Leukocytoclastic vasculitis (LCV) is a common form of small-vessel vasculitis, which commonly presents as palpable purpura or petechiae, caused by deposition of circulating immune complexes on vessels walls that attracts granulocytes which damage the vascular endothelium and leading to erythrocytes extravasation. The skin is the most commonly involved organ, but also renal, gastrointestinal, pulmonary, and neurological systems may be affected. Skin lesions may be the initial signs of systemic vasculitis. Systemic symptoms may be present, such as fever, myalgia, abdominal pain and arthralgia. The presence of neuropathy/mononeuritis multiplex is expression of severe vasculitic involvement. Herein, we describe the case of a patient with leukocytoclastic vasculitis associated to sensory neuropathy, responsive to intravenous immunoglobulins (IVIg) therapy, after the failure of classic systemic treatments.

**Key words:** Leukocytoclastic vasculitis, Sensory neuropathy, Intravenous immunoglobulins.
cardiovascular and neurological systems may be affected. Skin lesions may be the initial signs of systemic vasculitis. Systemic symptoms may be present, such as fever, myalgia, abdominal pain and arthralgia. The presence of neuropathy/mononeuritis multiplex is expression of a severe systemic vasculitic involvement (5-7).

**Case report**

A 35-year-old woman came to our attention for the occurrence of small reddish lesions on the back of the feet, then extended to the ankles and proximally to the knees. She reported that the lesions had appeared four months before and that she had been treated with topical steroids without benefit. The patient wasn’t taking any medication or recreational drug.

Physical examination revealed palpable petechial and purpuric lesions on the legs and feet. In the right pretibial region there were confluent lesions in necrotic areas (figure 1).

Close to the knees there were also erythematous macules. The right leg was slightly edematous. Patient’s vital signs were normal and she had no fever.

Laboratory tests showed normal hemoglobin levels (12.5 mg/dL, normal values: 12-15.5 mg/dL), a normal platelets count (250 × 10^9/L, normal values 150-400 × 10^9/L), but a neutrophilic leukocytosis with white blood cells 11.42 × 10^9/L (normal values: 4.5-11 × 10^9/L) and neutrophils 10.9 × 10^9/L (normal values: 2-8 × 10^9/L), and serum C reactive protein (PCR) was 19 mg/L (normal values: < 8mg/L). Hepatorenal function tests were normal. A low anti-nuclear antibodies (ANA) titer was observed (1:80) with a speckled nuclear pattern (IFI su HEP-2), ENA screen, rheumatoid factors, cryoglobulins and anti-neutrophil cytoplasmic antibodies (ANCA) were negative. Complements levels were within the normal ranges. Serological markers for hepatitis B virus, hepatitis C virus, Epstein-Barr virus, cytomegalovirus and HIV were negative. A chest X-rays was executed and resulted negative. A lower limbs echocolor doppler of the veins was performed but showed no alterations.

A skin punch-biopsy was performed on one of the most recent purpuric lesions of the right lower limb. The histologic findings revealed a leukocytoclastic vasculitis with a perivascular inflammatory infiltrate (mainly of polymorphonuclear leucocytes) and fragments of granulocytes’ nucleus (leukocytoclasia). There were also endoluminal thrombosis and thickening of the blood vessels wall (figure 2).

A treatment with prednisone 25 mg/day and dapsone 50 mg/day was started. Nevertheless, the patient gradually worsened with necrotic hemorrhagic evolution of the lesions of lower limbs (figure 3) and new onset of erythematous macules on the wrists and forearms.

The patient also reported the onset of hypoesthesia of the first three digits of the left hand associated

**Figure 1.** Necrotic lesions on the right pretibial region.

**Figure 2.** Histologic findings: leukocytoclastic vasculitis with perivascular inflammatory infiltrate, endoluminal thrombosis and thickening of the blood vessels wall.
with stiffness and tremor. She also reported hypoes-
thesia on the lateral side of the left ankle and foot,
as well as widespread arthromyalgias. Thus, electro-
myography and electroneurography (EMG/ENG)
of the upper and lower limbs was performed, but
resulted negative.

After a rheumatologic evaluation, dapsone 50
mg/day was stopped and azathioprine 100 mg/day
was started.

Two months later, the patient was admitted to
the hospital for an important worsening of the skin
conditions. The cutaneous examination of lower
limbs showed widespread purpuric lesions and pal-
pable petechiae, associated with exuding necrotic
lesions on the right pretibial region. A slight edema
of lower limbs and fovea sign were present. On the
wrists and forearms there were isolated erythematous
macules. Moreover, hypoesthesia and arthralgia of
upper and lower limbs were still present.

Another EMG/ENG of the upper and lower
limbs was performed, and showed signs of sensory
axonal multineuropathy, with mild damage of the
distal sensory fibers of the left median nerve and
severe damage of the sensitive fibers of the left sural
nerve. Furthermore, high-resolution ultrasound
revealed the increased left sural nerve cross sectional
area (CSA).

During the hospitalization, 25 mg/day of
prednisone, 100 mg/day of azathioprine and a sin-
gle infusion of 2 g/kg (for a total of 120 g) of IVIg
distributed over two days were administrated to the
patient, with a dramatic improvement of the skin
lesions (figure 4).

After discharge, the patient underwent other six
infusions of IVIg (2 g/kg over two days once a month
for six months) associated with prednisone 25 mg/
day, gradually tapered, and azathioprine 100 mg/day,
with a progressive clinical improvement.

Three months after the last IVIg infusion, the
patient was asymptomatic and neurological exami-
nation was negative, so oral prednisone was stopped
and but azathioprine 100 mg/day was maintained.

Actually, one year after the hospitalization, the
patient continues the therapy with azathioprine
100 mg/day, but her clinical conditions are in stable
remission, with occasional flare-ups on the skin, but
no more signs of sensory neuropathy.

**Discussion**

The treatment of LCV depends on two major fac-
tors: the etiology and the extent of disease, especially
in the cases of a systemic involvement. When LCV is
the manifestation of a systemic vasculitis process, the

![Figure 3](image3.png)

**Figure 3.** Necrotic hemorrhagic evolution of the lesions of lower limbs.

![Figure 4](image4.png)

**Figure 4.** Improvement of the skin lesions after a single infusion of IVIg (2 g/kg).
treatment generally requires a combination of steroids and immunosuppressive drugs. Systemic prednisone is the most widely used treatment. It may be very effective to treat acute or single episodic LCV, but it is not recommended for recurrent or chronic LCV. Dapsone is primarily an anti-inflammatory medication with a predominantly antineutrophilic effect that is frequently used in various vasculitic diseases and neutrophilic dermatoses. Azathioprine has been shown to be effective in preventing clinical recurrence, either as monotherapy or associated with a low-dose of prednisone (8–10). IVIg administration has shown to be effective in isolated severe cases with persistent ulcerations, suspected comorbid infection, or common variable immune deficiency, when added to traditional therapies.

IVIg is a purified product of normal polyspecific IgG obtained from the pooled blood of several healthy donors and it has been used for over 20 years to treat a wide variety of dermatologic autoimmune disorders, such as pemphigus vulgaris and foliaceus, bullous and mucous membrane pemphigoid, epidermolysis bullosa acquisita, dermatomyositis, systemic vasculitis, systemic lupus erythematosus and scleromyxedema. IVIg is usually administered at a dosage of 2g/kg bodyweight distributed over 2-5 days every 4 weeks (11).

Its mechanism of action is still unclear, but several hypothesis have been proposed. Its immunomodulatory effect depends on both the Fc portion and the variable regions of infused antibodies (Fab), which are able of competitive inhibition of the reticuloendothelial system, netralisation of pathogenic antibodies, anaphylotoxins and cytokines, complement scavenging, saturation of protective neonatal Fc receptors (FcRn), inhibition of B-cell functions, inhibition of Th17 differentiation and functions, expansion of regulatory T-cells and upregulation of inhibitory FCγRIIB or downregulation of activating FCγRIIB (12).

IVIg has been used successfully as a single agent and also as an adjuvant treatment in several autoimmune diseases. The first documented application of IVIg was reported in 1981 in a child with an idiopathic thrombocytopenic purpura (13).

Later, IVIg was used successfully treat some cases of Kawasaki disease (14,15), of livedoid vasculitis (16, 17), and in 1993 Dalakas et al. reported the first randomized controlled clinical trial of IVIg in dermatomyositis (18).

Recently, clinical guidelines for the use of IVIg in dermatology, first published in the European Dermatology Forum in 2009, were updated (19).

Regarding systemic vasculitis, data on IVIg in ANCA-associated vasculitis and in other several cases of different vasculitis reported beneficial effects of IVIg (20, 21).

Actually, European guidelines promote the use of IVIg in Kawasaki’s disease as a first-line treatment. In all the other systemic vasculitis the use of IVIg is intended for severe and recalcitrant cases, unresponsive to the classical therapies or if other therapeutic options are contraindicated (22).

The use of IVIg may be associated with mild systemic side-effects such as headache, backache, myalgia, chills, fever, nausea or vomiting, wheezing and, less often, changes in blood pressure and tachycardia. Less common side-effects include aseptic meningitis, anaphylactic reactions, renal failure and haemolytic anaemia (10–12).

In our patient, the use of IVIg healed a severe form of LCV, after the failure of the classical treatments.

In conclusion, we suggest to begin early IVIg therapy in patients with extensive disease associated to neurologic involvement with the aim to prevent permanent sequelae.

Conflicts of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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