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## What Is the Outcome of Undifferentiated Arthritis?<sup>☆</sup>



### ¿Cuál es la evolución de las artritis indiferenciadas?

To the Editor:

The use of a coding system in rheumatology improves the performance and quality of patient care. In the rheumatology department of our hospital, which has a reference area of 850 000 inhabitants, coding is carried out since 1984. Several rheumatologists prospectively collect, at 6 months of the first visit, filiation and diagnosis of patients seen in the clinic, patients admitted to hospital beds and admitted to other services that request an interconsultation. The nomenclature of the American College of Rheumatology (ACR) of 1983<sup>2</sup> was used and suitably modified to include a section of *undiagnosed arthritis* where mono, oligo and polyarthritis without an identified cause<sup>1</sup> are included. Between 2006 and 2011 13,767 first consultations were carried out and 154 patients with *undiagnosed arthritis* (1.12%) were classified. They retrospectively reviewed the medical records of these patients and the location of arthritis, follow up and final diagnosis reached up until December 2013 were collected, with an elapsed minimum 2½ years since the first visit (range 2.5–5 years). The distribution of arthritis was: 36 (23.3%) monoarticular, 71 (46.1%) oligoarticular and 47 (30.5%) polyarticular. Monoarticular forms affected the following joints: in 21 cases (58.3%) knee; 4 (11.1%) metatarsophalangeal; 3 (8.3%)

proximal interphalangeal; 2 (5.5%) tibioperoneoastragalus; 2 (5.5%) carpus; 2 (5.5%) metacarpophalangeal; 1 (2.7%) tarsus, and 1 (2.7%) elbow. The evolution of arthritis is summarized in Table 1.

It is noteworthy that of the 36 patients with monoarthritis, 4 evolved to seronegative oligo or polyarthritis and 3 oligoarthritis patients progressed to undifferentiated polyarthritis, also undifferentiated.

We conclude that undifferentiated arthritis may progress to a classifiable inflammatory disease, self-limit or persist undifferentiated, representing a challenge for the rheumatologist.<sup>3–5</sup> The percentage of spontaneous resolution in our series of cases is 44.4%, 9.8% and 14.9% for mono, oligo and polyarthritis, respectively. The former are more inclined to resolve spontaneously, whereas oligoarticular and polyarticular onset forms are more likely to become chronic. In the present series an established diagnosis was reached in 57 patients (65%) after an average of 8 months; mostly had an oligoarticular origin (65%). 11 patients (19%) were diagnosed with spondyloarthritis, whose onset was characterized as mono or oligoarticular; conversely, the 9 patients (16%) with a subsequent diagnosis of rheumatoid arthritis (RA) had an oligo or polyarticular onset. In addition, 10 patients (17.5%) were diagnosed with microcrystalline arthritis with a mono, oligo or polyarticular onset.

Most undiagnosed polyarthritis in the first 6 months, continued without cause after follow up. Interestingly, the percentage of

Table 1

	Undifferentiated arthritis n = 154		
	Monoarticular 36 (23.3%)	Oligoarticular 71 (46.1%)	Polyarticular 47 (30.5%)
<b>Evolution</b>			
Undifferentiated	9	27	31
67 (43.5%)	5 follow controls	16 follow controls	11 follow controls
	4 do not follow controls	11 do not follow controls	20 do not follow controls
self-limited	16	7	7
30 (19.5%)			
Diagnosis established	11	37	9
57 (65%)	3 spondyloarthritis	8 spondyloarthritis	2 rheumatoid arthritis
	2 microcrystalline	7 rheumatoid arthritis	2 microcrystalline
	2 juvenile idiopathic arthritis	6 microcrystalline	Lupus
	4 others <sup>a</sup>	3 palindromic rheumatism	1 palindromic rheumatism
		2 sarcoidosis	Psoriatic arthritis
		Still's disease	Two others <sup>c</sup>
		Lupus	
		9 others <sup>b</sup>	

<sup>a</sup> Arborescent lipoma, undifferentiated granulomatous synovitis and mechanical causes.

<sup>b</sup> Paraneoplastic, TBC, reflex sympathetic dystrophy, SAPHO syndrome, vasculitis and osteoarthritis.

<sup>c</sup> Polymyalgia rheumatic and osteoarthritis.

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patients who remain in follow-up is higher in classifiable than in undifferentiated arthritis (66.6 versus 32.9%).

Based on this, we can conclude that due to changes in the evolution of inflammatory joint diseases, rheumatology coding systems should be dynamic.<sup>1</sup> In general, the ACR classification criteria for different rheumatic diseases have little discriminatory value in the initial stages of the disease, so must be modified so that they allow us to distinguish these forms of early arthritis.<sup>3,6</sup> These criteria should be able to classify cases that will remain as undifferentiated arthritis, in which it has been shown that early treatment is paramount, even when not meeting established disease criteria.<sup>7,8</sup> In practice, the new criteria for RA and spondyloarthritis already been developed in this light.<sup>9,10</sup>

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## Parvovirus B19 chronic monoarthritis in a patient with common variable immunodeficiency<sup>☆</sup>



### *Monoartritis crónica por parovirus B19 en un paciente con inmunodeficiencia común variable*

Sir,

Human parvovirus B19 infection is mainly associated with erythema infectiosum or fifth disease in children and arthralgia/arthritis in healthy adults.

We describe the case of a patient who presented with chronic monoarthritis of the wrist due to parvovirus B19 and was found to have common variable immunodeficiency (CVID). A 48-year-old man was referred to the hospital because of right wrist monoarthritis lasting six months. Physical examination showed swelling of the right wrist not associated with erythema, warmth or skin lesions. Laboratory analyses showed a white blood cell count of 8300/mm<sup>3</sup> (91% granulocytes, 4% lymphocytes), an erythrocyte sedimentation rate (ESR) of 67 mm/h and a C-reactive protein (CRP) of 9.4 mg/l. Serum electrophoresis demonstrated hypogammaglobulinemia: 0.06 g/dl (IgG < 8.6 mg/dl, IgA < 7.8 mg/dl, IgM < 29.8 mg/dl). Rheumatoid factor and antinuclear antibodies were negative. Low values of C3 and C4 were found (64 mg/l and 1.5 mg/l, respectively). Serologic tests for *Borrelia burgdorferi*, hepatitis B and C, rubella and mumps virus, enterovirus, cytomegalovirus, Epstein Barr virus, human immunodeficiency virus and parvovirus B19 were negative. A bone gammagraphy showed marked fixation of the tracer in the right carpus, suggestive of arthritis. A magnetic resonance displayed

diffuse synovitis of the right distal radio-cubital joint, with no signs of necrosis or osteomyelitis. A synovial biopsy was performed; histopathological studies showed chronic nonspecific inflammatory changes and polymerase chain reaction (PCR) detected the presence of parvovirus B19 DNA in synovial tissue. PCR of parvovirus B19 DNA in blood was positive.

A diagnosis of parvovirus B19 monoarthritis in the setting of CVID was made, and prompt treatment with intravenous immunoglobulin (0.4 g/kg every 4 weeks) was administered with complete resolution of articular symptoms after the second infusion. Because of hypogammaglobulinemia, treatment with intravenous immunoglobulin was continued indefinitely. Human parvovirus B19 infection is detected in 3.3% of patients examined for acute reactive arthritis.<sup>1</sup> Joint symptoms usually resolve within two weeks; however, 0–17% of patients has chronic arthritis,<sup>2</sup> generally a symmetric polyarthritis that can resemble rheumatoid arthritis. Chronic monoarthritis is much less frequent. To our knowledge, five cases of parvovirus B19 chronic monoarthritis have been described: three children<sup>3,4</sup> and two adults.<sup>5</sup> Diagnosis of B19 infection in immunocompetent individuals is made by detection of B19 specific antibodies in blood. Caution should be made when interpreting serology for parvovirus B19 in immunodeficient patients and pregnant women because of their decreased capacity to mount an antibody response. In these patients, serology should be complemented by PCR analyses of B19 DNA.

In our patient, serologic tests for parvovirus B19 were negative and diagnosis was made by PCR of blood serum and synovial tissue. Even though the presence of parvovirus B19 DNA in synovial tissue does not allow a definite diagnosis, the absence of other causes and the rapid response to intravenous immunoglobulin, led us to assume the viral aetiology of the arthritis.<sup>6</sup>

CVID is a primary immune deficiency characterized by reduced levels of immunoglobulins of all classes despite normal numbers of circulating B cells. The deficiency in IgG production may lead to recurrent infections with encapsulated organisms, such as *Streptococcus pneumoniae* and *Haemophilus influenzae*,

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