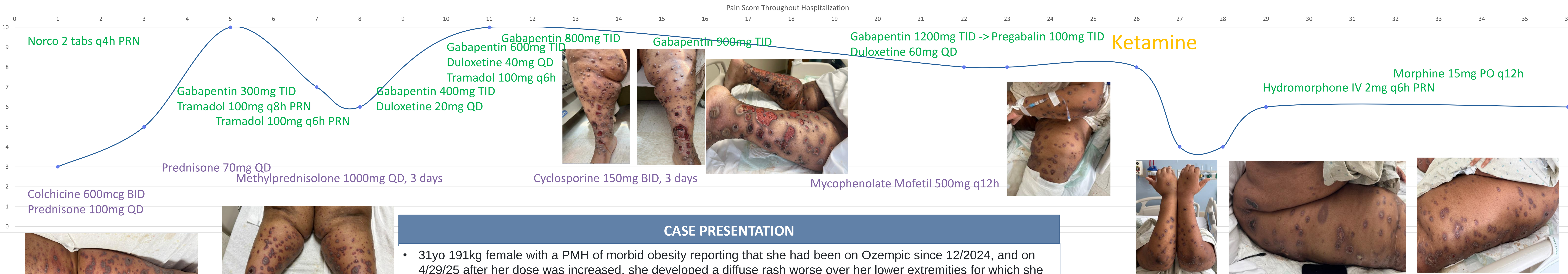


Pain Management in Semaglutide Induced Leukoclastic Vasculitis

Michael Lough D.O., Antoine Sioufi M.D., Gunar Subieta-Benito M.D.
Department of Anesthesiology and Pain Medicine, John H. Stroger Jr Hospital of Cook County



CASE PRESENTATION

- 31yo 191kg female with a PMH of morbid obesity reporting that she had been on Ozempic since 12/2024, and on 4/29/25 after her dose was increased, she developed a diffuse rash worse over her lower extremities for which she presented to our hospital and was diagnosed with leukoclastic vasculitis. Her HIV and hepatitis testing was negative. After consultation with Rheumatology, she started multiple immunosuppressing medications including prednisone 100mg daily, dapsone, mycophenolate as well as prophylactic antibiotics. Wound cultures were negative. Prednisone was weaned to 70mg daily
- Throughout her admission she was tachycardic, hypertensive, tachypneic complaining of generalized pain but worse on her legs. She reported chronic pain from her extensive wounds. The pain was initially management with opioid PCA, pregabalin, SNRIs in addition to the high dose steroids with partial response. The patient was then managed with ketamine inhalation at bed side due to isolation status and later with ketamine infusion at our clinic with significant relief of pain and mild improvement in her tachycardia

BENEFIT OF KETAMINE IN LEUKOCLASTIC CUTANEOUS VASCULITIS

- Ketamine is primarily a noncompetitive antagonist at phencyclidine binding site of n-methyl-D-aspartate(NMDA) receptor in prefrontal cortex and hippocampus which decreases frequency and duration of channel opening. NMDA receptor activation improves, chronic pain, opioid tolerance, and mood regulation. It can reduce central sensitization and windup. Also has opiate activity, greatest at mu receptor and less at kappa and sigma
- A randomized controlled trial found significantly decreased levels of the proinflammatory cytokines IL-1 beta, TNF-alpha, IFN-gamma and GM-CSF following a 0.5mg/kg ketamine infusion(9)
- Ketamine has additional areas of activity that can provide benefit including antagonism at nicotinic and muscarinic cholinergic receptors. It blocks sodium and potassium channels via hyperpolarization-activated cyclic nucleotide-gated channels as well as facilitation of GABA-A(10)
- Enhancement of descending modulatory pathways(11), prevention and reversal of opioid tolerance through ERK1/2 effect on mu-opioid activity, reduction of inflammation via the kynurenine pathway

DISCUSSION

- Semaglutide associated vasculitis, aggravation of inflammatory conditions and skin dysesthesias have been reported but the mechanism remains elusive but responsive to steroids (2,3, 4)
- Ketamine has been found to be effective in the management of dysesthesias (5), pain associated depression (6) and inflammatory pain (7) demonstrating its utility in this case. As GLP-1 receptor agonist use rises, clinicians should recognize LCV as a potential adverse effect and consider ketamine as an option refractory vasculitis-associated pain
- A case report highlights use of IVIg to improve rash and pain in a similar case resistant to conventional treatment which can be considered in future cases(8)

REFERENCES

- Goeser MR, Laniosz V, Wetter DA. A practical approach to the diagnosis, evaluation, and management of cutaneous small-vessel vasculitis. Am J Clin Dermatol. 2014;15(4):299-306. doi:10.1007/s40257-014-0076-6
- Pinheiro, M. M., de Souza, L. G., Nunes, G. P., Martin, I. F., de Oliveira, Y. U., Pinheiro, F. M. M., ... & Infante, M. (2024). The first report of leukocytoclastic vasculitis induced by once-weekly subcutaneous semaglutide. Current Medical Research and Opinion, 40(9), 1525-1531.
- Tran, M. M., Mirza, F. N., Lee, A. C., Goldbach, H. S., Libby, T. J., & Wisco, O. J. (2024). Dermatologic findings associated with semaglutide use: a scoping review. Journal of the American Academy of Dermatology, 91(1), 166-168.
- Castellanos, V., Workneh, H., Malik, A., & Mehta, B. (2024). Semaglutide-induced lupus erythematosus with multiorgan involvement. Cureus, 16(3).
- Kwatra, S. G., Kambala, A., Cornman, H., Reddy, S. V., & Cohen, S. P. (2023). Ketamine infusions for treatment-resistant neuropathic pruritus. JAMA dermatology, 159(9), 1011-1012.
- Voute, M., Lambert, C., Pereira, B., & Pickering, G. (2023). Assessment of initial depressive state and pain relief with ketamine in patients with chronic refractory pain. JAMA Network Open, 6(5), e2314406-e2314406.
- Urch, C. E., & Chamberlain, J. H. (1998). Ketamine analgesia in vasculitic pain. British journal of rheumatology, 37(6), 702-703.
- Strubchevska K, Kozyk M, Balanescu DV. A Case Report of Leukocytoclastic Vasculitis: Diagnostic Approach and Treatment. Am J Case Rep. 2023;24:e939541. Published 2023 May 30. doi:10.12659/AJCR.939541
- Nikkheslat N. Targeting inflammation in depression: Ketamine as an anti-inflammatory antidepressant in psychiatric emergency. Brain Behav Immun Health. 2021;18:100383. Published 2021 Nov 10. doi:10.1016/j.bbih.2021.100383
- Orumski CF, Izumi Y, Mennerick S. Ketamine: NMDA Receptors and Beyond. J Neurosci. 2016;36(44):11158-11164. doi:10.1523/JNEUROSCI.1547-16.2016
- Niesters M, Aarts L, Sartori E, Dahan A. Influence of ketamine and morphine on descending pain modulation in chronic pain patients: a randomized placebo-controlled cross-overproof-of-concept study. Br J Anaesth. 2013;110(6):1010-1016. doi:10.1093/bja/aes578
- Gupta A, Devi LA, Gomes I. Potentiation of μ -opioid receptor-mediated signaling by ketamine. J Neurochem. 2011;119(2):294-302. doi:10.1111/j.1471-4159.2011.07361.x
- Kopra E, Mondelli V, Pariente C, Nikkheslat N. Ketamine's effect on inflammation and kynurenine pathway in depression: A systematic review. J Psychopharmacol. 2021;35(8):934-945. doi:10.1177/02698811211026426

