Pneumoperitoneum by subcutaneous injections of GLP-1 analogues. A case report☆

Neumoperitoneo por inyecciones subcutáneas. A propósito de un caso

There has been a revolution in the treatment of diabetes mellitus in recent years with the introduction of the GLP-1 receptor agonists, among other drugs. Because of the still limited experience with these drugs, clinical practice may reveal previously unreported complications related to the drug substances themselves or to the administration protocol employed, as described below.

An 81-year-old woman reported to the emergency room due to a 10-day history of epigastric pain that worsened after meals. There was no associated fever or changes in bowel habit, though she did suffer nausea without vomiting. Guided questioning revealed no other symptoms. The patient had consulted four times because of these problems (the first visit being on 24 October), with all complementary tests (hematological and liver function parameters, abdominal X-rays and electrocardiogram) yielding normal results. Her personal history comprised cardiovascular risk factors (hypertension, type 2 diabetes and dyslipidemia under treatment), chronic ischemic heart disease subjected to revascularization in 2011, and persistent atrial fibrillation treated with anticoagulants. Her usual treatment consisted of rivaroxaban 20 mg, carvedilol 6.25 mg, valsartan 160 mg, amlodipine 5 mg, furosemide 40 mg, atorvastatin 40 mg nitroglycerin (NTG) patch 10 mg, omeprazole 20 mg, vildagliptin 5 mg/metformin 1 g/12 h, insulin Lantus® 16 IU and Trulicity (dulaglutide)® 1.5 every 7 days (this drug being started on 21 October 2017).

The physical examination, abdominal X-rays and blood and liver function tests proved normal.

Given the symptoms reported by the patient, an oral endoscopy was performed, with a diagnosis of antral biliary reflux. Computed tomography (CT) with abdominal contrast showed signs of pneumoperitoneum with the presence of bubbles both in the anterior abdominal wall – hollow organ perforation being discarded – and in the subcutaneous cellular tissue of the abdominal wall. This was probably related to subcutaneous injections, since the subcutaneous cellular tissue thickness in the anterior abdominal wall was 5 mm, reaching 3.8 mm in some zones (Fig. 1).

In view of the imaging findings, a repeat exploration was carried out and the patient was questioned again. Marked abdominal muscle separation (diastasis recti) was noted, becoming visible on the patient being raised. It should also be noted that the patient administered the dulaglutide doses in this abdominal muscle separation zone, the needle of the device being 5 mm in length. It was also seen that insulin administration was performed in the proximal region of both lower limbs.

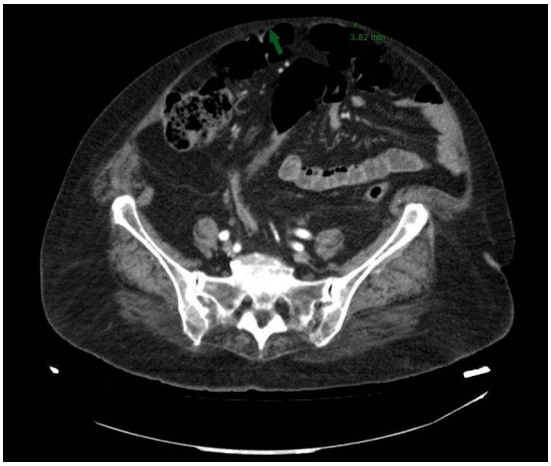

Figure 1 Axial CT scan of the abdomen, revealing the presence of bubbles in the anterior abdominal wall, which has a thickness of 3.8 mm in some areas.

After dulaglutide administration in the abdominal zone was discontinued, the patient was followed-up on in the outpatient clinic one month after hospital discharge, and was seen to be completely asymptomatic. Of note was the absence of abdominal pain.

Gastrointestinal adverse effects such as nausea or vomiting, among other problems, are known, though without reports of their manifestation as seen in our patient. Likewise, the incidence and severity of such effects are less in patients treated on a once-weekly basis.

Many studies have been made in patients treated with GLP1 agonists (dulaglutide), assessing the safety of the administering device[1] and reporting adverse effects in the form of bruising, subcutaneous emphysema and pain at the site of drug administration, as well as skin reactions such as rash.[2] However, to date there have been no reports of pneumoperitoneum, hollow organ perforation or other serious adverse effects. In our patient, pneumoperitoneum was caused because the drug was injected into an area which was unsuitable due to the extremely thin abdominal wall and muscle diathesis.

The etiology underlying pneumoperitoneum in our patient was established following the exclusion of other possible causes, with confirmation of the extreme thinness of the abdominal wall where the drug was administered, and with the resolution of the condition after its administration in this area was suspended.

A limitation in testing the hypothesis was the impossibility of determining the presence of the drug in the bowel contents, resulting from ineffective administration. This is due to the proteic composition of the drug, which facilitates its digestion and thus precludes its detection through testing.

The characteristics of the abdominal wall of the patient; the injection of the drug into the area presenting muscle diathesis; and the characteristics of the injection device make it reasonable to presume that the cause of the pneumoperitoneum was the administration of the drug.

Diathesis or separation of the abdominal muscles is not uncommon, particularly in obese individuals, in which GLP1 analogs are especially useful for the treatment of

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diabetes. In our opinion, this circumstance could represent a contraindication to the administration of the drug in the abdominal region. An alternative in this respect could be its administration in other body zones or specific training imparted by the nursing staff, emphasizing the so-called ''skin pinch technique'', which raises the skin and its underlying layers – thereby avoiding the risk of bowel loop perforation.

Acknowledgments

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Isabel Miras[a,*], Nieves Ramírez[b], Pablo Sánchez[a], Carlos Hernández[b], Domingo Acosta[c]

[a] *Unidad de Gestión Clínica de Oncología Médica, Radioterapia y Radiofísica, Hospital Universitario Virgen del Rocío, Sevilla, Spain*
[b] *Unidad de Gestión Clínica de Medicina Integral, Hospital Universitario Virgen del Rocío, Sevilla, Spain*
[c] *Unidad de Gestión Clínica de Endocrinología y Nutrición, Hospital Universitario Virgen del Rocío, Sevilla, Spain*

* Corresponding author.
E-mail address: isabelmiras92@gmail.com (I. Miras).

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Tako-Tsubo cardiomyopathy induced by pheochromocytoma☆

Cardiomiopatía de Tako-Tsubo inducida por feocromocitoma

Pheochromocytoma is a catecholamine-producing neuroendocrine tumor derived from the chromaffin cells of the adrenal gland. The annual incidence is between 0.005 and 0.1%,[1] though diagnostic difficulties result in an underestimation of the true incidence.[2] Infrequently, pheochromocytoma manifests as Takotsubo-like cardiomyopathy,[3] which is characterized by transient apical myocardial dysfunction simulating acute coronary syndrome, but with healthy coronary arteries. To date, a total of 84 cases of Takotsubo cardiomyopathy associated with pheochromocytoma have been reported.[1,4,5] We report the case of a patient requiring multiple admissions due to a myocardial dysfunction classified as recurrent Takotsubo cardiomyopathy secondary to pheochromocytoma.

A 70-year-old woman with no known family or personal history of disease presented with self-limiting symptoms of chest pain, palpitations and perspiration. She reported to the emergency room with the aforementioned symptoms, associated with dyspnea, normal blood pressure, and $SatO_2$ 84%. The ECG tracing showed ST depression on the lateral surface, and the laboratory tests revealed troponin elevation to 1200 ng/l (normal range: 0–13). The patient presented acute lung edema (ALE) requiring invasive mechanical ventilation (IMV) and diuretic and vasodilator medication. Echocardiography revealed severe contractile dysfunction with a left ventricular ejection fraction (LVEF) of 36% and posterolateral akinesis. With the suspicion of acute myocardial infarction (AMI), coronary artery catheterization was performed, but yielded no evidence of significant lesions. The condition was postulated to correspond to posterolateral AMI secondary to embolism. Control echocardiography 10 days after the acute event showed recovery of the LVEF (65%).

Two years later, under follow-up by her family physician, with good blood pressure control and no hyperadrenergic episodes, the patient returned to the emergency room in cardiogenic shock requiring noradrenalin, dobutamine, and IMV. The ECG tracing revealed marked negative T-waves on the anterolateral surface, with a positive troponin curve. Initial echocardiography showed a LVEF of 30–35%. The coronary catheterization findings were normal, and LVEF recovered two weeks later. A tentative diagnosis of Takotsubo cardiomyopathy was established. The patient reported again to the emergency room four months later due to ALE in the context of rapid atrial fibrillation, with a tendency toward hypotension. Vasoactive drugs were required. The acute phase echocardiographic study showed severe ventricular dysfunction. The Endocrinology department was consulted to rule out pheochromocytoma as the underlying cause. Twenty-four hour urine catecholamine measurements revealed no significant elevation (Table 1). The patient was under treatment with propranolol. Abdominal computed tomography (CT) with contrast injection identified an ovoid right adrenal mass measuring 30 × 20 mm in size. The lesion was hypodense, with fine capsular enhancement in the arterial and portal phases, with no features typical of pheochromocytoma. By contrast, scintigraphy with metaiodobenzylguanidine showed radioiodine uptake

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