GIANT SUPERINFECTED ULCERATIONS OF THE THIGHS AND TRUNK IN A PATIENT WITH UNBALANCED DIABETES MELLITUS

IOANA BALDOVIN*,**, ANDRA MARIA CRIVEANU*, BETTINIA ALEXANDRA FARKOS*, MARIA ROTARU*,***

Summary

Introduction: *Skin ulcers can be difficult to manage and can become a major source of morbidity. Abdominal and thigh localisation is rare. Necrotising panniculitis can occur anywhere, but the most common location is on areas exposed to injury and pressure.*

Clinical case: *We present here the case of a 78-year-old female patient, known to have insulin-dependent type II diabetes mellitus, hypertension, gastroesophageal reflux disease and morbid obesity, arriving at the medical office/clinic for multiple giant, round-oval ulcerations covered with necrosis and fibrin purulent secretions located on the abdomen and inner thighs. The onset was insidious, in the form of raised erythematous lesions on the thighs that subsided, but with a recurrence on the abdominal area two months ago, with rapid transformation into ulcerations. The patient underwent antibiotic treatment and topical therapy applied by the outpatient surgery service, but with an unfavourable outcome and was subsequently admitted to the dermatology ward. Bacteriological examinations revealed multibacterial superinfection of the ulcers with Klebsiella pneumoniae, E. Coli, Proteus and specific antibiotic therapy was initiated. Histopathological examination revealed focal changes of lipoid necrosis in the hypodermis. The differential diagnosis included pyoderma gangrenosum, necrotising panniculitis or allergic reaction to insulin.*

Conclusions: *Localisation of ulcerations at the abdominal level (at the site of insulin injection), but also on the thigh and in the intergluteal area is rare and poses diagnostic difficulties. Management of skin ulcers requires careful management of associated pathologies such as diabetes mellitus or hypertension, and morbid obesity in the patient.*

Key words*: ulcerations, ulcers, panniculitis, multi-bacterial superinfection, differential diagnosis.*

Received: 22.05.2023 *Accepted: 14.07.2023*

* Dermatology Clinic, Emergency Clinical County Hospital of Sibiu, Romania.
** Doctoral Studies, University of Medicine and Pharmacy „Victor Babeș" of Timișoara, Romania.
*** „Lucian Blaga" University of Sibiu, Faculty of Medicine, Sibiu, Romania.

Introduction

Skin ulcers can be difficult to manage and can become a major source of morbidity. Abdominal or thigh localisation is rare. Necrotising panniculitis can occur anywhere, but the most common location is on areas exposed to injury and pressure.

Clinical case

A 78-year-old female patient was admitted to the Dermatology Clinic in Sibiu for the presence of giant, well-defined, round-oval ulcerations, covered with necrosis and fetid fibrin purulent secretions, located on the abdomen, inner thighs and intergluteal area. The patient has associated intense local pain and perilesional cardinal signs of inflammation. The patient is known to have insulin-dependent type II diabetes mellitus, essential hypertension, gastroesophageal reflux disease and chronic venous insufficiency of the lower extremities stage C3 of CEAP.

Affirmatively, the disease started with erythematous lesions that appeared approx. 2 months ago with rapid transformation to ulcerations. The onset coincided with the initiation of insulin treatment (Tresiba - insulin degludec - insulin analogue). The patient was brought to the emergency ward and following consultations in General Surgery and Plastic Surgery, prior to admission, followed home treatment with ceftriaxone injections and local lavage with saline solution and betadine solution, with adverse outcome. The general clinical examination on admission revealed a mildly affected general condition, morbid obesity (BMI=45.77 kg/m^2), excess adipose tissue represented, bilateral gonalgia, BP=140/90 mmHg, VR (ventricular rate) =65 bpm, emphysematous thorax, tightened vesicular murmur, enlarged abdomen through adipose panniculus, painless spontaneously or on palpation, without other pathological changes.

The local clinical examination shows multiple round-oval painful ulcerations of various sizes, some giant, 2 to 15 cm in diameter, which are deep, well-defined, covered with dry and moist necrosis, with greenish-yellow fetid fibrin purulent secretions, with subcutaneous tissue, on an erythematous background, some accompanied by intense perilesional erythema, on the abdomen, thighs [Fig. 1], and in the intergluteal area [Fig. 2].

Figure 1. Ulcerations on the abdomen and thighs

Figure 2. Ulcerations at the interfacial level

Biologically there is hypoproteinemia with hypoalbuminemia, hypochromic anemia, normochromic anemia, low sideremia (mild iron deficiency anaemia), mild hypocalcemia, hyperglycemia, biological inflammatory syndrome, positive Adler test. Mycobacteriological examinations of ulcers revealed *Klebsiella Pneumoniae* ssp. pnemumoniae, ESBL (+) – on the abdomen, left thigh, and in the gluteal region, *Proteus* – on the abdomen, left thigh, and in the gluteal region, *Morganella Morganii* ssp. sibonii – on the abdomen, left thigh and in the gluteal region, and *Escherichia Coli* – in the gluteal region.

Multiple interdisciplinary consultations were carried out: Cardiology – a diagnosis of stage IIB hypertension was established and prophylactic anticoagulant treatment was recommended; Gastroenterology – a diagnosis of mild iron deficiency anaemia and occult gastrointestinal bleeding was determined and upper gastrointestinal endoscopy and colonoscopy were recommended; Diabetes and Nutrition Diseases – in order to adjust insulin doses; Infectious Diseases – to determine antibiotic therapy during hospitalisation; Allergology – to rule out an allergic reaction to insulin; and Plastic Surgery – to determine long-term treatment and assess the need to have skin defects repaired.

Upper gastrointestinal endoscopy was performed, which revealed an oesophagus with a 6 mm polyp at the level of the oesogastric junction, stomach with a polypoid-looking area at the level of the greater curvature and in the antrum portion with polypoid protrusions, from which biopsies were taken. The following were also revealed: permeable pylorus; duodenal bulb and second (descending) part of the duodenum without changes and colonoscopy in which small diverticula were found in the left colon without other changes and internal haemorrhoids without complications.

The histopathological examination revealed in the dermis sweat glands and blood capillaries, in the papillary portion: areas of mild and moderately increased chronic lymphocytic inflammatory infiltrate with disposed in the pericapillary matrix, without exocytosis, areas of degeneration of collagen fibres and dermal elastic fibres. Hypodermic adipose tissue with normal-appearing adipocytes and anucleate adipocytes with necrotic appearance, macrophagic reaction and presence of a lymphocytic inflammatory infiltrate at the interface with the dermis. All these histopathological changes suggested focal changes of lipoid necrosis in the hypodermis.

The following diagnosis is established: *ulcerative, necrotising panniculitis of abdomen and thighs*, infection of ulcers with Klebsiella pneumoniae, Proteus, Morganella Morganii, and Escherichia Coli, perilesional cellulitis on the abdomen, left thigh and in the gluteal region, complete with the following secondary diagnoses: chronic venous insufficiency of the lower extremities stage C3 of CEAP, insulin-dependent type II diabetes mellitus, stage IIB hypertension, gastrooesophageal reflux disease, oesophageal and stomach polyps, left colon diverticula, occult gastrointestinal bleeding, mild iron deficiency anaemia, morbid obesity.

The differential diagnosis is as follows:

Pyoderma gangrenosum – initially manifesting as nodules, plaques or pustules with progressively enlarging ulceration formation, with a raised, purplish margin and erythema around, are painful and are usually located on post-trauma areas; histopathological examination shows perivascular or intramural lymphocytic infiltrate or dermal neutrophilic infiltrate.

Lipoid necrobiosis – clinically manifesting as oval or irregular plaques, with a yellowish atrophic centre, with a raised, purplish periphery, and the most common location is pretibial are, but 15% of cases may occur in other topographic regions, and a third may ulcerate.

Allergic skin reaction to insulin administration – erythema, pruritus, induration, nodules and lipoatrophy frequently occur at the injection site, subside spontaneously, and the patient did not have lesions only at the insulin injection site.

Calciphilaxis – this is necrosis of skin or subcutaneous tissue that occurs by occlusion of small vessels, caused by calcification of vessel walls. It occurs frequently in patients with significant kidney dysfunction or other risk factors, such as obesity, female sex, diabetes mellitus, hypoalbuminemia. Nevertheless, upon histopathological examination on the patient, the absence of calcium deposits is observed.

Differential diagnosis with other panniculitis, such as infectious-induced panniculitis - this can

be caused by a wide variety of bacteria, fungi, viruses, or parasites. It frequently occurs in immunocompromised or diabetic patients, it is clinically manifested by plaques, nodules or abscesses with purulent discharge, and it frequently affects the lower extremities but also the upper extremities, face or trunk. The histopathological examination frequently shows lobular panniculitis and neutrophilic infiltrate. Another differential diagnosis panniculitis is pancreatic panniculitis - this is located in the lower limbs and manifested by subcutaneous nodules that ulcerate spontaneously; paraclinically - serum lipase and amylase are elevated and histopathological examination reveals lobular panniculitis and intense adipocyte necrosis.

Panniculitis due to AAT deficiency frequently occurs between 30-60 years of age, is associated with pulmonary (COPD), liver (cirrhosis) pathologies, and clinically manifests as painful erythematous nodules and plaques, cellulitis, fluctuating abscesses. The most frequent localisation is in the in the gluteal region, proximal extremities, and histopathological examination reveals rapid necrosis of subcutaneous tissue and liquefactive necrosis. Drug-induced panniculitis appears after treatment with vemurafenib or ponatinib. Traumatic or factitial panniculitis is manifested by nodules, plaques, various ulcerations - this was refuted by personal medical history.

Systemic antibiotic treatment was initiated with teicoplanin 400 mg every 12 hours, 3 doses, then 400 mg every 24 hours for 5 days, ceftazidime 1 g every 8 hours for 9 days, gentamicin 100 mg every 12 hours for 10 days, then piperacillin/tazobactam 4g/0.5g every 8 hours for 12 days, antifungal treatment, corticotherapy, PPI, probiotics, analgesics, antihistamines, prophylactic anticoagulants, albumin, insulin, and vascular trophic treatment.

The evolution of ulcers was slowly favourable under topic treatment, with improvement of periulcer erythema rapidly and clearance of fibrin purulent secretions and necrosis, with reduction of ulcer depth during hospitalization. [Fig. 3, Fig. 4]

The particularity of the case lies in the rarity of the location of the skin ulcers (abdomen, at the site of insulin injection, but also in the thighs and in the intergluteal area), in the rapid worsening of their evolution, and also in the association of insulin-dependent type II diabetes mellitus and obesity, the complexity of the case posing diagnostic and treatment problems.

Discussions and conclusions

The localisation of ulcerations at the abdominal level, which coincides with the insulin injection site, but also on the thigh and in the intergluteal area is rare and poses diagnostic

Figure 3. Evolution during hospitalization

Figure 4. Evolution 2 months after discharge

difficulties. Innovations in insulin therapy in recent times have drastically reduced the incidence of adverse reactions, with less than 0.1% currently reported. Despite changes in the insulin manufacturing process, the preservatives and some of the excipients have remained the same, and the bacteria used in these processes appear to have the potential to act as an antigen – adverse reactions to insulin therapy can be considered, but in the patient's case, the localisation of lesions in regions other than the injection sites ruled out a possible adverse reaction.

Difficult healing of ulcerations in a diabetic patient is the result of complex pathological physiology. Hyperglycemia is mainly correlated to impaired microcirculation, which leads to reduced tissue oxygenation, but also to poor leukocyte migration to affected areas, which puts patients at greater risk of infection. Adjustment of insulin therapy and rebalancing of diabetes mellitus has helped the lesions heal in a short time.

The patient required treatment of underlying disease, but also additional supportive treatment and treatment of complications. Also of major importance is the reduction of risk factors and the multidisciplinary team approach was essential in this case.

Because of the multiple associated pathologies, treatment of comorbidities was also required.

Management of skin ulcers requires careful management of associated pathologies such as diabetes mellitus or hypertension, and morbid obesity in the patient.

Bibliography

1. Fitzpatrick's Dermatology 9th edition S Kang, M Amagai, A Bruckner, A Enk, D Margolis, A McMichael, J Orringer – McGrow Hill Education
2. Boli dermatologice și infecții sexual-transmisibile Ediția a IV-a – Virgil Pătrașcu, Craiova 2018
3. Schmieder SJ, Krishnamurthy K. Pyoderma Gangrenosum. [Updated 2022 Jul 5]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-.
4. Natali KM, Goldman JD. Insulin Allergy: A Case Report and Review of Literature. J Pharm Technol. 2016 Oct;32(5):210–5. doi: 10.1177/8755122516655544. *Epub* 2016 Jun 23.
5. Bzowyckyj AS, Stahnke AM. Hypersensitivity reactions to human insulin analogs in insulin-naïve patients: a systematic review. *Ther Adv Endocrinol Metab.* 2018 Feb;9(2):53-65
6. Spampinato SF, Caruso GI, De Pasquale R, Sortino MA, Merlo S. The Treatment of Impaired Wound Healing in Diabetes: Looking among Old Drugs. Pharmaceuticals (Basel). 2020 Apr 1;13(4):60

Conflict of interest

NONE DECLARED

Correspondance address: Andra Maria Criveanu
Dermatology Clinic
Emergency Clinical County Hospital of Sibiu, Romania
E-mail: dr.andra.criveanu@gmail.com