



Fig. 2. Villous proliferation in the synovium. Inset: adipose infiltration.

Five months after the synovectomy, she noted inflammation in the left knee and functional disability. Nuclear magnetic resonance and ultrasound led to a diagnosis of lipoma *arborescens*.

She underwent surgery, and the pathological study of the synovial membrane confirmed the diagnosis (Fig. 2).

Nuclear magnetic resonance can be highly useful in the evaluation of noninflammatory processes in patients with atypical monoarthritis.

## References

1. Murphey MD, Carroll JF, Flemming DJ, Pope TL, Gannon FH, Kransdorf MJ. From the archives of the AFIP: benign musculoskeletal lipomatous lesions. *Radiographics*. 2004;24:1433–66.

2. Hirano K, Deguchi M, Kanamono T. Intra-articular synovial lipoma of the knee joint (located in the lateral recess): a case report and review of the literature. *Knee*. 2007;14:63–7.
3. Coll JP, Ragsdale BD, Chow B, Daughters TC. Best cases from the AFIP: lipoma arborescens of the knees in a patient with rheumatoid arthritis. *Radiographics*. 2011;31:333–7.
4. Al-Ismaïl K, Torreggiani WC, Al-Sheikh F, Keogh C, Munk PL. Bilateral lipoma arborescens associated with early osteoarthritis. *Eur Radiol*. 2002;12:2799–802.
5. Patil PB, Kamalapur MG, Joshi SK, Dasar SK, Rao RV. Lipoma arborescens of knee joint: role of imaging. *J Radiol Case Rep*. 2011;5:17–25.
6. Martín S, Hernández L, Romero J, Lafuente J, Poza AI, Ruiz P, et al. Diagnostic imaging of lipoma arborescens. *Skeletal Radiol*. 1998;27:325–9.
7. Vilanova JC, Barceló J, Villalón M, Aldomà J, Delgado E, Zapater I. MR imaging of lipoma arborescens and the associated lesions. *Skeletal Radiol*. 2003;32:504–9.
8. Narváez JA, Narváez J, Aguilera C, de Lama E, Portabella F. MR imaging of synovial tumors and tumor-like lesions. *Eur Radiol*. 2001;11:2549–60.
9. Sheldon PJ, Forrester DM, Leach TJ. Imaging of intraarticular masses. *Radiographics*. 2005;25:105–19.

Maria Dolores Ruiz Montesino,<sup>a,\*</sup> Virginia Moreira Navarrete,<sup>b</sup> Carmen Vargas Lebrón,<sup>b</sup> Juan J. Rios-Martín<sup>c</sup>

<sup>a</sup> Unidad de Gestión Clínica de Reumatología, Unidad de investigación (Imagen), Hospital Universitario Virgen Macarena, Sevilla, Spain

<sup>b</sup> Unidad de Gestión Clínica de Reumatología, Hospital Universitario Virgen Macarena, Sevilla, Spain

<sup>c</sup> Unidad de Gestión Clínica de Anatomía Patológica, Hospital Universitario Virgen Macarena, Sevilla, Spain

\* Corresponding author.

E-mail address: [lruizmontesino@yahoo.es](mailto:lruizmontesino@yahoo.es) (M.D. Ruiz Montesino).

2173-5743/

© 2016 Elsevier España, S.L.U. and Sociedad Española de Reumatología y Colegio Mexicano de Reumatología. All rights reserved.

## Cutaneous Leishmaniasis: An Opportunistic Infection<sup>☆</sup>



### Leishmaniasis cutánea. Una infección oportunista

To the Editor,

Leishmaniasis is a parasitic disease caused by the intracellular protozoa *Leishmania*. It is transmitted by through the bite of a mosquito: the female phlebotomus. There are 21 species of *Leishmania*. The species most widespread in Spain is *Leishmania infantum* and its major reservoir is the dog.<sup>1</sup>

A number of cases of leishmaniasis have been reported in patients with different rheumatic diseases who were being treated with biological drugs.

We describe a case of cutaneous leishmaniasis in a woman with rheumatoid arthritis who was receiving an anti-tumor necrosis factor (TNF)- $\alpha$  and methotrexate. The patient was 54 years old and had been born in Murcia, a city in southeastern Spain. She had been diagnosed with rheumatoid arthritis 5 years earlier, and was positive for rheumatoid factor and anti-cyclic citrullinated peptide antibodies. She was being treated with subcutaneous methotrexate (25 mg each week) together with adalimumab at a dose of 40 mg every 15 days. She had no significant medical history or

harmful habits. The patient was in clinical remission and it was decided to increase the interval between adalimumab doses to 21 days. Weeks later, she developed a nodular and ulcerated lesion on the palmar side of her left carpus (Fig. 1). Biopsy led to a diagnosis of cutaneous leishmaniasis. Immunosuppressive therapy was discontinued and she underwent an analytical and imaging study, which ruled out visceral leishmaniasis. The patient was treated with amphotericin B at a dose of 3 mg/kg body weight/day for 5 days, and the lesion disappeared. Intralesional treatment was not performed and there were no secondary effects of the therapy.

In Spain, according to a report of the Ministry of Health dated 2012, the autonomous communities that had reported cases of leishmaniasis during the preceding decade were: Andalusia, Aragon, Balearic Islands, Cantabria, Castile-León, Catalonia, Valencian Community, Extremadura, Community of Madrid, Region of Murcia, Chartered Community of Navarre and La Rioja. According to the registry of the Center for the Coordination of Health Warnings and Emergencies, between 2002 and 2010, 82 cases were reported in Murcia.

The disease can present in 3 clinical forms<sup>2</sup>: cutaneous, mucocutaneous and visceral leishmaniasis. In the cutaneous and mucocutaneous forms, the diagnosis is reached by biopsy and visualization of *Leishmania* in the cells.

The mucocutaneous form presents with erythema, erosion and ulcers around the lips and nose; the differential diagnosis should include Wegener granulomatosis, among others. In the cutaneous form, we find lesions in areas of exposed skin, like face, arms

<sup>☆</sup> Please cite this article as: Moreno Martínez MJ, Moreno Ramos MJ, Sánchez Pedreño P. Leishmaniasis cutánea. Una infección oportunista. *Reumatol Clin*. 2017;13:181–182.



**Fig. 1.** Cutaneous leishmaniasis lesion in carpus (Oriental sore).

and legs. Each lesion represents a bite. Visceral leishmaniasis can present with a febrile syndrome with constitutional symptoms and manifestations depending on the affected organs (spleen, liver, bone marrow, among others).<sup>2</sup>

Tumor necrosis factor- $\alpha$  is a cytokine implicated in the immune response against intracellular parasites. It has been involved in granuloma formation and in containing the protozoa.<sup>3</sup>

Since the introduction of anti-TNF- $\alpha$  agents, there have been several cases of leishmaniasis.<sup>4</sup> According to the reports, it seems that the risk is greatest during the first year of treatment, and to a greater extent with infliximab than with the subcutaneous drugs.<sup>5,6</sup> There have also been cases with other types of immunosuppressive agents, like azathioprine, methotrexate, cyclosporine, steroid and cyclophosphamide.<sup>7</sup>

In immunocompromised patients, the risk of reactivation, and thus, of active visceral leishmaniasis is increasing.<sup>4,7</sup> In regions in which it is endemic, in an immunocompromised patient with fever, asthenia, splenomegaly and pancytopenia, this diagnostic possibility should be considered.<sup>4</sup> In our case, the patient was receiving treatment with an immunosuppressive agent, and came from an area in which leishmaniasis is endemic. Thus, upon the first diagnostic suspicion, after the development of the skin lesion, the latter was biopsied and immunosuppressive therapy was discontinued.

## References

- Lucientes J, Castillo JA, Gracia MJ, Peribáñez MA. Flebotomos, de la biología al control. Revista Electrónica de Veterinaria REDVET. Available in: <http://www.veterinaria.org/revistas/redvet/n080805.html> [accessed 14.10.13].
- David CV, Craft N. Cutaneous and mucocutaneous leishmaniasis. *Dermatol Ther.* 2009;22:491–502.
- Engwerda CR, Ato M, Stager S, Alexander CE, Stanley AC, Kaye PM. Distinct roles for lymphotoxin and tumornecrosis factor in the control of leishmania donovani infection. *Am J Pathol.* 2004;165:2123–33.
- Cascio A. Leishmaniasis and biologic therapies for rheumatologic diseases. *Semin Arthritis Rheum.* 2010;40:e3–5.
- Martin-Mola E, Balsa A. Infectious complications of biologic agents. *Rheum Dis Clin N Am.* 2009;35:183–99.
- Guedes-Barbosa LS, Costa IP, Fernandes V, Mota LM, Menezes I, Scheinberg MA. Leishmaniasis during anti-tumor necrosis factor therapy: report of 4 cases and review of the literature (additional 28 cases). *Semin Arthritis Rheum.* 2013;43:152–215.
- Van Griensven J, Carrillo E, Lopez-Velez R, Lynen L, Moreno L. Leishmaniasis in immunosuppressed individuals. *Clin Microbiol Infect.* 2014;20:286–99.

María José Moreno Martínez,<sup>a,\*</sup> Manuel José Moreno Ramos,<sup>a</sup> Paloma Sánchez Pedreño<sup>b</sup>

<sup>a</sup> *Departamento de Reumatología, H.C.U. Virgen de la Arrixaca, Murcia, Spain*

<sup>b</sup> *Departamento de Dermatología, H.C.U. Virgen de la Arrixaca, Murcia, Spain*

\* Corresponding author.

E-mail address: [mjmorenomartinez@gmail.com](mailto:mjmorenomartinez@gmail.com) (M.J. Moreno Martínez).

2173-5743/

© 2016 Elsevier España, S.L.U. and Sociedad Española de Reumatología y Colegio Mexicano de Reumatología. All rights reserved.

## Autoimmune pitfalls in treatment with TNF $\alpha$ inhibitors



### Los escollos autoinmunes en el tratamiento de pacientes con anti-TNF $\alpha$

Dear Editor,

Systemic lupus erythematosus (SLE) may be induced by several drugs, including the anti-TNF $\alpha$  agents.

As time passes, and after an experience of almost 15 years with these drugs in a wide variety of rheumatic diseases, there are questions still unanswered.

In fact, despite the frequent and well-established development of autoantibodies, such as anti-nuclear antibodies (ANA) and anti-double stranded DNA (anti-dsDNA), among patients treated with anti-TNF $\alpha$  agents, the occurrence of clinical SLE still remains a rare adverse event.<sup>1,2</sup> Its aetiology, triggering factors and temporal association are still unknown. From case-reports published in

the literature and some data available from registries, it seems more common in rheumatoid arthritis patients under infliximab<sup>3</sup>. However, as new drugs are becoming available, new cases have been reported.<sup>4</sup>

In our cohort, from 401 rheumatic patients (with rheumatoid arthritis, spondylarthritis and psoriatic arthritis) exposed to anti-TNF $\alpha$  agents, only three of them developed drug induced lupus after a mean time of exposure of  $4.11 \pm 4.71$  months.

The first case is a 52-year-old male patient suffering from ankylosing spondylitis for 7 years and treated with infliximab (450 mg, 8/8 weeks). After 20 months of treatment, he started complaining of asthenia, fever, dyspnoea and arthralgia. The chest X-ray showed bilateral pleural effusion. Laboratory investigation revealed normal blood cell count, raised erythrocyte sedimentation rate (ESR) (87 mm, normal <20 mm/h) and c-reactive protein (CRP) (76.6 mg/L, normal <0.3 mg/L). Additionally he had positive ANA (1/640, homogeneous pattern), positive anti-DsDNA (263 UI/mL, normal <200), complement consumption (C3 76 mg/dL, normal >83 and C4 11 mg/dL, normal >12). Anti-histone antibodies,