

# Novel therapeutic approach for loxoscelism: efficacy of cefixime and netilmicin sulfate combination therapy

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Dear Editor,

Loxoscelism, resulting from bites by *Loxosceles* spiders – particularly *Loxosceles reclusa* – is characterized by necrotic skin lesions and, in severe cases, systemic symptoms such as hemolysis, acute renal failure, and disseminated intravascular coagulation (DIC). The venom's sphingomyelinase D (SMD) enzyme induces direct tissue damage and an inflammatory response, leading to cell death, dermal necrosis, and increased vascular permeability, which can result in hemolysis and thrombosis.<sup>1,2</sup> Additionally, SMD activates endothelial cells and neutrophils, contributing to vasculitis, a factor often overlooked in treatment considerations. This mechanism may explain the efficacy of dapsone in certain stages of loxoscelism. In Italy, particularly in the southern regions,

there has been an increase in reported *Loxosceles* spider bites over the past decade, correlating with climate changes and urban expansion into previously uninhabited areas.<sup>3</sup> This rise underscores the need for effective treatment protocols.

Five patients presented to our clinic with confirmed *Loxosceles* spider bites, all exhibiting initial necrotic lesions (Figure 1 A,B). Previous treatments included local and systemic corticosteroids, topical antibiotics, and systemic antibiotics such as azithromycin and amoxicillin (administered separately), without significant improvement. The time between the spider bite and the initiation of these treatments ranged from 24 to 72 hours. Given the potential for secondary bacterial infections, we administered a combination of netilmicin (300 mg intramuscularly once daily) and cefixime (400 mg orally once daily) for 10 days. Netilmicin, an aminoglycoside antibiotic, is effective against a broad spectrum of gram-negative bacteria, including *Pseudomonas aeruginosa*,<sup>4</sup> and some gram-positive bacteria. Cefixime, a third-generation oral cephalosporin, provides coverage against gram-positive organisms like *Streptococcus pyogenes* and gram-negative bacteria, including *Enterobacteriaceae*.<sup>5</sup>

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Consent for publication: the patients included in this manuscript have given written informed consent to the publication of their case details and any accompanying images.

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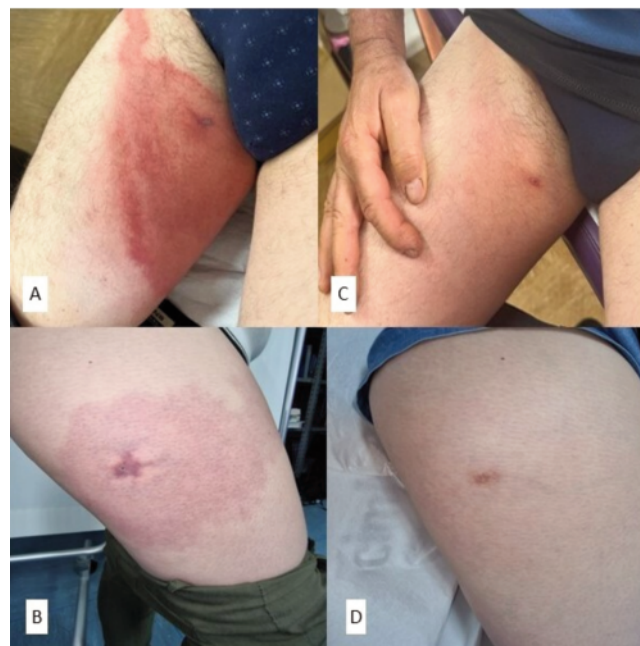
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**Figure 1.** A, B) Initial clinical manifestation consisted of a central necrotic area surrounded by erysipelas-like reaction. Lymphangitis is shown in panel A; C) after 5 days of combined antibiotic treatment, the erythema has significantly faded; D) complete resolution occurred after 10 days of treatment.

Patients reported significant improvement in pain and local inflammation within the first five days of treatment (Figure 1C). All patients experienced resolution of their necrotic ulcers without the need for surgical intervention or further complications (Figure 1D). No side effects were reported. Wound cultures from two patients, taken before antibiotic administration, revealed the presence of *Staphylococcus aureus* and *P. aeruginosa*, both of which were effectively cleared by the combination therapy. The combination of netilmicin and cefixime offers broad-spectrum antibacterial coverage, addressing both gram-positive and gram-negative bacteria, including potential polymicrobial infections. This approach may be advantageous over conventional therapies that typically involve a single antibiotic or supportive wound care alone. However, the use of prophylactic antibiotics in loxoscelism should be carefully considered, as current guidelines do not universally recommend their use without clear signs of infection. In our cases, the presence of necrotic lesions and positive wound cultures justified the antibiotic therapy. The combination of netilmicin and cefixime may provide an effective treatment for necrotic lesions resulting from *Loxosceles* spider bites, particularly when secondary bacterial infection is a concern. Further studies are warranted to establish the long-term efficacy and safety of this treatment protocol.

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