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Case Report

Pseudoseptic arthritis as a complication of intra-articular infiltration of hyaluronic acid in a patient with rheumatoid arthritis



Chafik Chacur,* Anastasia Mocritcaia, Raimon Sanmartí

Servicio de Reumatología, Hospital Clínic, Barcelona, Spain

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ABSTRACT

Pseudoseptic arthritis is a rare complication of hyaluronic acid (HA) injections that often is difficult to differentiate from septic arthritis. Patients present acute pain, swelling and joint effusion normally around 24 h after the second or third HA infiltration. We describe a female patient with seropositive rheumatoid arthritis and flare-ups of knee arthritis with pseudoseptic features in the past, who develops pseudoseptic arthritis of the knee following her first injection of hyaluronic acid.

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Artritis pseudoséptica como complicación de infiltración intraarticular de ácido hialurónico en una paciente con artritis reumatoide

RESUMEN

La artritis pseudoséptica es una complicación infrecuente de las inyecciones intraarticulares de ácido hialurónico (AH), que puede ser difícil de diferenciar de la artritis séptica. Los pacientes presentan dolor agudo y derrame articular, alrededor de 24 horas después de la segunda o tercera infiltración de AH. Presentamos el caso de una paciente con artritis reumatoide seropositiva y brotes previos de artritis pseudosépticas de rodilla, que ha desarrollado una artritis de rodilla de características similares después de su primera inyección de ácido hialurónico.

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Palabras clave:

Artritis pseudoséptica

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Artritis reumatoide

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Introduction

Intra-articular injections of hyaluronic acid (HA) are a common treatment for patients with osteoarthritis of the knee which, in exceptional cases, can be complicated by pseudoseptic arthritis. We present a patient diagnosed with rheumatoid arthritis (RA) and secondary osteoarthritis in the knees, with a previous history of pseudoseptic arthritis, who developed acute pseudoseptic monoarthritis after HA infiltration.

Case report

We present the case of a 77-year-old woman diagnosed with seropositive and erosive RA, with high titres of rheumatoid factor (2,730 U/mL) and anti-CCP antibodies (>1,600 U/mL), with 27 years of evolution and a history of 4 outbreaks of pseudoseptic arthritis in both knees (leukocyte counts in synovial fluid between 25,400 and 160,000 leukocytes/mm³). At the time of examination, she was in remission, continuing treatment with etanercept (50 mg/week), methotrexate (15 mg/week), and methylprednisolone (4 mg/day). In addition, she suffered from osteoarthritis in her right knee. As a result of controls at another healthcare centre she received intra-articular infiltration of HA (Proyal 60 H).

After 24 h, the patient presented with severe pain in the infiltrated knee and significant functional impotence. The examination showed knee arthritis with marked inflammatory signs and joint

* Corresponding author.

E-mail address: Chacur10@hotmail.com (C. Chacur).

Table 1
Comparison between the characteristics of our patient and the patients from a systematic review.

	Case report	Systematic review (Sedrak et al.) (n = 27 patients/28 knees)
Gender	Woman	Women (23/27; 85.2%)
Age (years)	77	60,8 (31–79)
Time to symptomatology (h)	24	<24 h (22/28; 78,6%) <12 h (15/28; 53,5%)
Affected joint	Knee	Range: 1 h–9 days Knee (28/28; 100%)
Number of injections received (before developing arthritis)	1 Infiltration	1 infiltration: 3/28 (10.7%) 2 infiltrations: 7/28 (25%) 3 infiltrations: 5/28 (17.9%) 4 or more injections: 13/28 (46.4%)
Leukocytes in peripheral blood	8.250	11,116.7 (range 9,200–16,000; 6 patients)
CRP (mg/dl)	3,11	9.26 (range 0.6–28.2; 7 patients)
ESR (mm/h)	57	72.5 (range 12–112; 7 patients)
Synovial fluid analysis		
Leukocytes/mm ³	22.700	24,430.2 (range 2,115–103,000; 26 patients)
Neutrophils (%)	76%	59.0 (range 13–87; 23 patients)
Microcrystals	Absent	Absent (24/24; 100%)
Cultures	Negative	Negative (27/27; 100%)

effusion. In the laboratory analysis, the elevation of inflammatory parameters was notable. Arthrocentesis was performed with inflammatory fluid (22,700 leukocytes/mm³) (Table 1); no microcrystals were visualized and Gram stain and culture were negative. The affected knee was infiltrated with glucocorticoids, with significant improvement in the following 48 h and no symptoms throughout the follow-up.

Discussion

Intra-articular HA is commonly used for the management of knee osteoarthritis. Side effects are usually mild, including pain after infiltration. The development of arthritis is rare, although cases of microcrystalline and septic arthritis have been described.¹ Pseudo-septic arthritis is an exceptional complication that usually develops after the second or third infiltration, after sensitisation to the inoculated agent.² The pathophysiology could be related to a cell-mediated hypersensitivity reaction, with secondary activation of the complement.³

In a systematic review that included 27 patients with gonarthrosis, mostly women, with 28 cases of HA-induced pseudo-septic arthritis,⁴ joint pain and effusion had occurred in the majority of cases (80%) 24 h after injection.⁴ Arthritis was observed in 3 cases (10.7%) after the first infiltration.^{5–7} The analysis of the synovial fluid showed inflammatory characteristics, with some counts over 50,000 leukocytes/mm³ and negative cultures (Table 1).⁴

Our patient developed acute knee monoarthritis 24 h after infiltration. The characteristics of the synovial fluid, together with the absence of microcrystals; the negativity of the cultures; and the favourable outcome after glucocorticoid infiltration, indicated HA-induced pseudo-septic arthritis. The product used in this case

(Proyal 60 H) consists of a high molecular weight HA (2.5–3.5 million daltons) obtained from the biofermentation of *Streptococcus equi* bacteria, which is characterised by high viscoelasticity. On this point, it has been pointed out that products made from this technique have a better safety profile than those derived from avian materials.⁸

Pseudo-septic arthritis has been exceptionally described in patients with RA, even in the context of anti-TNF treatment, in a similar way to our patient.⁵ The reason for HA infiltration was the presence of symptomatic osteoarthritis, which was administered during a period of RA remission. Few studies have analysed the effectiveness and adverse effects of HA in patients with RA and osteoarthritis.⁹ Among these, a Chinese study shows beneficial results with no relevant adverse effects.¹⁰ Our patient, however, had previously presented episodes of pseudo-septic arthritis in both knees, with no identifiable cause other than her underlying disease. It could therefore be hypothesised that there is a greater predisposition towards this complication, in addition to the fact that this treatment should be indicated with caution in analogous cases.

Conclusions

Pseudo-septic arthritis is an uncommon complication of HA infiltration. The present case demonstrates the need for an adequate characterisation of the patients selected for its use, since the presence of underlying inflammatory diseases and previous episodes of pseudo-septic arthritis could increase the risk of this complication.

Informed consent

Informed consent was obtained from the patient.

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Conflict of interest

The authors have no conflicts of interest to declare for this study.

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