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Lack of response of Chikungunya chronic infection with low-dose naltrexone: a case series

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ABSTRACT:

— ***Background:*** The Chikungunya virus (CKV) has been associated with chronic joint involvement in 14.4% to 87.2% of cases. Analgesics, non-steroidal anti-inflammatory drugs, glucocorticoids, and hydroxychloroquine are used successfully. These drugs may present side effects or may not work in some cases. Low-dose naltrexone (LDN) has been studied in painful and inflammatory conditions such as rheumatoid arthritis with good outcomes.

— ***Case report:*** In this article, two cases of patients with chronic CKV who were treated with LDN were reported. Both patients had a chronic CKV course, one with chronic polyarthralgia and the second with polyarthritis, but refused glucocorticoids and immunosuppressive drugs. LDN was tried for at least three months, although no beneficial effect was observed during follow-up.

— ***Conclusions:*** This article evaluated the effects of LDN in chronic CKV, and but no improvement in this condition was registered. Future studies, however, need to confirm the present data.

— ***Keywords:*** Chikungunya, Viral infection, Arthritis, Naltrexone.

BACKGROUND

The Chikungunya virus (CKV), a member of the Togaviridae family, Alphavirus genus, was first isolated from humans in 1952 in the coastal area of Muawiya, Makondo, and Rondo, currently known as Tanzania. Brazil had a large outbreak of CKV between September 2014 and 2017[1]. Until the 37th epidemiological week, 236,287 probable cases of CKV were evaluated, and 116,523 were serologically confirmed. In the literature, 14.4% to 87.2% of these cases may evolve into chronic joint involvement[2]. Usually, analgesic, non-steroidal anti-inflammatory drugs, and hydroxychloroquine are used successfully. Nevertheless, some refractory patients are treated with immune suppressive agents such as glucocorticoids and methotrexate. The French guidelines[3] advise using methotrexate (MTX), leflunomide, and sulfasalazine according to the clinical stage of the CKV disease. In addition, the Brazilian guidelines[4] recommend the use of MTX plus hydroxychloroquine and low-dose oral steroids for 6-8 weeks. In refractory cases, guidelines advise using biological agents such as anti-tumor necrosis factor[5].

It is well known that these drugs bring together plenty of side effects[2]. It is reasonable to speculate that other medications with minimal adverse effects should be used, such as low-dose naltrexone (LDN).

LDN refers to a dosage of 1-6 mg/day. Recently, a systematic review[6] on LDN in rheumatic diseases observed beneficial effects on pain and well-being in fibromyalgia patients, Sjogren's syndrome, and improved pruritus in scleroderma. At such low levels, naltrexone exhibits paradoxical anti-inflammatory and analgesic properties. The analgesic effect of LDN results from the blockage of mu- and delta-opioid receptors and, to a lower extent, kappa-opioid receptors in the central nervous system, leading to a feedback-mediated increase of these receptors and improving the endorphin system[6]. In this study, two cases of chronic CKV infection with polyarthritis treated with LDN are described.

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CASE PRESENTATION

Case 1

A 39-year-old female patient started polyarthralgia in 2019, associated with erythematous rash and fever. She was treated with paracetamol, and fever and pain improved, but the rash disappeared spontaneously. However, some years later, she came to our private clinic for the persistence of polyarthralgia over her knees, ankles, elbows, and wrists, which improved with movements. She was treated with non-steroidal anti-inflammatory drugs. Her physical examination showed only polyarthralgia; no other abnormalities were detected. Laboratory tests revealed normal blood cell count, C-reactive protein of 0.8 mg/dL (normal range: < 3 mg/dL), erythrocyte sedimentation rate of 4 mm/1st hour (nr: < 20 mm/1st hour), normal TSH of 2.2 mU/L and negative HLA-B27. Serologies for infectious diseases, such as HIV 1 and 2, HTLV I and I, syphilis, rubella, mononucleosis, hepatitis B and C virus, parvovirus B19, and cytomegalovirus were all negative. IgG serology for Chikungunya was positive. Antinuclear antibodies, anti-CCP, and rheumatoid factor were all negative. X-rays were normal. A diagnosis of polyarthritis secondary to Chikungunya infection was determined. She referred to a pain analogic visual scale (AVS) 6.0 and a well-being AVS 6.0. Since the patient did not have arthritis and inflammatory biomarkers were normal, we treated her with low-dose naltrexone (4.5 mg/day at bedtime). After 3 months, she had no response to LDN. Methotrexate was then initiated, and after 2 months, a marked improvement was observed.

Case 2

A 53-year-old woman with diabetes and hypertension had a fever, skin rash, and polyarthritis 1 year before coming to our clinic. She was treated with glucocorticoid 40 mg/day of prednisone for 2 months without improvement. She complained of persisting polyarthritis over her knees and ankles that improved with movements and worsened with rest. The ESR was 45 mm/1st hour, and the CRP was 13 mg/dL. Antinuclear antibodies, anti-CCP, and rheumatoid factor were all negative. IgG serology for Chikungunya was positive. X-rays were normal. A diagnosis of polyarthritis secondary to Chikungunya infection was determined. She refused to take glucocorticoid or immunosuppressive drugs. Hence, we started LDN 4.5 mg/day. After 2 months, her symptoms persisted, and she reported no amelioration of the polyarthralgia. Therefore, we started methotrexate 15 mg/week, and she significantly improved her condition.

DISCUSSION

This is the first description of the use of LDN in chronic CKV polyarthritis; in these two patients, this medication did not improve the joint condition.

Studies have demonstrated the safety and efficacy of LDN in rheumatic disease[5]. In fact, in 2019, a study[7] evaluated the role of LDN in 360 patients with rheumatoid arthritis in a controlled before-after study. The authors found that for persistent LDN users, a reduction in 13% of rheumatic drugs (NSAID, opioids, DMARDs, and TNF blockers) and analgesics was observed[5]. Regarding pain control, in seven previous studies[8-15] using LDN for treating fibromyalgia patients, the authors demonstrated in a total of 121 patients improvement of pain, FM scales, and inflammatory parameters, such as cytokines, after LDN treatment. Most studies in literature revealed no side effects or mild effects such as insomnia or vivid Dreams.

Strengths and Limitations

This article's strengths include the diagnosis of the two patients involved in CKV infection based on positive serologies, and the main autoimmune rheumatic conditions were excluded by absent autoantibodies.

The limitations of this manuscript are the low number of participants and the relatively small follow-up. However, since it is the first time that LDN is used in CKV chronic arthritis potentially resulting from a previous Chikungunya infection, a low number of patients is expected.

CONCLUSIONS

This report showed no clinical improvement in LDN in patients with chronic CKV joint involvement. Further studies are necessary to investigate the use of LDN in individuals with chronic Chikungunya arthritis.

Conflict of Interest:
None.

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Informed Consent:
Informed consent was obtained from all study participants.

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