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## Familial Chondrocalcinosis: Report of the Case in Two Sisters

Chondrocalcinosis is a chronic and progressive inflammatory joint disease with acute episodes of arthritis, which may be associated with other metabolic diseases or transmitted as a genetic disorder. We report a case of chondrocalcinosis in two sisters.

**Keywords:** chondrocalcinosis, familial, Iran

### Introduction

Chondrocalcinosis is known as chondrocalcinosis articularis, pseudogout, calcium pyrophosphate dehydrate-crystal deposition arthritis (CPPD-CDA) and crystal-induced rheumatism. Knowledge about CPPD-CDA has increased recently; however, the relationship between CPPD crystals and arthritis remains unclear.<sup>1,2</sup> Chondrocalcinosis is known to be arthritis that occurs after the fifth decade of life, and thus most frequently, patients are the elderly.<sup>3</sup> Radiographic studies reveal age-related increase of chondrocalcinosis so that by the ninth decade almost 50% of individuals have chondrocalcinosis.<sup>4</sup> Chondrocalcinosis is an unusual finding in young adults; however, there are some case reports in young patients.<sup>5</sup> CPPD-CDA has been found in patients with diabetes mellitus, hyperparathyroidism, hemochromatosis, gout, etc. which highly suggests a relationship between pathogenesis of CPPD-CDA and certain metabolic diseases. Although there is insufficient data to confirm racial predisposition, familial affinity is well reported in CPPD-CDA.<sup>6-9</sup> To our knowledge this is the first report of familial chondrocalcinosis in two Iranian young sisters.

### Case Report

#### Case 1

A 38-year-old lady referred with an asymmetrical polyarthritis. She had pain and swelling on the dorsum of right foot, right knee, both wrists, and left shoulder which was aggravated during pregnancy. Previous intermittent episodes of painful reddish swelling had occurred over the same areas. History of morning stiffness and synovial thickening were not found. Erythrocyte sedimentation rate (ESR) had been constantly elevated, rheumatoid factor (RF), anti-nuclear antibody (ANA), anti-DNA antibody, serum uric acid and other laboratory tests were negative. x-rays of hips, knees (Figure 1), and shoulders (Figure 2) showed characteristic calcifications. Mildly positive-birefringence crystals were reported in the fluid tapped from the right knee.

#### Case 2

The 36-year-old sister of our first case, also referred to our clinic with asymmetrical polyarthritis in the form of swelling in both knees and the right wrist, and intense pain in the left hip joint, and also arthralgia in metacarpophalangeals

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**Table 1.** Clinical findings in both patients

	Case 1	Case 2
Joint swelling and pain	right foot, right knee, both wrists, left shoulder	both knees, right wrist, left hip, bilateral MCPs and PIPs
Fever	Negative	Negative
Morning stiffness	Negative	Negative

and proximal interphalangeal joints of both hands. x-ray studies of involved joints revealed characteristic calcifications in knees, shoulders and ankles (Figure 3). She did not permit us to aspirate synovial fluid from the knee joint.

Clinical and laboratory findings are summarized in Tables 1 and 2.

## Discussion

CPPD is a calcium salt that can be deposited in hyaline- and fibrocartilage, appearing as chondrocalcinosis on radiological films.<sup>10</sup> On the other hand chondrocalcinosis is a radiological entity that shows CPPD deposition in synovial joints to any causes. Chondrocalcinosis is frequent in elderly but as a generalized chronic polyarticular disorder in younger individuals is rare. Based on the recognized predisposing factors, CPPD-CDA is classified as hereditary, idiopathic (sporadic), or associated with various metabolic diseases or trauma.

Most cases of CPPD-CDA are idiopathic. Advanced age is the most common risk factor for the development of CPPD-CDA. It is very rare in young adults unless in cases with injury or operation performed on

a joint, positive family history of CPPD-CDA, or with other predisposing diseases.

With our presented cases, history of similar symptoms was there in their father that had died many years ago. Most patients with the familial CPPD-CDA show an autosomal dominant inheritance.<sup>2</sup> A variety of metabolic and endocrine disorders are associated with CPPD-CDA, particularly among young patients.

Hemochromatosis is the most common disease associated with the CPPD-CDA.<sup>11,12</sup> Other rare metabolic diseases that predispose the patients to CPPD-CDA include hyperparathyroidism, hypophosphatasia, hypomagnesemia, Wilson's disease, hypothyroidism, acromegaly, and X-linked hypophosphatemic rickets.<sup>13-18</sup> Our patients were evaluated for the possible hormonal and metabolic disorders, which showed to be normal (Table 2).

In familial chondrocalcinosis, the pattern of inheritance varies but two distinct clinical phenotypes have been described. The first phenotype has an early onset (3<sup>rd</sup> – 4<sup>th</sup> decades) with florid polyarticular arthritis, and the second type with a late onset (after 7<sup>th</sup> decade) in the form of oligoarticular involvement. In the majority of reported CPPD-CDA series, male gender predominates, but in familial cases female gender predominates with a female to male ratio of 2 to 1.<sup>8</sup>

Age of onset in the polyarticular form is often in the middle age, which may have some diagnostic problem with RA, a disease of high incidence in the middle aged people. Attention to the morning stiffness, steady synovial thickening, symmetrical involvement and remissions during pregnancy could be useful in the differentiation of RA. In our patients, neither clinical nor laboratory findings of RA were detected. In addition, in the first patient, her symptoms and signs had aggravated during pregnancy.

Associated metabolic diseases and familial predispositions are rarely identified in CPPD-CDA and routine screening for hereditary or metabolic diseases is

**Table 2.** Laboratory findings in both patients

	Case 1	Case 2
Uric Acid (mg/dL)	3.2	3.6
Calcium (mg/dL)	8.8	8.8
Phosphorus (mg/dL)	3.4	4.1
Serum Fe (µg/dL)	62	69
TIBC (µg/dL)	280	320
ASO (Todd units)	200	200
CRP	2+	1+
RF	Negative	Negative
ESR (mm/h)	38	42
T3 (ng/mL)	90	98
T-3RU (%)	32	36
T4 (µg/dL)	6	7
TSH (µU/dL)	2.1	2.5

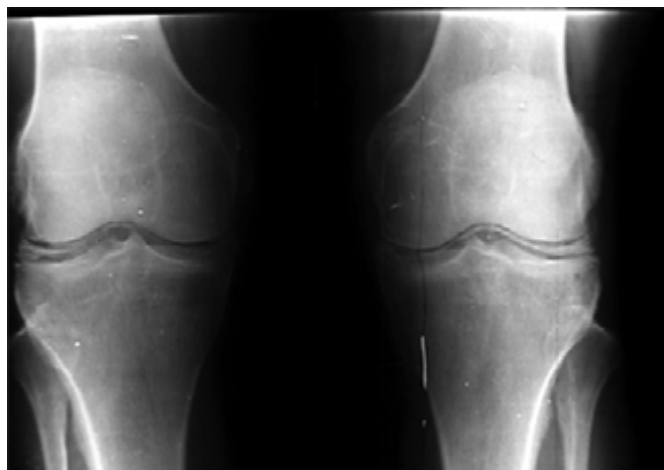


Fig 1. a,b: Knee x-rays show characteristic calcification in both knee joints.

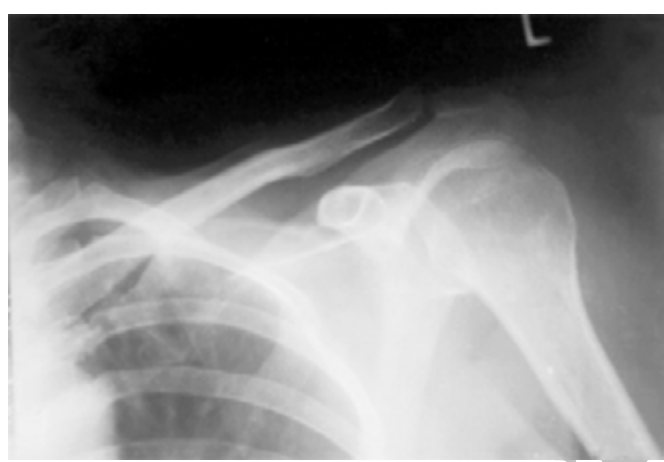
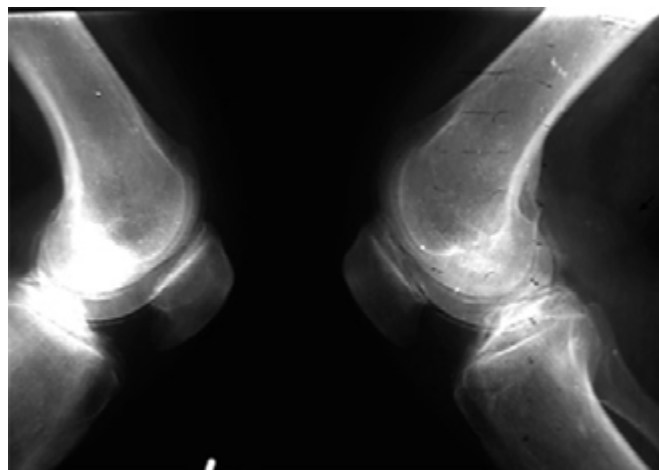


Fig 2. Left shoulder shows arc like calcification on x-ray.



Fig 3. Right ankle x-ray shows characteristic calcification in thalocalcaneal joint.

not indicated in CPPD-CDA patients.<sup>13</sup> However, in young onset polyarticular chondrocalcinosis investigations for the predisposing metabolic conditions is indicated.<sup>4</sup>

CPPD-CDA can be well due to other treatable and preventable conditions, therefore, screening of symptomatic family members is important since life-threatening complications can be avoided by appropriate treatment of hemochromatosis, hypomagnesaemia or hypophosphatasia.<sup>11</sup>

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