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Aseptic Abscess Syndrome in a Patient with Rheumatoid Arthritis: A Case Report

Miguel González-Velásquez[1], Carlos Jaime Velásquez-Franco[2], Santiago Bernal-Macías[3], Johann Gutiérrez-Bolaños[4]

[1] Internal Medicine Resident, Universidad Pontificia Bolivariana, Medellin, Colombia.
[2] Professor of Internal Medicine and Rheumatology, Universidad Pontificia Bolivariana, Medellin, Colombia.
[3] Rheumatologist, San Ignacio University Hospital, Bogotá, Colombia.
[4] Internal Medicine Physician, Clinica Universitaria Bolivariana, Medellin, Colombia.

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Correspondence:
Miguel González-Velásquez;
miguelgonv41@gmail.com

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ABSTRACT

Aseptic abscess syndrome is a rare and possibly underdiagnosed condition characterized by the presence of sterile neutrophilic collections in various tissues that do not respond to antimicrobial therapy but rather require anti-inflammatory treatment. There is limited literature linking this condition to rheumatoid arthritis. Here, we present the case of a patient with rheumatoid arthritis, presenting with prolonged febrile syndrome and multiple sterile abscesses. A diagnosis of aseptic abscess syndrome was made, and successful resolution of the abscesses was achieved following treatment with glucocorticoid pulses and infliximab. Clinicians should consider this condition in patients with inflammatory diseases who develop abscesses in different tissues where no causative microbiological agent can be identified.

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Síndrome de abscesos asépticos en paciente con artritis reumatoide: reporte de caso

Miguel González-Velásquez[1], Carlos Jaime Velásquez-Franco[2], Santiago Bernal-Macías[3], Johann Gutiérrez-Bolaños[4]

[1] Residente de Medicina Interna, Universidad Pontificia Bolivariana, Medellín, Colombia.
[2] Profesor titular de medicina interna y reumatología, Universidad Pontificia Bolivariana, Medellín, Colombia.
[3] Reumatólogo, Hospital Universitario San Ignacio, Bogotá, Colombia.
[4] Médico internista, Clínica Universitaria Bolivariana, Medellín, Colombia.

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RESUMEN

El síndrome de abscesos asépticos es una condición poco frecuente, probablemente subdiagnosticada, que se caracteriza por la aparición de colecciones neutrofílicas estériles en diferentes tejidos, las cuales no responden a antimicrobianos y cuyo tratamiento es basado en terapia antiinflamatoria. La literatura que relaciona dicha condición con la artritis reumatoide es escasa. Se presenta el caso de un paciente con artritis reumatoide, con síndrome febril prolongado y múltiples abscesos estériles en quien se hizo diagnóstico de síndrome de abscesos asépticos, con resolución de las colecciones luego del tratamiento con pulsos de glucocorticoides e infliximab. Se debe sospechar esta condición en pacientes con enfermedades inflamatorias que desarrollan abscesos en diferentes tejidos en los que no se logra identificar ningún agente microbiológico causal.

INTRODUCTION

The Aseptic Abscess Syndrome (AAS) is a rare autoinflammatory condition, primarily associated with Inflammatory Bowel Disease (IBD). It involves the formation of abscesses in various organs, without the presence of infectious microorganisms (1). It is distinguished by a lack of response to antibiotic therapy and the resolution of the abscesses following glucocorticoid treatment. Patients often undergo prolonged antimicrobial treatments and unnecessary invasive procedures, which can be avoided with proper diagnosis; hence, it is vital to recognize this condition (2). We report the case of a patient with Rheumatoid Arthritis (RA) and prolonged febrile syndrome who developed multiple abscesses in soft tissues and muscles without any microbiological isolation.

CLINICAL CASE

A 56-year-old male with a history of RA (positive rheumatoid factor and anti-citrullinated protein antibodies, ACPA) and type 2 diabetes mellitus was under treatment with leflunomide 20 mg daily, methotrexate 15 mg weekly, prednisolone 5 mg/day, insulin glargine 30 IU/day, and metformin 850 mg/day. The patient sought medical attention due to a four-month history of fever and a weight loss of 20 kg. He had been hospitalized in another facility for one month, until five days prior to admission to our department. During that hospitalization, a left psoas abscess was documented and drained twice (purulent material with negative cultures for aerobes, mycobacteria, and fungi). He was treated with cefepime 1 g IV every 8 hours and metronidazole 500 mg IV every 8 hours for 28 days. He was discharged to continue outpatient antibiotic therapy, but persistent febrile episodes were noted three weeks post-antibiotic therapy, prompting his return.

Upon admission, his vital signs were stable, but he appeared emaciated with mucocutaneous pallor. Additionally, he had bilateral axillary lymphadenopathy and inflammatory changes in multiple joints (right elbow, left knee, both wrists, and metacarpophalangeal joints of the second and third fingers of the left hand).

Laboratory tests on admission highlighted a leukocyte count of 13,130 cells/mm^3 due to neutrophils, normocytic and normochromic anemia, C-reactive protein (CRP) of 25 mg/dL, and an erythrocyte sedimentation rate of 68 mm/hour. Blood cultures, urine cultures, rapid plasma reagin (RPR), fluorescent treponemal antibody absorption (FTA-ABS), and tests for HIV and hepatitis B and C viruses were negative. A contrast-enhanced computed tomography (CT) scan of the abdomen revealed a hypodense image measuring 10.5 x 6.4 mm in the left psoas consistent with a residual collection. Given the suspicion of an active infectious process, prednisolone was prescribed at 10 mg orally daily, and both methotrexate and leflunomide were discontinued. From the time of admission, the patient was not on any antimicrobial medications. Figure 1 illustrates the chronological sequence of significant events during the hospital stay. Figure 2 plots the evolution of CRP levels and the glucocorticoid doses administered to the patient. Table 1 lists the relevant laboratory findings and their progression during hospitalization, while Table 2 provides the microbiological studies.

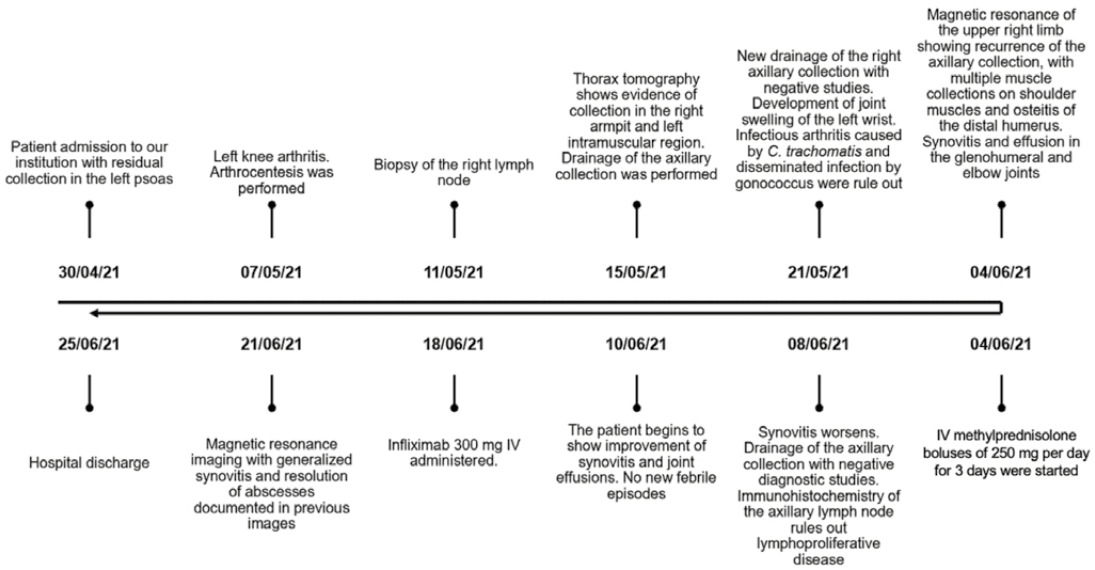

Figure 1. Significant events during hospitalization

Source: Own elaboration

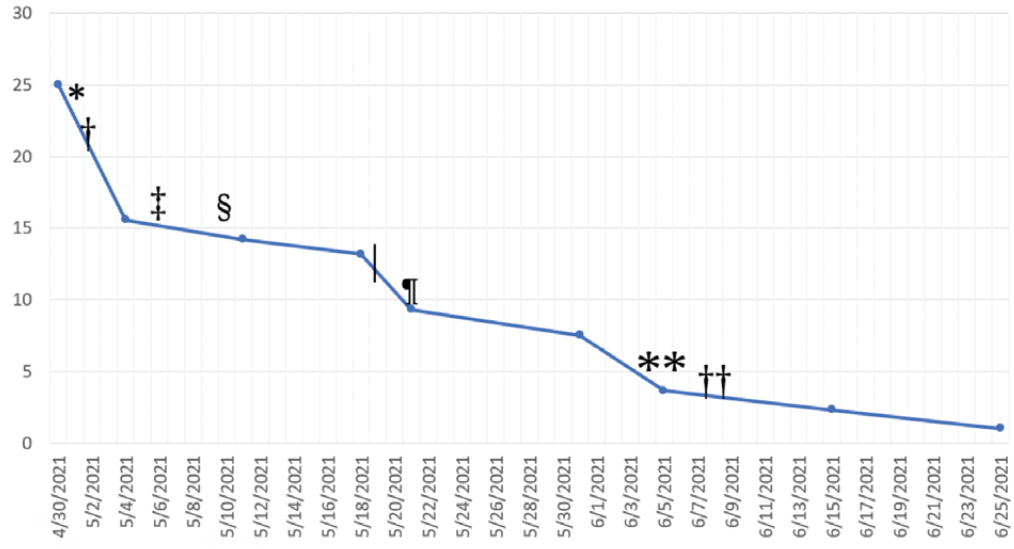

Figure 2. C-reactive protein (CRP) and glucocorticoid dose (in prednisolone equivalence) during hospital stay.

X-axis: date, Y-axis: C-reactive Protein concentration (mg/dL). Equivalent prednisolone doses: * 10 mg, † 25 mg, ‡ 15 mg, § 20 mg, | 30 mg, ¶ 40 mg, ** 312,5 mg (methylprednisolone pulses: 250 mg IV/day for 3 days), †† 50 mg.

Source: Own elaboration

Table 1. Laboratory tests during hospitalization

Test/ Date	30/04/21	04/05/21	18/05/21	21/04/21	31/05/21	05/06/21	19/06/21	25/06/21	Reference value
Hemoglobin (g/dL)	10,7	8,4	8,6	7,9	9,7	9,8	11,3		13 - 18
Leukocytes (cells/mm^3)	13130	7720	13740	14290	11980	13310	10240		4500 - 11000
Neutrophils (cells/mm^3)	10510	4910	10450	10320	8580	11540	8320		2000 - 7500
Platelets (cells/mm^3)	458000	410000	584000	591000	552000	482000	438000		140000 – 400000
C-reactive protein (mg/dL)	25	15.56	13.18	9.3	7.5	3.63	2.31	1.02	0 - 5
Sedimentation rate (mm/hour)	53	68					48		0 - 20
Ferritin (ng/mL)		9005			747.1			699.1	30 - 400

Source: Own elaboration

Table 2. Microbiological studies

Procedure (date)	Sample	Test	Result
Blood culture (30/04/21)	Blood	Bacterial culture	Negative
Urine culture (30/04/21)	Urine	Bacterial culture	Negative
Arthrocentesis of left knee (07/05/21)	Synovial fluid	Gram	Without bacteria
		Aerobic culture	Negative
		Molecular test for *M. tuberculosis*	Non detectable
		M. tuberculosis culture	Negative
Biopsy of right axillar lymphatic node (11/05/21)	Lymph node	Gram	Without bacteria
		KOH	Without fungi
		Bacilloscopy	Negative
		Molecular test for *M. tuberculosis*	Non detectable
		Aerobic culture	Negative
		Fungal culture	Negative
		M. tuberculosis culture	Negative
Percutaneous drainage of right axillary collection (15/05/21)	Secretion	Gram	Without bacteria
		KOH	Without fungi
		Bacilloscopy	Negative
		Molecular test for *M. tuberculosis*	Non detectable
		Aerobic culture	Negative
		Fungal culture	Negative
Percutaneous drainage of right axillary collection (21/05/21)	Secretion	Gram	Without bacteria
		Aerobic culture	Negative
Percutaneous drainage of right axillary collection (08/06/21)	Secretion	Gram	Without bacteria
		KOH	Without fungi
		Bacilloscopy	Negative
		Molecular test for *M. tuberculosis*	No detectable
		Aerobic culture	Negative
		Fungal culture	Negative
		M. tuberculosis culture	Negative

Source: Own elaboration

The patient's fever remained, furthermore, the inflammation of the left knee worsened, so an arthrocentesis was performed, from which a cloudy, non-viscous fluid was obtained with 17,760 leukocytes (91% neutrophils). Microbiological studies were conducted on the fluid, yielding negative results. An excisional biopsy of the axillary lymph nodes was performed and sent for histopathological and microbiological examinations, both of which returned negative. Among the differential diagnoses, there was a consideration that the patient might have a lymphoproliferative syndrome. However, this was ruled out with histopathological and immunohistochemical studies of the axillary lymph nodes and flow cytometry.

The patient developed inflammatory changes on the right dorsal side, leading to a CT scan of the chest. This revealed a 75 x 75 mm collection in the right axilla and a 22 mm intramuscular collection behind the left scapula (Figure 3). The axillary collection was percutaneously drained, yielding 25 mL of seropurulent material. Various microbiological tests were conducted on this material, including Gram stain, KOH, bacilloscopy, aerobic culture, fungal culture, and the GeneXpert molecular test for *Mycobacterium tuberculosis*. All these tests were negative. Subsequently, the patient showed worsening synovitis of the wrist, flexor tenosynovitis in both wrists, and persistent knee arthritis despite adjustments made to the glucocorticoid doses. Because the patient presented with additive polyarthritis, the following differential diagnoses were considered: infectious endocarditis, reactive arthritis due to *Chlamydia trachomatis,* and disseminated gonococcal infection. A transesophageal echocardiogram and a polymerase chain reaction for sexually transmitted pathogens were performed, ruling out the aforementioned diagnoses. The glucocorticoid dose was increased, and the CRP decreased by approximately 50% (Figure 2). The patient developed progressive swelling of the right upper limb, prompting an angio-CT scan. The scan showed the persistent collections in the right axilla in close proximity to vascular structures but without compression and no associated thrombosis. The patient underwent another percutaneous drainage of the collections, yielding 65 mL of citrine fluid with negative microbiological tests. During the drainage, a collection was observed anterior to the distal humerus with an apparent periosteal involvement, prompting a magnetic resonance imaging (MRI) to rule out osteomyelitis. After the second drainage and adjustment of the glucocorticoid dose, the fever subsided.

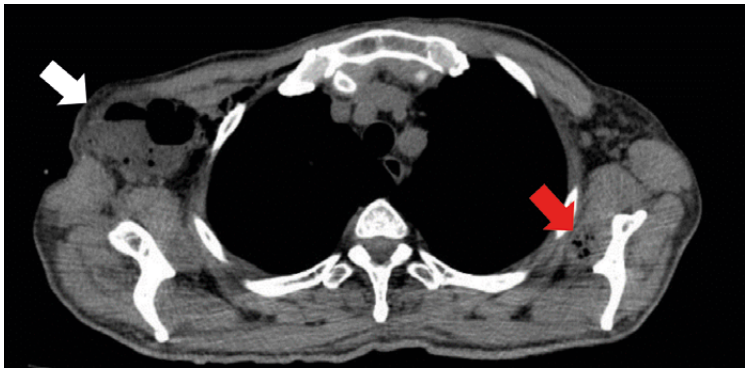

Figure 3. Contrast-enhanced chest CT scan.

Right axillary collection measuring 75 x 75 mm, with internal bubbles and air extending to the soft tissues of the anterior chest wall (white arrow). Left intramuscular collection posterior to the scapula with internal air measuring 22 mm (red arrow).
Source: Own elaboration

The magnetic resonance imaging (MRI) of the right upper limb revealed an osteitis zone in the distal humerus without osteomyelitis along with multiple collections in the rotator cuff muscles and the known axillary collection. The orthopedics department did not consider performing surgical drainage; instead, they requested percutaneous drainage of the axillary collection. Having reasonably ruled out both infectious and lymphoproliferative causes, combined with the presence of recurrent abscesses, AAS was considered. As a result, pulses of methylprednisolone were ordered (250 mg IV daily for 3 days due to hypoalbuminemia), and treatment with prednisolone continued at 1 mg/kg/day. On 06/08/21, the last percutaneous drainage of the right axillary collection was performed with negative microbiological studies. From 06/10/21, improvement in arthralgias and arthritis began to be noticed, the swelling of the RUL decreased, and the acute phase reactants (APR) normalized. A total body MRI was performed to rule out hidden abscesses, none were found, and a colonoscopy, which did not show findings suggestive of IBD, was performed. Due to the presence of active rheumatoid arthritis, despite receiving leflunomide, methotrexate, and glucocorticoids, and the diagnosis of AAS, treatment with infliximab was initiated at a dose of 300 mg IV, with good tolerance by the patient and without adverse effects.

After this, the swelling of the RUL completely improved, and the joint involvement significantly decreased. The total body MRI showed synovitis in the shoulders, wrists, and hips; but these did not present abscesses or collections, so it was decided to discharge the patient from the hospital with management using corticosteroids and infliximab.

DISCUSSION

AAS is characterized by neutrophilic and sterile infiltration with a granulomatous reaction in different organs (1–3). Less than 100 cases have been reported in the literature (4), mainly in Europe, although there are reports in Asia and America (1,2,5). This condition is primarily associated with Inflammatory Bowel Disease (IBD) (in 66% of cases), but it is also associated with neutrophilic dermatoses, relapsing polychondritis, monoclonal gammopathy of uncertain significance, and myelodysplastic syndromes (1,5-6). There are two reported cases of AAS associated with rheumatoid arthritis (7-8), one of them with concomitant disease activity (8), which is similar to the presented case.

Patients exhibit fever (which may precede the abscesses), weight loss, diaphoresis, myalgia, and arthralgias. They may experience arthritis; skin involvement in the form of abscesses or lesions compatible with neutrophilic dermatoses (like pyoderma gangrenosum or Sweet's syndrome), ulcers, hepatosplenomegaly, or lymphadenopathy. In paraclinical examinations, leukocytosis, and elevated acute phase reactants (APR) will be found. The spleen is the most affected site, but collections can affect any tissue (liver, lungs, kidneys, pancreas, testicles, lymph nodes, brain, pharynx, and muscle) (1,3,9-10). Regarding the symptoms related to this disease, the patient had abscesses in different muscular planes and soft tissues, which did not resolve despite antibiotic therapy. Also supporting the diagnosis was the fact that no microbiological isolation was achieved despite multiple studies of the abscesses, and the patient had a constitutional syndrome with elevated APR. Additionally, the patient improved after intensifying the immunosuppressive regimen. While the synovitis the patient had could correspond to RA activity, AAS could have been the trigger for the activity and contributed to the worsening of symptoms.

AAS should be suspected in patients with deep abscesses, in whom an infectious cause cannot be demonstrated despite exhaustive studies (1). It is a diagnosis of exclusion, and while there are no diagnostic criteria, André et al. (1) recommend the inclusion criteria used in the French registry. To the criteria mentioned, the response to treatments other than glucocorticoids is added for diagnosis (Table 3). Due to the association between AAS and IBD, a colonoscopy is recommended as a screening test (3).

Table 3. Proposed Diagnostic Criteria for AAS *

Deep Abscesses on Imaging Studies: Predominantly neutrophilic when aspiration or biopsy is performed.
Negative Diagnostic Tests: Negative blood cultures, negative serologies, and, when punctures or biopsies are carried out, negative microbiological studies.
Therapeutic Failure with Antibiotics: When prescribed for at least 2 weeks for conventional therapy and 3 months for antituberculous therapy.
Rapid Clinical Improvement After Glucocorticoid Prescription: Quick clinical improvement the day after prescribing glucocorticoids (at least 0.5 mg/kg/day), followed by radiological improvement after one month. A similar response with colchicine, anti-TNFα, and anti-IL-1 may also be considered.

*All criteria must be met
Source: Adapted form references (1, 11)

The majority of patients respond quickly to glucocorticoids. However, approximately 66% experience relapses when tapering off (1-2,11); therefore, adjuvant drugs are required for maintenance (12). Among the drugs used as adjuvants are azathioprine, colchicine, cyclophosphamide, cyclosporine, methotrexate, mycophenolate mofetil, and dapsone. However, the optimal maintenance therapy remains unknown (1,4). In refractory cases or those with frequent relapses, biological therapy with anti-TNFα (infliximab, adalimumab, and etanercept), anti-IL-1 (anakinra and canakinumab), and anti-IL-6 (tocilizumab) has been used, achieving a complete response (4-5,9,11). In patients receiving azathioprine, adalimumab, or infliximab as maintenance therapy, no relapses have been reported (12). Splenectomy has been utilized due to the frequent involvement of the spleen, but its use has become less common nowadays (1,13). Despite frequent relapses, the prognosis is good, with no reported fatal cases to date (1-2).

CONCLUSIONS

AAS is a diagnosis of exclusion that should be considered in patients presenting abscesses and where an infectious etiology cannot be demonstrated despite thorough investigation. Even though it is mostly associated with IBD, it can occur in other inflammatory diseases. To the best of our knowledge, this is the first reported case of AAS in Colombia in a disease other than IBD.

ETHICAL CONSIDERATIONS

Written informed consent was obtained from the patient for the publication of this case report, and it was approved by the ethics committee of the institution where the care was provided.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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