Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Cocaine/Levamisole-Associated Autoimmune Syndrome: A Case Report☆

Síndrome autoinmune cocaína-levamisol. Presentación de un caso

To the Editor:

A 55-year-old man visited the emergency department with clinical signs and symptoms that had appeared some days earlier, consisting of progressive dyspnea accompanied by fever of up to 39 °c, productive cough, and flat, red-violaceous reticulated lesions with a purplish appearance on the left outer ear (Fig. 1), left malar region, right nostril, and both arms. The patient was an ex-intravenous drug abuser and had a history of stage-2 infection with the human immunodeficiency virus (HIV), hepatitis B virus, hepatitis C virus, which was cured spontaneously, and presented chronic neutropenia. Laboratory tests showed leukopenia and thrombocytopenia, creatinine levels of 6 mg/dL, procalcitonin of 3.74, C-reactive protein (CRP) of 313, and a glomerular filtration rate of 9 mL/min. Antineutrophil cytoplasmic antibodies (ANCAs) and lupus anticoagulant were positive, whereas cryoglobulins were negative. A chest x-ray showed bilateral disperse alveolar-interstitial infiltrates and the patient was therefore diagnosed with lobar pneumonia and acute kidney failure.

A punch biopsy of one of the skin lesions was performed and revealed massive occupation of the capillaries by mixed thrombi, with some trapped polymorphonuclear cells, without the characteristic abnormalities of leukocytoclastic vasculitis (Figs. 2 and 3). The differential diagnosis

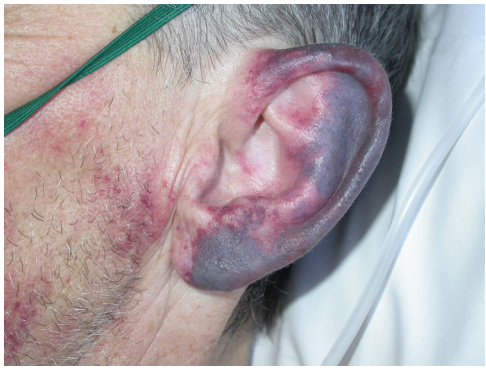

Figure 1 Purplish lesion on the outer ear.

included thrombotic thrombocytopenic purpura, disseminated intravascular coagulation, cryoglobulinemia, and retiform purpura associated with cocaine use. The first 2 entities were ruled out clinically and the third was ruled out due to the absence of cryoglobulins. The patient subsequently admitted to using cocaine. The skin lesions remitted

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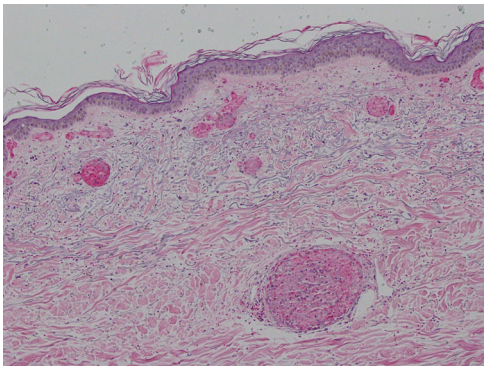

Figure 2 (hematoxylin–eosin, x100) Massive occupation of dermal blood vessels by thrombi.

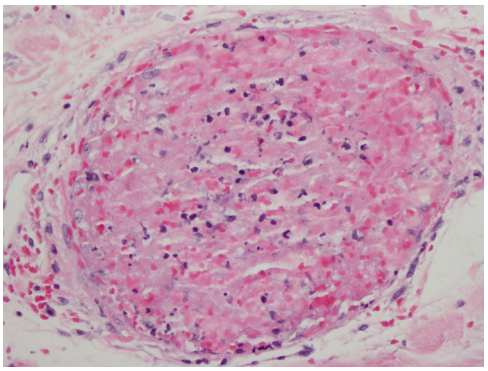

Figure 3 (hematoxylin–eosin, x200 Higher-magnification image of a thrombosed blood vessel without leukocytoclastic vasculitis.

after administering treatment with methylprednisolone and the patient was referred to a mental-health center for cessation of cocaine use.

Levamisole is an anthelminthic drug that, due to its immunomodulatory effect, was used in the past to treat rheumatoid arthritis, collagenopathies, inflammatory bowel disease, pediatric nephrotic syndrome, and cancer. In 2000, the US Food and Drug Administration (FDA) withdrew the drug from the market due to its severe adverse effects, such as vasculitis and blood disorders (especially agranulocytosis)[1–3]; the drug was, however, maintained for veterinary use.[4,5]

It has gained notoriety since 2008 through its use as an adulterant for cocaine due to its similar consistency, its availability, and its synergic activity.[2] A syndrome has therefore been described in users of this drug that is characterized by retiform purpura,[1–3] pauci-immune crescentic glomerulonephritis, pulmonary hemorrhage with vasculitis, pulmonary hypertension,[2,5] and arthritis deformans, with variable frequency.[6] Serology reveals higher titers of perinuclear antineutrophilic antibodies than in idiopathic vasculitis. Its association with antinuclear antibodies (ANAs), anti-double stranded DNA (anti-dsDNA), and antiphospholipids such as lupus anticoagulant and anticardiolipin has also been reported.[2,3] A study carried out in Spain in 2009 determined that 48% of cocaine samples studied contained levamisole.[7]

The most notable symptom, and the one that causes patients to seek consultation, is the cutaneous symptom.[2] It has also been found that 60% of these patients have blood disorders and between 95% and 100% have high ANCA titers.[3] It usually manifests as retiform purpura involving the outer ear, zygomatic arches, and extremities, while sparing the torso. Typical histopathology findings include small-vessel leukocytoclastic vasculitis with fibrinoid necrosis of the vascular wall, extravasation of erythrocytes, karyorrhexis and angiocentric inflammation, and multiple fibrin thrombi in the vessels of the superficial and deep dermis.[1–3,5] These findings may present together or separately; microvascular thrombosis is the most consistent of these findings[1] and was the only one found in our case.

Cascio and Jen[2] have suggested naming this constellation of abnormalities cocaine/levamisole-associated autoimmune syndrome (CLAAS). As well as the retiform purpura with the characteristic pattern, our patient presented a thrombotic vasculopathy, thrombocytopenia, neutropenia, lupus anticoagulant, and ANAs. Although the patient presented acute kidney failure, there is no clinical confirmation that this was due to the use of cocaine and levamisole.

The diagnosis of CLAAS is by exclusion. It should be considered in all patients with a history of cocaine use who present with purpura of the characteristics described above, joint pain, neutropenia, and high ANCA titers[5] in the absence of other apparent etiologies.[8] The basis of treatment is ceasing cocaine, and thus levamisole, use.[1,2,5] The literature shows treatment data similar to those for primary vasculitis: immunosuppression, anticoagulation, and antiaggregation.[6] In our patient, the dermal lesions remitted after treatment with methylprednisolone.

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Conflicts of Interest

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Inflammatory Tinea Capitis Due to *Trichophyton rubrum*☆

Tinea capitis inflamatoria por *Trichophyton rubrum*

Dear Editor:

A 78-year-old woman, living in an urban area, reported an approximately 3-month history of an inflammatory purulent lesion on the scalp and a 1-year history of toe nail onychomycosis and tinea pedis treated with topical ciclopirox and sertaconazole. Examination findings showed a wide scarring alopecia area on the scalp with perifollicular pustules and crusts which, after having been removed, exhibited a bleeding, erosive surface (Fig. 1). No adenopathies and no general symptoms of infection were found. There was no history of animal contact and no clinical signs of immunodeficiency.

For diagnosis, swab samples of yellowish secretion of the pustules were obtained and *Trichophyton rubrum* was identified by culture and microscopic examination. We also took a biopsy, in which histopathological study showed perivascular infiltration by lymphocytes in the upper dermis. Septate hyphae were not revealed by periodic acid-Schiff staining (PAS). Bacterial cultures showed mixed microbiota.

Finally, a diagnosis of tinea capitis due to *T. rubrum* was made.

In the matter of treatment, the patient improved her condition with a course of twelve weeks of two hundred and fifty milligrams per day of oral terbinafine and topical ketoconazole treatment (Fig. 2).

Tinea capitis is common in children, but several studies have shown that it also can be seen in adults, particularly in postmenopausal women, a phenomenon that may be explained by the involution of sebaceous glands following decreased blood oestrogen levels,[1,2] and immunocompromised people, as immunologic dysfunction may increased risk of infection through an impaired cell-mediated response.[3]

In our geographical area, most of the cases of tinea capitis affecting the adult population are caused by species of the genus *Trichophyton*.[1]

However, *T. rubrum* is a very uncommon cause of tinea capitis in the general population. This particular dermatophyte led to a robust case of tinea capitis in our patient, likely due to autoinoculation from tinea pedis and onychomycosis. In contrast to other dermatophyte species, *T. rubrum* can cause both an endothrix and an ectothrix infection in the setting of hair invasion, maybe this is what allows long-term colonization.[2,3,4]

Adult tinea capitis may have polymorphic and atypical clinical presentations, leading to difficulty in diagnosis and a delay in treatment. The differential diagnosis in our area included erosive pustular dermatosis of the scalp, folliculitis decalvans and cutaneous cryptococcosis. Erosive pustular dermatosis of the scalp is a rare inflammatory disease of unknown aetiology that usually occurs in the elderly and is a diagnosis of exclusion. Patients commonly present tiny pustules on the scalp, forehead or temples. The pustules are usually sterile, but they can become secondarily colonized by bacteria. Folliculitis decalvans is a highly inflammatory form of cicatricial alopecia where perifollicular papules and pustules complete the clinical picture. Often, *Staphylococcus aureus* can grow. Finally, cutaneous cryptococcosis is an infection caused by *Cryptococcus neoformans*[5]. The skin lesion sometimes consists of large crusted ulceration on the scalp that could resemble tinea capitis, but this usually occurs in immunocompromised hosts.

In terms of treatment, the choice of the antifungal drug depends on the characteristics of the patient, the type and extent of infection, and the possibility of drug interactions.

Situations where systemic therapy is indicated include tinea involving two or more areas, tinea corporis with extensive involvement, tinea pedis such as moccasin or vesicular type, and failure of treatment with topical agents[6].

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