## Elasomeran/tozinameran

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## Worsening of complex regional pain syndrome: 3 case reports

In a case series, 3 patients (2 women and 1 man) aged 21–49 years were described, who developed worsening of complex regional pain syndrome (CRPS) following immunisation against COVID-19 with tozinameran or elasomeran [*doses and routes not stated*].

Case 1: A 23-year-old woman, who had a history of right lower extremity CRPS type I, underwent a series of lumbar sympathetic blocks and physical therapy for 1 year with over 90% improvement of the right ankle and foot pain and symptoms. Thereafter, she could function well and was only receiving paracetamol [acetaminophen]. Later, she was immunised against COVID-19 with the first dose tozinameran [BNT162b2 COVID-19, mRNA-based COVID-19 vaccination; manufactured by Pfizer/BioNTech]. However, after 3h of immunisation, she experienced a severe exacerbation of the burning pain in the right foot extending proximally to the entire right lower extremity. She developed sensitivity to touch, swelling, colour changes and temperature changes in the right leg, ankle and foot. Additionally, she developed intense lower extremity myoclonus in the entire right lower extremity. Worsening of CRPS was suspected secondary to tozinameran. The woman was treated in the emergency room with ketorolac, hydromorphone and diazepam with minimal improvement of the pain and symptoms. Subsequently, she was admitted for further management. She was treated in the intensive care unit with multiple medicines which included ketamine, hydromorphone, patient-controlled analgesia and diazepam and diphenhydramine as needed for muscle spasms. A partial improvement of the right lower extremity pain and myoclonus was observed. However, she was still complaining of intermittent severe muscle spasms approximately every 4h. She started receiving lorazepam, baclofen, diphenhydramine as needed for muscle spasms and hydromorphone as needed. She underwent physical therapy twice a day during hospitalisation. On hospital day 2, she underwent a right-sided lumbar sympathetic block under fluoroscopic guidance because of persistent pain and spasms. Thereafter, she reported over 70% improvement in the pain and symptoms. Thus, within 1 day, her ketamine was stopped after the sympathetic block and patient-controlled analgesia was weaned off over 2 days and she was transferred to the regular inpatient room. On hospital day 6, she was discharged home with hydromorphone, baclofen, lorazepam and diphenhydramine as needed for muscle spasms. She could stop all the medications within 10 days after discharge from the hospital with the improvement of the right lower extremity pain and symptoms to baseline which needed only naproxen and paracetamol. Before the second dose of tozinameran, it was decided to treat her before vaccination with the anticipation that there might be a worsening of the symptoms again. She underwent lumbar sympathetic block 2 days before the second dose of tozinameran and was started receiving diphenhydramine orally every 8h around the clock and 48h before the second dose of vaccination. She did not report any significant worsening of the right lower extremity pain and symptoms following the second dose of vaccination. She was followed up for 5 months after the second dose and there was no significant worsening of the CRPS-related pain and symptoms. She complained of mild baseline pain and symptoms, which required naproxen and paracetamol as needed.

Case 2: A 21-year-old man, who was diagnosed with bilateral lower extremity CRPS type I, 2 years before, had completed physical therapy, underwent a series of bilateral lumbar sympathetic blocks and was maintained with gabapentin. He was stable with gabapentin treatment with mild baseline pain without interfering with daily activities. He was immunised against COVID-19 with the first dose of elasomeran [mRNA COVID-19 vaccination, mRNA-1273 vaccine, manufactured by Moderna]. Within 24h, he reported that severe exacerbation of bilateral lower extremity burning pain. He was consulted on the phone and the dose of gabapentin was further increased and no other medication was needed for controlling pain. Approximately 2 weeks after immunisation, he could wean to the baseline dose of gabapentin. He again developed worsening bilateral lower extremity burning pain with intermittent colour and temperature changes, following the second dose of elasomeran, 4 weeks after the first dose. Thus, the dose of gabapentin was increased for pain control. He could wean gabapentin successfully back to baseline, following 3 weeks, after the second dose of pain medication and was stable with mild pain on the baseline dose of gabapentin. His worsening of the CRPS was suspected secondary to elasomeran.

Case 3: The 49-year-old woman had been diagnosed with a right lower extremity CRPS type I, 3 years ago. She also had a history of migraine headaches for which she was receiving topiramate. She underwent a series of intermittent lumbar sympathetic blocks, physical therapy, medication management, activity modification, home exercises and dorsal root ganglion neurostimulator implantation, after a successful trial, 18 months before. With all these treatments, moderate pain control was noted. She was receiving pregabalin for neuropathic pain and indomethacin as needed. She could function and work despite the requirement for ice application to the right lower extremity, which seems to relieve the burning sensation from time to time. She was immunised against COVID-19 with the first dose of elasomeran [mRNA COVID-19 vaccination, mRNA-1273 vaccine, manufactured by Moderna] and within 24h, she reported that the severe worsening of the right lower extremity, burning pain, colour changes and temperature changes. She was consulted over the phone and the dose of pregabalin was further increased. As there was still significant pain the next day, she started receiving duloxetine. She continued with indomethacin with a more frequent ice pack application to the lower extremity for pain relief. She received the second dose of elasomeran, 4 weeks after the first dose and she did not report any significant worsening of the CRPS-related pain and symptoms. She could wean pregabalin to the initial dose and continued with duloxetine and indomethacin as needed 2 months after the second dose of vaccination. Finally, her worsening of CRPS was considered secondary to the first dose of elasomeran.

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