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Neurology® 2019;93:1009-1011. doi:10.1212/WNL.0000000000008584

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Neutrophilic dermatoses are a heterogeneous group of inflammatory skin conditions all characterized by sterile neutrophilic infiltrates in cutaneous and subcutaneous tissues, usually leading to ulcers or erythematous plaques. They can be associated with extracutaneous sterile neutrophilic infiltration occurring mainly in the lung, liver, spleen, or lymph nodes, whereas aseptic neutrophilic myositis is extremely rarely reported. Isolated muscular neutrophilic infiltrates never occur in autoimmune myopathy, and this feature usually suggests an infectious muscle disease.

Recently, it was reported that pyoderma gangrenosum or necrotizing Sweet syndrome (2 distinct clinical entities belonging to the spectrum of neutrophilic dermatoses) may be mimickers of necrotizing fasciitis.[1] The authors coined the unifying term of "necrotizing neutrophilic dermatosis" to define this subgroup of neutrophilic dermatoses with systemic inflammation and emphasized the importance of not misdiagnosing them as necrotizing fasciitis to avoid inappropriate management. We report herein 2 cases of severe aseptic neutrophilic myositis, which mimicked as well necrotizing fasciitis, although concomitant skin manifestations were mild or initially absent, and which responded dramatically to infliximab.

We examined a 47-year-old man with a mild painful proximal weakness and deep palpable subcutaneous nodules of the legs associated with high fever, night sweats, and leukocytosis. Electromyogram and creatine kinase levels were normal. The skin biopsy showed a neutrophilic panniculitis, and the muscle biopsy a neutrophilic myofasciitis, without infection. Malignancy and hemopathy were ruled out. Within the next weeks, following a diarrhea onset, Crohn disease was diagnosed. Initially, the patient was refractory to 4 weeks of corticosteroids 1 mg per kg per day, but dramatically improved with infliximab 5 mg per kg.

A 75-year-old woman, bedridden, with a 23 kg weight loss, was also referred to our department for a neutrophilic myositis without initial cutaneous lesions. She had a history of Janus kinase 2–mutated thrombocythemia, complicated with myelofibrosis. She was ambulant at disease onset and had developed during the last 3 years a proximal painful weakness, night sweats, and high fever with chronic blood inflammation (leukocytosis 28 x 10^9/L and C-reactive protein 121 mg/L). Previous explorations showed asymmetric plurifocal myositis (thigh muscle MRI, figure) with a significant hypermetabolism in PET. Electromyogram showed myogenic features, and the creatine kinase level was normal. Myopathologic analysis revealed a disruption of muscle architecture with dense fibrosis, and polymorphic nodular inflammatory infiltrates mostly composed of altered neutrophils (figure). Muscle analysis ruled out infectious (including 16S rRNA gene sequencing) or malignant diseases. Of note, various large spectrum antibiotic courses had been initiated without effect. She was also refractory to oral corticosteroids 1 mg per kg per day during 3 weeks. When she arrived in our unit, she did not show any sign of skin involvement, but we considered this aseptic neutrophilic myositis as a neutrophilic

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Go to Neurology.org/N for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

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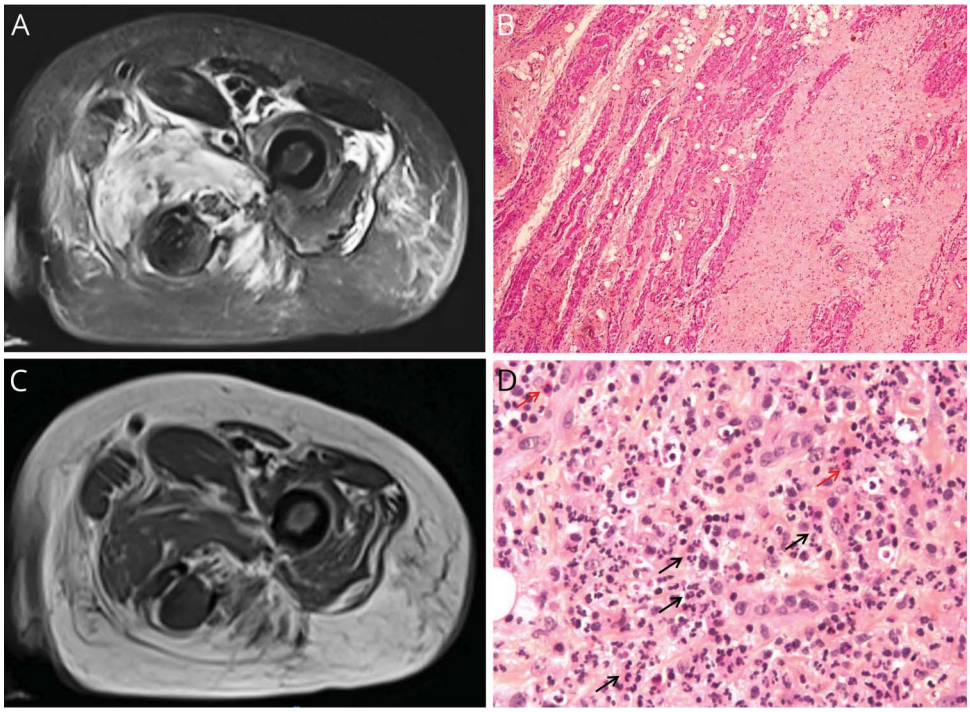
Figure Muscle biopsy and MRI



(A) Thigh muscle MRI STIR showing hypersignal within the following muscles: the vastus lateralis, the adductor longus, and the adductor brevis. There is also a moderate hypersignal on the gracilis muscle. No abnormal contrast in the fascia nor in the bone. (B) Hematoxylin and eosin staining of the vastus lateralis muscle biopsy showing fatty and fibrosis replacement (20× magnification). (C) Thigh muscle MRI T1 showing some degree of atrophia and fatty replacement, which mostly involved these muscles: the vastus lateralis, the biceps femoris, and the end of the gluteus maximus. (D) At higher magnification (200× magnification), the dense polymorphic nodular infiltrate is mainly composed of neutrophils (black arrows). Of note, few eosinophils are present (red arrows).

systemic disease associated with her acquired myeloproliferative disorder. She quickly and dramatically improved (apyrexia and C-reactive protein level normalization) following infliximab initiation (1 infusion 5 mg per kg followed by 1 infusion 2 and 8 weeks later) regaining the use of her limbs. Because of an early immunization against infliximab, she relapsed developing concomitantly an erythematous and edematous plaque, without skin breakdown, of the left leg. She responded to a second line of treatment with tocilizumab and without antibiotic therapy.

Five other cases of histologically confirmed aseptic neutrophilic myositis without skin manifestations[2–4] or skin breakdown[5,6] have been reported. Muscle histology always showed neutrophilic infiltrates, with necrosis in 3 cases. Creatine kinase levels were normal (n = 1) or high (n = 3) between 467 and 4471 UI/L and not available in 1 case. Aseptic neutrophilic myositis was associated with acute myeloid leukemia (n = 2), myeloproliferative disorder (n = 1), inflammatory bowel disease (n = 1), or was the unique feature (n = 1). All patients were treated with corticosteroids and achieved remission, except for 1 who died of myocardial infarction. The use of tumor necrosis factor (TNF) alpha inhibitors has proved safe and effective in other neutrophilic dermatoses such as pyoderma gangrenosum, especially when associated with underlying diseases such as inflammatory bowel diseases, rheumatoid arthritis, or ankylosing spondylitis.[7] We here report the first 2 cases of aseptic neutrophilic myositis, one of which developing concomitantly Crohn disease, that responded dramatically to a TNF-alpha inhibitor.

This rare condition shows that extracutaneous organs may be solely affected by aseptic neutrophilic infiltration; it can nevertheless be considered as part of the spectrum of neutrophilic dermatoses *sine dermatosis* and as a variant of the necrotizing neutrophilic dermatosis mimicking necrotizing fasciitis.[1] The mainstay of treatment remains systemic corticotherapy, but in cases of resistance or contraindication, TNF-alpha inhibitors, namely infliximab, should be considered as alternative therapy.

Author contributions

P. Guillaume-Jugnot: drafting/revising the manuscript, data acquisition, study concept or design, accepts responsibility for conduct of research and will give final approval, and acquisition of data. S. Guégan: drafting/revising the manuscript, data acquisition, study concept or design, analysis or interpretation of data, accepts responsibility for conduct of research and will give final approval, and study supervision. S. Léonard-Louis: analysis or interpretation of data, accepts responsibility for conduct of research and will give final approval, and acquisition of data. S. Barete: drafting/revising the manuscript, analysis or interpretation of data, accepts responsibility for conduct of research and will give final approval, and acquisition of data. O. Benveniste: drafting/revising the manuscript, analysis or interpretation of data, accepts responsibility for conduct of research and will give final approval, acquisition of data, and study

supervision. Y. Allenbach: drafting/revising the manuscript, data acquisition, study concept or design, analysis or interpretation of data, accepts responsibility for conduct of research and will give final approval, and study supervision.

Acknowledgment

The authors thank Quentin Monzani, who helped us actively for the MRI pictures, and Gonzague de Pinieux and Elodie Miquelestorena-Standley for the histology.

Study funding

No targeted funding reported.

Disclosure

The authors report no disclosures relevant to the manuscript. Go to Neurology.org/N for full disclosures.

Publication history

Received by *Neurology* April 21, 2019. Accepted in final form September 3, 2019.

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Neurology 2019;93;1009-1011 Published Online before print October 29, 2019
DOI 10.1212/WNL.0000000000008584