



Letters to the Editor

False Negatives of Synovial Fluid in Septic Arthritis*



Falsos negativos del líquido sinovial en la artritis séptica

To the Editor,

The analysis of the synovial fluid (SF) is a fundamental tool in the study of monoarthritis, as it reflects changes in the synovial membrane and underlying articular cartilage. The findings in the SF are essential in infectious and crystal arthritis.^{1,2}

To date, SF culture continues to be the gold standard for the microbiological diagnosis of septic arthritis.^{3,4} The pathogen most frequently isolated in septic joint processes is *Staphylococcus aureus* (50%–60%), followed by streptococci, found in up to 20% of the cases. Gram-negative bacilli are the cause in only 5%–10% of the cases of septic arthritis.⁵

We report the case of a patient who experienced an episode of septic arthritis in which the SF study showed no evidence of inflammation.

The patient was a 49-year-old man with no toxic habits. He had a history of untreated Rendu–Osler–Weber disease. He presented with monoarthritis in the left knee that had developed several days earlier, without fever or any other accompanying symptoms.

On physical examination, he was afebrile. The only significant finding was joint effusion with functional impairment and inflammation in left knee. He underwent arthrocentesis, which yielded 10 mL of SF with inflammatory features: 12,500 leukocytes/mm³, predominance of polymorphonuclear cells (95%) and glucose level of 82 mg/dL. No crystals were observed in a microscopic study. Gram stain was negative. Laboratory tests revealed no evidence of leukocytosis (6100×10^9 leukocytes, 62% neutrophils and 27% lymphocytes), but showed elevated acute phase reactants (C-reactive protein 1.4 mg/dL; fibrinogen: 600 mg/dL). The study was completed with radiographies of the knees, which revealed conserved alignment and mineralization, and no periosteal reaction or erosions. While waiting for the results of the microbiological study, we started treatment with nonsteroidal anti-inflammatory drugs (NSAID). Five days after this episode, he presented with more intense pain, without fever or any other symptoms. The physical examination revealed joint effusion and inflammation in left knee, with no other significant changes. Arthrocentesis was repeated, and yielded 38 mL of SF with no inflammatory features: 1960 leukocytes/mm³, 35% polymorphonuclear cells and glucose level of 84 mg/dL. However, methicillin-sensitive *Staphylococcus aureus* was identified in 2 separate SF cultures. Urine sediment was normal and blood and urine cultures were negative. The study

was completed with bone scintigraphy and labeled white blood cell scan—both of which were positive for septic arthritis—and chest radiography and echocardiography, which ruled out lung and cardiac involvement. Laboratory tests revealed positivity for HLA-B27. Antibiotic therapy was begun with ceftriaxone 2 g every 24 h and cloxacillin 2 g every 6 h. Emergency surgical joint lavage with saline solution was carried out. Subsequent cultures were negative. No cancer cells were found in the pathological study. The patient remained in the hospital until he had completed a 15-day intravenous treatment. He experienced clinical improvement, remission of the infectious process and recovery of knee function.

Although the study of the SF is fundamental and of great help in monoarthritis, in certain specific situations (immunosuppression, previous antibiotic use, and chronic or very acute conditions), the results do not clearly reveal what is taking place at the level of the joints. Thus, the microbiological study continues to be the gold standard for the diagnosis of septic arthritis.^{3,4} In these situations, tests like bone scintigraphy or positron emission tomography (PET) lend great support to the diagnosis. Moreover, we found that the Gram stain currently used for SF is of no value in the diagnosis of septic arthritis, as the rate of false negatives ranges from 25% to 50%, according to the literature,^{6,7} and was as high as 78% in a retrospective study conducted by the Manchester Royal Infirmary.⁸ This makes the technique a tool of little use when the clinical picture constitutes an orthopedic emergency with significant morbidity and a mortality of up to 11%.^{3,4,9} Investigation is underway to find alternative diagnostic techniques, such as the use of lithium heparin containers for SF sample collection to prevent coagulation. These modifications are being assessed in order to quantify the extent to which they will reduce false negatives with Gram staining in SF.^{7–10}

Finally, we can conclude that early diagnosis is essential to limit the morbidity and mortality. A delay in the treatment of septic arthritis can lead to the rapid destruction of the articular cartilage.^{3–8} Thus, given the high rate of false negatives with Gram staining, it is necessary either to improve the diagnostic techniques or dissociate SF from the process taking place at the level of the joint.

References

1. SemFYC. Aparato locomotor: exploraciones complementarias en Atención Primaria. Barcelona: Sociedad Española de Medicina de Familia y Comunitaria; 2007. Available from: <http://www.semfyce.es> [accessed 30.11.14].
2. Freire González M. Pruebas de laboratorio en Reumatología. Guía fisterra. Available from: <http://www.fisterraocom> [accessed 04.05.12].
3. Coakley G, Mathew C, Field M, Jones A, Kingsley G, Walker D, et al., British Society for Rheumatology Standards, Guidelines and Audit Working Group. BSR & BHP, BOA, RCGP and BSAC guidelines for management of the hot swollen joint adults. *Rheumatology (Oxford)*. 2006;45:1039–41.
4. Kaandorp CJ, Krijnen P, Moens HJ, Habbema JD, van Schaardenburg D. The outcome of bacterial arthritis a prospective community-based study. *Arthritis Rheum*. 1997;40:884–91.
5. Carpenter CR, Schuur ID, Everett WW, Pines JM. Evidence-based diagnosis: adult septic arthritis. *Acad Emerg Med*. 2011;18:781–96.

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6. Shemerling RH. Synovial fluid analysis. A critical reappraisal. *Rheum Dis Clin North Am.* 1994;20:503–12.
7. Goldenberg DL. Septic arthritis. *Lancet.* 1998;351:197–202.
8. Stirding P, Faroung R, Amanat S, Ahmed A, Armstrong M, Sharma P, et al. False negative rate of Gram-stain microscopy for diagnosis of septic arthritis: Suggestions for improvement. *Int J Microbiol.* 2014;2014. Article ID 830857.
9. Vostrel P, Legout L, Hoffmeyer P. Septic arthritis (non-gonococcal) of the adult: practical aspects. *Rev Med Suisse.* 2006;2:2924–30.
10. Denton J. Synovial fluid analysis in the diagnosis of joint disease. *Diagn Histopathol.* 2012;18:159–68.

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Allergic Contact Dermatitis in Medical Professionals Due to Exposure to Ultrasound Gel*



Dermatitis alérgica de contacto en profesionales médicos por exposición a gel ecográfico

To the Editor,

There are numerous publications describing the development of allergic contact dermatitis caused by the presence of isothiazolinone, a preservative used in household cleaning and personal care products, as well as in materials for industrial use, such as paint and varnish.

Isothiazolinones are found in those products as a mixture of methylchloroisothiazolinone and methylisothiazolinone in a proportion of 3:1 (a compound known commercially as Kathon CG). They are heterocyclic organic components with powerful antibacterial and antifungal activities. However, they interact with epidermal proteins, and can induce allergic sensitivity. In Europe, they are the second most common cause of allergic dermatitis secondary to preservatives, preceded only by formaldehyde releasers; they have even been considered responsible for an “authentic allergy epidemic” because of their widespread presence in the market.¹

Isothiazolinones are used as preservatives in ultrasound gels, and there are publications dealing with patients who have developed allergic contact dermatitis, in most cases after undergoing gynecological ultrasound or other procedures that involve the use of these gels.^{2,3} However, there are few reports in the literature describing allergic contact dermatitis caused by ultrasound gels in health care professionals who carry out ultrasound studies.^{4,5}

We present the case of a 28-year-old man, a rheumatologist with no history of allergies, who has worked for the last 10 years in a rheumatology department where he performed musculoskeletal ultrasound, without gloves, on a regular basis, using the ultrasound gel Mebaline® (Esteer PHARMA GmbH, Reilingen, Germany). The patient reported the appearance of pruritic, eczematous lesions on the outer side of the pads of the 4th and 5th fingers and in the middle segment of the 3rd finger of his dominant hand (Fig. 1). Erythema with a few vesicles and scaling were observed and painful fissures appeared that developed into skin atrophy over a 2-month period. The lesions did not improve with the application of moisturizing cream or intermediate-potency topical corticosteroids.

The composition of the ultrasound gel used was glycerin, carbomer, sodium hydroxide, propylene glycol, methylisothiazolinone, iodopropynyl, butylcarbamate and sodium chloride. As

dermatitis secondary to prolonged contact with the ultrasound gel was suspected (the lesions coincided with the areas of skin exposed to the gel during manipulation of the ultrasound transducer), patch tests were carried out for methylisothiazolinone and the ultrasound gel, with positive results for both substances (Fig. 2). The patient began to use latex gloves to avoid contact with the allergen and a moisturizer for his skin, and 3–4 weeks later, there was a marked improvement. In addition, the ultrasound gel was replaced by a hypoallergenic product.

Allergic contact dermatitis generally appears as a subacute or chronic eczema, especially on the hands and face (in the case of cosmetic use), and can sometimes mimic chronic irritant dermatitis. Logistic regression analyses have identified painters, blacksmiths, operators of industrial machinery and individuals whose profession involves the use of cosmetics as being at risk, especially those over the age of 40 years.² In the case we report here, the principal sensitizer was methylchloroisothiazolinone and the cause was prolonged exposure to this compound.

Allergic dermatitis produced by ultrasound gels is rare, and has mainly been associated with substances like propylene glycol, methyldibromo glutaronitrile, parabens, imidazolidinyl urea and isothiazolinones. The series published to date mention cases in which patients have undergone ultrasound examinations, but the medical literature makes no reference to health care professionals.

Informative message: any eczema located on the dominant hand in health care professionals who perform ultrasound examinations may be secondary to contact dermatitis caused by the ultrasound gel.



Fig. 1. Eczematous lesions with fissures in the skin on the outer side of the pads of the 3rd, 4th and 5th fingers of the dominant hand. Erythema with a few vesicles, scaling and painful fissures in the skin are observed.

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