Vasculitis associated with cocaine-levamisole use

Vasculitis asociada a consumo de cocaína-levamisol

To the Editor,

Cocaine is a stimulant drug of the central nervous system, a vasoconstrictor, and a local anesthetic derived from the coca leaf. Currently, derivatives are produced at different stages of processing, such as coca paste, cocaine hydrochloride, and freebase cocaine, known as "crack." It is consumed intranasally, intravenously, or smoked.[1]

Levamisole is a drug used as a veterinary antiparasitic agent, but it is not authorized for human use due to adverse effects such as agranulocytosis, hepatotoxicity, and vasculitis. In many countries, such as the United States, it is used as a cocaine adulterant.[2,3]

We present the case of a 53-year-old man with a past medical history of polysubstance abuse (tobacco, ethanol, cannabis, and cocaine), type 2 diabetes mellitus, and schizophrenia, who presented to the Emergency Department with a several-day history of skin lesions on the lower extremities and difficulty walking, without fever or other associated symptoms. He reported that his last use of cocaine had occurred 3 and 10 days prior to his consultation, after a 4-month abstinence. On physical examination, multiple purpuric papules and plaques were observed on the lower limbs, umbilicus, periumbilical area, and dorsum of the hands—some with crusted-necrotic centers and others with vesiculobullous centers containing hemorrhagic fluid (Figure 1a).

Supplementary tests showed a C-reactive protein (CRP) of 5.19 mg/dL, leukocytosis of 15,470/mm^3, normocytic-normochromic anemia, negative blood cultures, and growth of coagulase-negative *Staphylococcus* in lesion smear cultures. Autoimmunity studies showed: normal anti-β^2 glycoprotein, normal complement levels, negative antinuclear antibodies (ANA), minimally elevated anti-Ro, negative anti-neutrophil cytoplasmic antibodies (ANCA), moderately positive antinuclear IgG$^{3-4}$ with a speckled pattern, and negative cytoplasmic antibodies.

Toxicological urine screening tested positive for benzodiazepines and cocaine. Gas chromatography/mass spectrometry (GC/MS) analysis revealed the presence of cocaine metabolites ecgonine methyl ester (EME) and benzoylecgonine (BE). Levamisole was not detected, probably due to the prolonged interval between drug use and sample collection (5 days). A skin biopsy showed thrombotic vasculopathy, unrelated to other causes, consistent with the clinical suspicion of being caused by cocaine/levamisole use (Figure 1b).

Empirical antibiotic treatment with amoxicillin-clavulanate, oral corticosteroids,

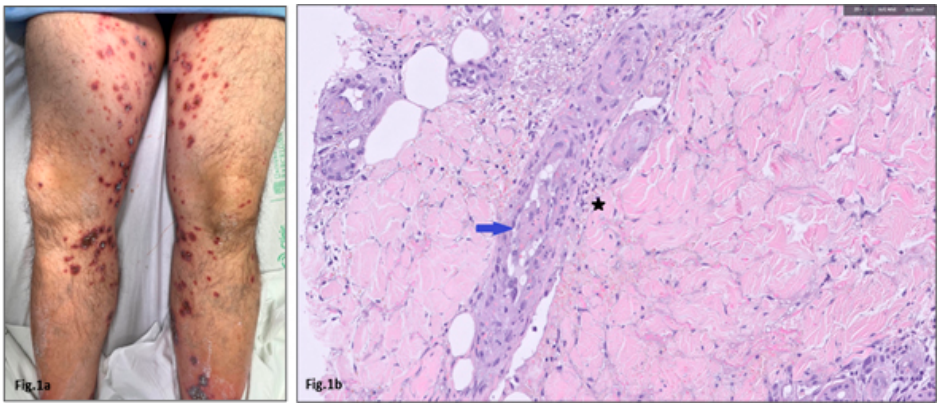

Figure 1. A) Multiple purpuric papules and plaques on the lower limbs. B) Histological image corresponding to cutaneous tissue, a small-calibre vascular structure with a fibrin thrombus adhered to the endothelium (blue arrow), with haematic extravasation and scarce associated inflammatory infiltrate (black asterisk), without evidence of karyorrhexis can be identified in the mid dermis. The endothelia are oedematous and swollen (haematoxylin-eosin, 10x).

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and topical wound care were administered, with good clinical progress, and the patient was discharged after 10 days.

From a pathophysiological standpoint, cocaine acts on blood vessels by stimulating the release of endothelin-1, a potent vasoconstrictor, and inhibiting the production of nitric oxide, the main vasodilator, which induces endothelial damage, promotes platelet aggregation and a prothrombotic state, leading to systemic and local ischemia. Notably, it causes midline destructive lesions and may contribute to vasculitis mechanisms associated with ANCA or inflammatory processes triggered by *Staphylococcus aureus* superantigens.[4,5]

Levamisole may influence immune function by activating neutrophils and inducing ANCA formation.[6] The elimination half-life of levamisole is 5–6 hours,[7] which is faster than the elimination of cocaine metabolites BE and EME, which can be detected in urine for up to 5 days post-consumption.

In our case, an association was demonstrated between cocaine use (likely adulterated with levamisole) and the appearance of skin lesions, after ruling out infection and confirming inflammatory markers and a biopsy compatible with vasculitis due to levamisole-adulterated cocaine.[8] These are uncommon cases that should be considered in the differential diagnosis of chronic cocaine users presenting to emergency services.[9]

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Comment on "A nonketotic hyperglycemic hemichorea emergency"

Hemicorea hiperglucémica no cetósica en emergencias

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To the Editor,

We have paid very close attention to the letter by Sánchez J *et al.* published in your journal.[1] We were surprised and strongly intrigued to see that a metabolic lesion could be visualized on imaging, and we would like to congratulate the authors. However, we would like to clarify certain aspects regarding the pathophysiology of diabetes and hyperglycemia.

Diabetes mellitus is a metabolic disease with various clinical forms. In all of them, there is a deficit in insulin function, which leads to alterations in metabolic pathways involving carbohydrates, lipids, proteins, water-electrolyte balance, and acid–base equilibrium.

Clinically, on the one hand, acute decompensations are described (simple hyperglycemia, diabetic ketoacidosis, hyperosmolar state, and hypoglycemia), which are often the first manifestation of the disease[2]. On the other hand, there are the so-called chronic complications, which result from sustained hyperglycemia over time, causing different types of damage through the following mechanisms: 1) Alteration of the polyol pathway due to the conversion of excess glucose into sorbitol, which accumulates in certain tissues, disrupting cellular function and nerve conduction; 2) Hemorheological changes, creating a hypercoagulable state due to increased plasma viscosity, decreased red blood cell deformability, and increased platelet aggregability; e) Excess glucose binds to various proteins (lipoproteins, collagen, hemoglobin, etc.). Therefore, ischemic mechanisms are not the only cause of neurological damage, even if these late complications have traditionally been categorized by the size of the blood vessels they affect. These are referred to as microangiopathic (retina, kidney, nervous system) and macroangiopathic lesions, which may lead to ischemic heart disease, ischemic stroke, and lower limb ischemia.[2]

In the presented case, although plasma osmolality is not mentioned, we believe it describes a hyperosmolar state, for which the term "non-ketotic" need not be specified, as by definition it involves hypernatremic dehydration caused by osmotic diuresis due to sustained and intense hyperglycemia. In this condition's pathophysiology, ketogenesis is not triggered because there is an insulin deficiency, but not a complete absence. Nevertheless, it is extremely interesting to highlight the neurological symptoms and the hyperintense lesion on computed tomography (CT) described as "non-ischemic." Acute decompensations of diabetes can exhibit a variety of neurological symptoms, including focal neurological deficits. In this case, they are first described as abnormal movements, possibly corresponding to hemichorea–hemiballismus, and later as weakness graded 3/5.

Although the metabolic causes of hemiballismus are very rare, they may be underdiagnosed, even in hyperglycemia. A combination of pathophysiological mechanisms has been proposed: hyperglycemia may impair the function of basal ganglia neurons, leading to decreased GABA levels, along with plasma hyperviscosity in the hyperosmolar state that may trigger an ischemic mechanism.[3] This would appear on CT as a hyperintense signal, although magnetic resonance imaging (MRI) is more sensitive for diagnosis.[4]

We thank the authors for presenting such an interesting case and believe it is essential to remember that both hyperglycemia and hypoglycemia can lead to a variety of neurological alterations, which—because they share symptoms—may be mistaken for ischemic lesions.

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Complicated internal hernia in a patient with a history of laparoscopic bariatric surgery

Hernia interna complicada en paciente con antecedente de cirugía bariátrica laparoscópica

To the Editor,

Given the rise of bariatric surgery as a treatment for obesity, the number of surgical procedures is increasing, with Roux-en-Y gastric bypass being one of the most frequently performed.[1] This technique is mainly done laparoscopically, which results in fewer intestinal adhesions. However, it is proposed that it may act as a risk factor for the development of internal hernias, with an estimated incidence between 0.9% and 4.5%.[2] These can lead to severe complications if they progress, such as bowel strangulation in a Petersen's hernia. Occasionally, the symptoms are subtle, making the diagnosis challenging.[3-5] This is the reason for our interest in reporting the present case.

A 64-year-old woman with a past medical history of hypertension, depression, and obesity treated with laparoscopic Roux-en-Y gastric bypass in 2016 (body mass index –BMI– prior to surgery was 43.5 kg/m^2; at the time of evaluation, 26.7 kg/m^2), cholecystectomy, and appendectomy, began experiencing epigastric abdominal pain radiating to the back and a single episode of vomiting. Vomiting did not recur, but the pain progressively worsened.

She first presented to the Emergency Department 24 hours after symptom onset, where general condition deterioration was noted, yet there were no clinical signs of peritoneal irritation. Bloodwork and abdominal X-ray were performed, with no pathological findings. Analgesia was prescribed and, after pain control, she was discharged. She returned 4 days later due to persistent abdominal pain, again without signs of peritoneal irritation. Analgesia was once more prescribed, and after symptom improvement, she was discharged again without further diagnostic studies.

Finally, she presented a 3rd time after another 4 days, reporting baseline ab-

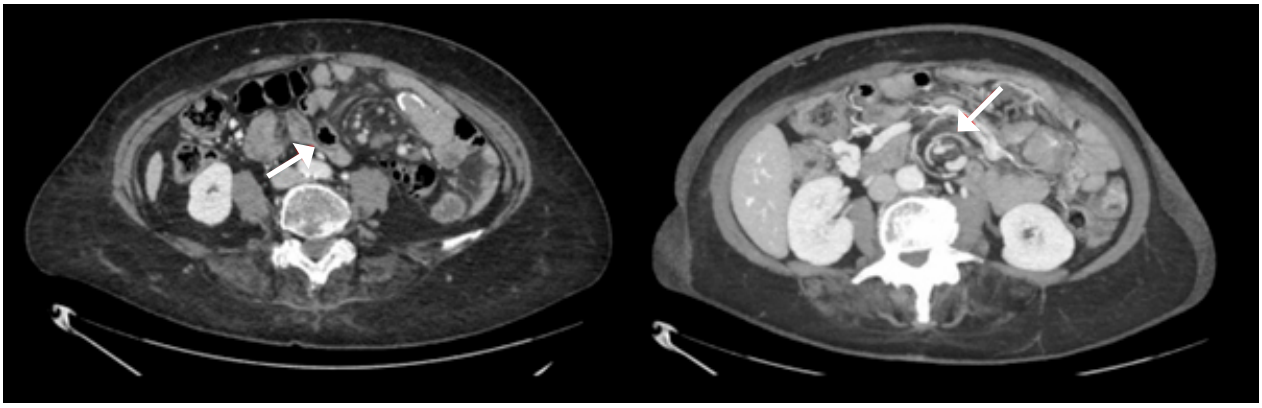

Figure 1. CT scan of the abdomen with contrast. The image on the left shows the herniated intestinal loop through of Petersen's defect (arrow), a virtual space created after Roux-en-Y ileostomy. The image on the right, shows marked distortion of the mesenteric anatomy manifested by elongation and anomalous narrowing of arterial and venous vascular structures with 'whirlpool sign' at the root of the mesentery (arrow), with segmental inversion of the arrangement of the superior mesenteric vein and artery, which generates vascular compromise at that level.

dominal pain rated 8/10 with severe exacerbations reaching 10/10, radiating in a belt-like pattern. Initially, she denied any relation to food intake, but upon specific questioning, she noted worsening after meals. There was marked deterioration of general condition with a grave appearance, although again, no signs of peritoneal irritation were found. Analgesia was administered with partial relief. A drop in hemoglobin to 9.6 g/dL was noted (previously 12 g/dL 24 hours earlier), but there was no elevation in acute phase reactants. A chest X-ray was performed to rule out pneumoperitoneum or referred pain from basal pneumonia, with no abnormal findings.

As no cause was found to explain the symptoms, an abdominal computed tomography (CT) scan with contrast was performed due to the patient's deteriorated condition and the severity of pain. The CT revealed the presence of an internal hernia through the transmesenteric Petersen's defect, causing torsion of vascular pedicles of small bowel loops, without luminal obstruction (Figure 1). Based on these findings, the general surgery team was consulted and decided to perform emergency surgery. The hernia was successfully reduced without complications, and the Petersen's defect was closed with continuous non-absorbable polypropylene suture. The following day, the patient was asymptomatic with only first-line analgesia and discharged 4 days later.

Internal hernias often escape early diagnosis, as they are not palpable like external hernias and do not produce signs of peritoneal irritation as in intestinal perforation.[3,4] They may cause severe abdominal pain and deterioration of general condition and can even become life-threatening due to intestinal ischemia caused by mesenteric vascular torsion, requiring emergency surgery for reduction.[1,2] In other cases, they may present as a chronic condition with recurrent postprandial pain, raising differential diagnosis with functional or psychiatric causes.[3]

We present this case as an example of the difficulty of its diagnosis, reminding us that we must be guided by clinical examination and seek serious underlying causes when the general condition is affected, using diagnostic tools such as abdominal CT[1-3] due to its high diagnostic yield. A history of laparoscopic bariatric surgery in a patient presenting with significant, unexplained abdominal pain should raise suspicion for this disease.[2]

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Historical note on cardiopulmonary resuscitation in the Spanish Society of Emergency Medicine (SEMES)

Otros apuntes históricos sobre la RCP en la Sociedad Española de Medicina de Urgencias y Emergencias

To the Editor,

I have read the article on cardiopulmonary resuscitation (CPR) in the Spanish Society of Emergency Medicine (SEMES), and I would like to make a few comments.[1]

We all remember the signing of the SEMES–AHA agreement in the 2000s, undoubtedly a milestone in the history of CPR within SEMES and one that carried significant implications. We can only look back fondly on that moment in our history and thank those involved for their important work at that time.

That said, CPR within SEMES clearly cannot be summarized by that one event. From 2005 onwards, the story continued, and we must highlight the important contributions of key figures such as Dr. Carlos Bibiano,[2] who led the development of the first course management platform and the updating of instructor databases, or Dr. Verónica Almagro,[3] who played a crucial role in advancing both basic and advanced CPR courses and in establishing a complete network of regional coordinators for SEMES CPR. Later, Dr. Carlos Alonso[4] led the dual training pathways through SEMES (via ERC or AHA) and became the first president of CERCP representing SEMES. The current coordinator, Dr. Ana Beltrán, is guiding SEMES toward integrating all courses into its E-CRM (Emergency Crisis Resource Management) platform and exploring new training approaches using artificial intelligence, along with various agreements with national security forces and public and private entities for CPR training.

All of them have been notable SEMES coordinators and leaders of SEMES CPR over the years. We should also highlight the support received from the training secretariats (Dr. Carmen Del Arco, Dr. José Ramón Casal), who have helped position SEMES as a leader in scientific[5] and educational activities—with our motto: "not a single week should go by without an emergency physician having access to training."

The drive of many members and anonymous instructors has brought this society to 2024, the year the Emergency Medicine specialty was officially established.

We should not forget the enormous contribution of EMTs (TES) and nurses in recent years through their involvement in basic and advanced CPR and advanced life support courses, the countless agreements signed with various institutions for CPR training, the school programs developed by the regional SEMES branches, the CPR research projects conducted in both prehospital emergency systems and hospitals, the public education campaigns[7], the publications by prominent members of the society, the promotion of CPR quality contests, and all instructors and students who have made SEMES what it is today.[6]

The article by García-Vega is a historical note on CPR in SEMES. In summary, the pioneering work of the 2000–2005 period was followed by that of other leaders and anonymous members. We hope that all these contributors—and those who follow them—will continue developing high-quality CPR[11] using the tools we now have (e-learning,[8] advanced simulation,[9] A.I.,[10] etc.), extending its reach to the entire population,[12] and that both the challenges and achievements serve as a foundation for our future residents to understand the roots of their specialty.

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