid decrease in blood glucose [16–18]. Therefore, it is likely that acute hypoglycemia may trigger ischemia and cardiovascular events [13]. Increased counter-regulatory hormones, which are caused by hypoglycemia or rapid decrease in blood glucose, may induce vasoconstriction, platelet aggregation, and thereby ischemia [12, 19, 20]. Indeed, animal studies have also documented such an effect exerted by hypoglycemia on myocardial ischemia/reperfusion injury [17], and both animal and human studies showed that hypoglycemia may increase myocardial infarct size [2, 3, 17]. Hypoglycemia-induced silent myocardial ischemia has also been suggested by multiple authors [3, 21]. For instance, Koh and coll. [22] showed that patients affected by coronary artery disease being not diabetic may present ischemic ECG changes during hypoglycemia. In patients affected by type 1 diabetes without coronary artery disease, Russell and coll. [23] demonstrated that myocardial adaptation to hypoglycemia is impaired during hypoglycemia. Finally, other potential mechanisms by which hypoglycemia may lead to myocardial ischemia are secondary to an increased release of some markers of endothelial dysfunction, such as VIII factor, von Willebrand factor, interleukins, cytokines levels, and endothelin-1 [24–26].

CONCLUSION

In sum, diabetic patients are predisposed to myocardial ischemia and electrical instability consisting of QTc-interval prolongation. Therefore, hypoglycemia needs to be carefully considered and recognized in these patients, as it can lead to ECG changes and silent myocardial ischemia.

As shown in this case of diabetic patient who was diagnosed with silent cardiac ischemia, emergency physicians should be aware that overdosing on insulin can cause prolonged hypoglycemia requiring ECG monitoring to early detect any electrocardiographic ischemic signs of myocardial ischemia.

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