

# Chondrocalcinosis and Hypomagnesemia: Clinical and Radiological Progression

José González Domínguez,<sup>a</sup> Alejandro Escudero Contreras,<sup>b</sup> Verónica Pérez Guijo,<sup>b</sup> Francisco Ginés Martínez Sánchez,<sup>b</sup> Miguel Ángel Caracuel Ruiz,<sup>b</sup> and Eduardo Collantes Estévez<sup>b</sup>

<sup>a</sup>Servicio de Reumatología, Hospital Clínico San Cecilio, Granada, Spain

<sup>b</sup>Sergicio de Reumatología, Hospital Universitario Reina Sofía, Córdoba, Spain

Hypomagnesemia is a rare secondary metabolic disorder associated with calcium pyrophosphate dihydrate crystal deposition disease in joint structures and may cause asymptomatic chondrocalcinosis (linear calcification of cartilage), pseudogout, and chronic arthropathy.

We report 2 young men with relapsing acute knee monoarthritis with chondrocalcinosis and hypomagnesemia. After follow-up clinical and radiological events at least for 5 years and treatment with magnesium lactate, these patients have not shown new pseudogout attacks. We discuss knee radiological evolution in both patients, outstanding major knee radiological deterioration in the patient with early symptoms and a familial chondrocalcinosis association, in spite of clinical asymptomatic status.

**Key words:** Chondrocalcinosis. Hypomagnesemia. Calcium pyrophosphate.

---

### Chondrocalcinosis e hipomagnesemia: evolución clinicorradiológica

Entre las causas secundarias infrecuentes de la enfermedad por depósitos de cristales de pirofosfato cálcico se incluye la hipomagnesemia.

Se presentan 2 casos de pacientes jóvenes con ataques repetidos de monoartritis en rodillas con chondrocalcinosis articular e hipomagnesemia. Tras seguimiento clinicorradiológico y tratamiento con lactato de magnesio

durante al menos 5 años, los pacientes no han presentado nuevos ataques de seudogota en rodillas. Se discute la evolución clinicorradiológica de las rodillas afectadas en ambos pacientes; destaca el mayor deterioro radiológico en sus rodillas del paciente con inicio más precoz y antecedentes familiares de chondrocalcinosis articular, a pesar de seguir clínicamente asintomático.

**Palabras clave:** Chondrocalcinosis. Hipomagnesemia. Pirofosfato cálcico.

---

### Introduction

Hypomagnesemia can be among the secondary causes of joint chondrocalcinosis (JCC),<sup>1-3</sup> which can be the cause of its pathogenesis.

Its early diagnosis is very important because, upon ionic correction of the hypomagnesemia,<sup>4</sup> clinical, and radiological progression of JCC can be avoided.

In the present study we describe the clinical and radiological progression of 2 young patients with repeated bouts of acute monoarthritis with JCC and hypomagnesemia.

### Clinical Cases

#### Case 1

A 40-year-old male patient presented his first episode of monoarthritis at 26 years of age on the right knee and afterward, until he was 35, was attended by our department and had presented 3 bouts of acute monoarthritis.

Upon visiting our outpatient clinic, the patient was treated for an episode of right knee monoarthritis and underwent arthrocentesis and received a steroid infiltration. Radiologically, he was diagnosed with JCC of both knees, mainly the right one, with a discreet impingement of the internal femorotibial joint line. No JCC was detected either on the wrist or the pubic symphysis.

---

Correspondence: Dr. J. González Domínguez.  
Servicio de Reumatología. Hospital Clínico San Cecilio.  
Avda. Dr. Oloriz, 16. 18012 Granada. España.  
E-mail: jose.gonzalez.dominguez.sspa@juntadeandalucia.es

Manuscript received June 5, 2006; accepted for publication October 23, 2006.

A complete analysis included: complete hemogram, erythrocyte sedimentation rate (ESR), CRP, blood chemistry (glucose, urea, creatinine, Na, K, Cl, Ca, P, AST, ALT, GGT, alkaline phosphatase, creatinase [CPK], lactate dehydrogenase [LDH], uricemia, total cholesterol, triglycerides), and all were normal, except cholesterol, 233 mg/dL (normal value, 220 mg/dL) and magnesemia, 1.4 mg/dL (normal value, >1.8 mg/dL). Urine test and sediment, also normal; T4 and thyrotropin (TSH), normal; parathyroid hormone, normal.

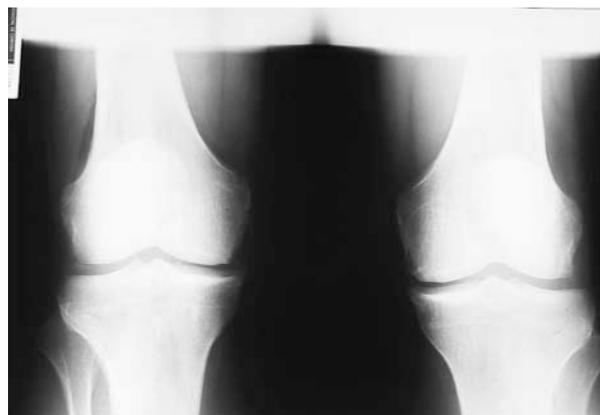
The patient was treated with non-steroidal antiinflammatory drugs (NSAID) (in the acute stage of the disease) and continuously with magnesium at a dose of 1 g/day (with an equivalence to 94.8 mg of Mg ion) and colchicine 0.6 mg/day for 1 year. After the start of treatment with magnesium, the patient has not had any more recurrences of acute monoarthritis; he is still asymptomatic although occasionally he has moderate pain on the knees. In posterior analytical controls the patient maintained magnesium levels between 1.7 and 1.8 mg/dL. On the knees, and after 5 years of disease, there was progression of the radiologic lesions (Figures 1 and 2). Additionally, an x-ray family study was carried out on the patients living first degree relatives: his mother, 2 sisters (35 and 32 years old, respectively), and a brother (27 years old), only detecting JCC in his mother.

## Case 2

A 43-year-old patient who was treated in our outpatient clinic at 39 years of age was sent by the emergency department due to acute monoarthritis of the right knee; in the previous 2 months he had presented 2 bouts of monoarthritis. Radiologically, his knees presented JCC in the femorotibial compartment of his right knee. There were no valuable signs in the pelvis x-ray and carpal bones. Complementary analysis included: a complete hemogram, ESR, CRP, blood chemistry (glucose, urea, creatinine, Na, K, Cl, Mg, Ca, P, AST, ALT, GGT, alkaline phosphatase, CPK, LDH, uricemia, total cholesterol, triglycerides) which were normal, except CRP, 10 (normal, 8); serum magnesium, 1.6 mg/dL (normal, >1.8 mg/dL). Rheumatoid factor was negative. Urine testing and sediment were normal. T4 and TSH, normals. Urinary calcium and phosphate were normal.

After 1 year of treatment with magnesium 1 g/day and colchicine 0.6 mg/day, the patient presented a relapse of arthritis of the elbows and the right wrist, with a serum magnesium level of 1.6 mg/dL. X-rays of the hands, feet, and elbows showed no valuable findings. The episode was resolved after a few days of anti-inflammatory treatment and did not present again.

During these years, the patient has received magnesium supplements with regularity and has been clinically asymptomatic. The radiological aspect of his knees has



**Figure 1.** Antero-posterior x-ray of the knees in which calcification of the joint cartilage can be seen.



**Figure 2.** Antero-posterior x-ray of the knees after a 5-year progression in which internal femoro-tibial joint impingement can be appreciated, as well as subchondral sclerosis, and marginal osteophytes which are better appreciated on the right knee. There is also an increase in intensity and extension of the cartilage and meniscal calcification of both knees, and a cystic image on the internal side of the upper third of the right tibia.

been unchanged but the calcified tissue has not disappeared (JCC) from the right knee. He has no other family members who are affected.

## Discussion

Hypomagnesemia has been associated to calcium pyrophosphate crystal deposit disease (CPPD), which is one of the secondary causes of JCC.<sup>1,4</sup> Magnesium is known to be one of the cofactors of many pyrophosphatases and there is a direct relationship between the solubility of the calcium pyrophosphate and the serum

concentration of Mg.<sup>5</sup> Hypomagnesemia can produce crystal deposition disease (CPPD) due to the pyrophosphates' enzymatic activity dependence on Mg ions. Precipitation of these CPPD crystals in the joint produces episodes of pseudogout<sup>4</sup> similar to the ones described in our patients.

Occasionally, chondrocalcinosis and hypomagnesemia have been associated to Bartters' syndrome (BS),<sup>6,8</sup> which is characterized by hypokalemia, metabolic alkalosis, hyperaldosteronism, and renal loss of chloride and potassium, indicating a defect in chloride reabsorption in the ascending segment of Henle's loop. CPPD deposit disease and hypomagnesemia have also been associated to a hereditary variant of hypocalciuric BS known as Gitelman's syndrome (GS)<sup>7-9</sup> and characterized by hypokalemia and hypomagnesemia of a renal origin next to hypocalciuria.<sup>8</sup>

Several causes for idiopathic familial and secondary JCC have been described.<sup>10</sup> The prevalence of the primary familial crystal CPPD deposit disease associated to endocrine or metabolic illnesses is unknown. A study carried out in Spain<sup>11</sup> revealed that an elevated proportion of sporadic cases of CPPD crystal deposit disease can have a familial origin. In most of the patients CPPD crystal deposit disease presents itself as an idiopathic or sporadic form, and there occasionally can be found a rare familial form associated to certain metabolic alterations among which hyperparathyroidism, hemochromatosis, hypophosphatemia, and hypomagnesemia can be included.<sup>12</sup> There are 2 clinical forms of CPPD crystal deposit disease. One of them is relatively benign, starts at an early age (patients are usually younger than 50 years old), and is characterized by polyarticular affection (knees, wrists, shoulders, elbows, and hips) with recurrent episodes of pseudogout and JCC, and scarce, or non-existent joint deformity. The second form of presentation is more destructive, starts later in life (patients are older than 50), and is manifested as oligoarthritis that can affect knees, wrists, shoulders, and hips, developing progressive and deforming arthrosis (chronic pyrophosphate arthropathy). We have described 2 cases of secondary chondrocalcinosis associated with hypomagnesemia in young patients who presented several bouts of acute monoarthritis of the knees and in whom a low level of magnesium was shown and whom, after treatment was started with magnesium supplementation, have not presented any new episodes of arthritis in their course over the past 4 years. In our patients, the values of Na, K, Cl, Ca, and P were normal, considering that the patients were not affected by either

BS or its variant (SG). It is important to mention that, in the first case described, a familial association was shown, with the patient's mother also presenting with chondrocalcinosis of the knees. In addition, the patient presented his first bout of monoarthritis at a young age, 26 years. In this patient, in spite of staying asymptomatic after the start of supplementation with magnesium, an unfavorable radiologic progression was seen on his knees.

This patient developed a degenerative arthropathy of the knees, in spite of early development of disease, in direct contrast with the second familial clinical form of JCC which starts later in life. These facts indicate that, in the patients with familial chondrocalcinosis and hypomagnesemia, joint deterioration is larger than in patients with idiopathic JCC and hypomagnesemia. In the patients with familial JCC, magnesium supplementation seems to limit the episodic nature of the bouts of arthritis, but do not stop the radiological deterioration. Due to all of this, we reiterate the convenience of a determination of serum ions that includes magnesium, especially in young patients with JCC and, if possible, the performance of a family study.

## References

1. Jones AC, Chuck AJ, Arie EA, Green DJ, Doherty M. Diseases associated with calcium pyrophosphate deposition disease. *Semin Arthritis Rheum.* 1992;22:188-92.
2. Zarco P, Jaller JJ, Rapado A, Herrero-Beaumont G, Traba ML, Grant C, et al. Estudios metabólicos en 2 casos de condrocalcinosis con hipomagnesemia. *Rev Clin Esp.* 1989;185:77-81.
3. Erickson AR, Yeun JY, Enzenauer GJ. Chronic calcium pyrophosphate crystal deposition disease arthropathy associated with hypomagnesemia. *J Clin Rheumatol.* 1997;3:51-4.
4. Pérez-Ruiz F, Testillano M, Gastaca MA, Herrero-Beites AM. "Pseudoseptic" Pseudogout associated with hypomagnesemia in liver transplant patients. *Transplantation.* 2001;71:696-8.
5. Smilde TJ, Haverman JF, Schipper P, Hermus AR, van Liebergen FJ, Jansen JL, et al. Familial hypokalemia/hypomagnesemia and chondrocalcinosis. *J Rheumatol.* 1994;21:1515-9.
6. Muñoz-Fernández S, Pantoja L, Martín-Mola E, Miguel E, Gijón Baños J. Chondrocalcinosis associated with Bartter's syndrome and hypomagnesemia. *J Rheumatol.* 1994;21:1782-3.
7. Gascón A, Cobeta-García JC, Iglesias E. Hypomagnesemia and chondrocalcinosis in Gitelman syndrome. *Am J Med.* 1999;107:301-2.
8. Calo L, Punzi L, Semplicini A. Hypomagnesemia and chondrocalcinosis in Bartter's and Gitelman's syndrome: review of the pathogenetic mechanisms. *Am J Nephrol.* 2000;20:347-50.
9. Hang-Korng EA, Blanchard A, Dougados M, Roux Ch. Chondrocalcinosis secondary to hypomagnesemia in Gitelman's syndrome. *J Rheumatol.* 2005;32:1840-2.
10. Maldonado I, Reginato AM, Reginato AJ. Familial calcium crystal diseases: what have we learned? *Curr Opin Rheumatol.* 2001;13:225-33.
11. Fernández-Dapica MP, Reginato AJ. Familial chondrocalcinosis in Spain. *Arthritis Rheum.* 1992;35:S45.
12. Fam AG. What is new about crystals other than monosodium urate? *Curr Opin Rheumatol.* 2000;12:228-34.