

Cellulitis at GLP-1 Agonist Injection Site: Rare But Relevant

Celulite no Local de Injeção do Agonista de GLP-1: Rara, Mas Relevante

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Abstract

We present a case of cellulitis complicating with abscess formation as a possible complication of treatment with injectable GLP-1 agonists on a sixty-one-year-old woman. Pus cultures showed isolation of *Streptococcus anginosus* and clindamycin was started as targeted therapy but absence of improvement prompted a consultation with the surgery department and a manual surgical debridement was performed. A second isolate of *Eikenella corrodens*, which is frequently resistant to clindamycin, was identified. We opted for a switch to ceftriaxone and after nineteen days, having achieved clinical improvement, plans were made for her to continue to change her wound dressing at her local health center and for a short-term reevaluation at a surgery outpatient consultation. Caring for social needs and assuring continuity across multiple care levels can be fundamental in preventing adverse effects from self-injectable drugs.

Keywords: cellulitis; abscess; GLP-1 agonist; obesity; social needs.

Resumo

Apresentamos um caso de celulite com formação de abscesso, numa mulher de 61 anos, como possível complicação do tratamento com agonistas de GLP-1. Das culturas de pus foi isolado *Streptococcus anginosus* e iniciada clindamicina, mas a ausência de melhoria motivou referência ao Departamento de Cirurgia que realizou um desbridamento cirúrgico manual. Foi identificado um segundo isolado de *Eikenella corrodens*, frequentemente resistente à clindamicina. Optou-se por mudar para ceftriaxona e, após dezanove dias de tratamento, com melhoria clínica, foi planeado que a doente continuasse a mudar o penso no seu centro de saúde local e fosse alvo de uma reavaliação a curto prazo na consulta ambulatória de Cirurgia. Cuidar das necessidades sociais e garantir continuidade nos múltiplos níveis de cuidados pode ser fundamental na prevenção dos efeitos adversos dos medicamentos auto-injetáveis.

Palavra-chave: celulite; abscesso; agonista do GLP-1; obesidade; necessidades sociais.

> INTRODUCTION

Injection site cellulitis with or without abscess formation as a complication is a well-known adverse effect, described for drugs such as several immunizations and, of course, insulin. ⁽¹⁾ Obese patients are proven to be at higher risk for cellulitis. ⁽²⁾ For years now there have been explicit criteria for its diagnosis and guidelines for data collection. ⁽³⁾ However, and to our knowledge, this is the

first reported case of this presentation following a GLP-1 agonist injection. So much that such a possible adverse event is not included on the drug side effect list. ⁽⁴⁾ Moreover, this class of incretin mimetics has been on the market for more than ten years now but only recently was their role in reducing cardiovascular events in high-risk patients with type 2 diabetes was fully established ⁽⁵⁾ which makes it that more likely that there be an increase in patients prescribed with this class of agents in coming years.

> CASE DESCRIPTION

We present the case of a woman, sixty-one years old, that is admitted to our emergency department. She has a skin lesion that appeared four days ago and for the last two, she has been feeling feverish. She remembered

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clearly that the inflamed region corresponded to the site of her last dulaglutide administration because she started to feel pain in that area and noticed it had become red just the day after.

Upon physical examination, she had a body temperature of 37,8°C and her blood glucose was 333 mg/dl. Abdominal exam showed a 5-cm tumefaction located to the paraumbilical region on the left, with inflammatory signs such as erythema and tenderness upon palpation. Adjacent skin looked rough, "orange peel" like. There were no other positive findings to point out.

She has type 2 diabetes and was being treated with lispro insulin since 2013 and also metformin 1000mg, dapagliflozin 10mg and a GLP-1 agonist - dulaglutide - that she administers herself, once a week. Her last determination of glycosylated hemoglobin was 8,2%. She also has a medical record of class III obesity (estimated body index of 53,8 kg/m²) and was referred to start initial assessment for bariatric surgery but she skipped consultation. Other relevant diagnoses are sleep apnea (with indication to use a continuous positive airway pressure - CPAP - therapy that she stopped using a year ago), hypertension, hypercholesterolemia, bilateral gonarthrosis and depression. She never learned how to read but understands numbers and is able to manage medication on her own.

From a performance status point of view, her weight and chronic knee pain has diminished her ability to move (she does so with a crutch) and take care of herself. She lives alone in a first-floor house, accessible only through a staircase which accounts for her difficulties with attending her medical appointments.

Initial blood work revealed leukocytosis (17,29 x10⁹ cells/L) with neutrophilia (12, 54 x10⁹ cells/L) and a C-reactive protein of 140,0 mg/L, without relevant changes in red blood cell count, platelet count renal or hepatic functions. Blood and urine cultures were drawn (and turned out to be negative). Assuming a case of infected insulin lipodystrophy we started empiric antibiotic therapy with intravenous amoxicillin and clavulanic acid [1,2 g every 12 hours, administered intravenously (IV)], and the patient was transferred to our infirmary for continuing treatment.

Two days after admission, patient was complaining with worsening pain. The abdominal region was tense on the left side and there was palpable fluctuation over the wound, suggesting formation of an abscess, which was drained. Pain improved immediately, with the release of haemopurulent fluid which was sampled for culture. At this point, given the presence of a purulent collection,

we added clindamycin (600mg every 6 hours, IV) to our empiric regimen in order to ensure proper coverage for anaerobes. An isolate of *Streptococcus anginosus* was obtained, which was sensitive to both penicillin G and clindamycin.

As she maintained local induration and residual spontaneous purulent drainage, we protracted antibiotic therapy de-escalation and consulted with the surgery department which performed a manual surgical debridement and collected a fluid sample for culture. The patient was kept on a daily dressing regimen using octanedione. On day eleven, after as many days of amoxicillin + clavulanic acid and seven days of clindamycin, we obtained an isolate of *Eikenella corrodens*, a gram-negative rod which is usually present in the oral cavity, and frequently resistant to clindamycin. At this point, approximately 48h after surgical approach, the patient was clinically better and the isolated microorganism was theoretically sensitive to amoxicillin + clavulanic acid with which she was being treated with. However, considering that the cultured sample originated from deep tissue within the wound – which makes contamination unlikely – and that she was already on her eleventh day of seemingly targeted therapy, we opted for expanding gram-negative coverage. For this reason, we switched antibiotic therapy to ceftriaxone (1g every 24h, IV) that was administered to her for 7 days, having achieved clinical and analytical improvement. We made plans for her to continue to be able to change her wound dressing every two days at her local health center and for a short-term reevaluation at a surgery outpatient consultation. During her stay, we are able to obtain optimal glycemic control with insulin alone at a much lower dosage than the one she usually had at home. For this reason, our nutrition department prepared an adjusted meal plan and her outpatient medication was adjusted, suspending metformin and dulaglutide and maintaining dapagliflozin and insulin to be administered on her arms instead of the abdominal wall.

> DISCUSSION

We can only speculate as to the cause of infection as well as the factors contributing to it. Both isolated organisms are part of the commensal flora. Proper administration technique was reviewed with the patient but given her precarious living arrangements it is likely that she used expired medication, stored it deficiently or that asepsis was not ensured leading to contamination of the needle with usually harmless bacteria that were inoculated into the subcutaneous tissue, causing cellulitis

Contributing to the severity of the infectious process was also her extreme obesity which is a known risk factor and also her decompensated diabetes: both a cause of immunosuppression and consequence of said process. In this case, high level of suspicion of infection with a second agent and multidisciplinary work to ensure infection source control and antibiotic penetration was instrumental.

From a social point of view, we were also faced with a challenge as this was a patient that had completely disconnected herself from the healthcare system as a result of multiple adverse circumstances - her trouble moving, poor social resources and even personal self-esteem. Discharging her with safety involved targeting all those aspects as well.

> CONCLUSION

Cellulitis with or without abscess formation is a potential adverse consequence of injectable drugs, including GLP-1 agonists. Preventing and treatment of such harmful events requires multidisciplinary work and continuity across different care levels. <

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