Calcium pyrophosphatase dihydrate (CPPD) crystal deposition disease in a teaching hospital in Kuwait

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Abstract

Objective—A Medline electronic search showed a paucity of reports on calcium pyrophosphate dihydrate crystal deposition disease (CPPD-CDD) from the Gulf region. To date only a single case report has been published from this region. Therefore, this study aimed, firstly, at finding out the prevalence of chondrocalcinosis in adult Arabs in Kuwait presenting with knee arthritis and, secondly, at carrying out an observational study of CPPD-CDD among Arabs in Kuwait. **Methods**—For the study of the prevalence of chondrocalcinosis 100 consecutive adult patients presenting with knee arthritis were radiologically examined. For the observational study the clinical, laboratory, and radiological findings were analysed in patients with CPPD-CDD seen over a period of five years. **Results**—This study showed the presence of chondrocalcinosis in two (2%) of the 100 adult Kuwaiti and other Middle-Eastern Arab patients (70 men, 30 women, median age 50 (range 45–80)) who presented to the rheumatology clinic for the evaluation of knee pain. When the younger age of the group (only three patients aged >70) is taken into account the figure was comparable with that reported from Western countries. Over a period of five years a total of 2726 new patients were evaluated at the rheumatology clinic of this institution. A diagnosis of crystal arthritis was made in 85 patients (3%). Fourteen of these 85 (that is, 16.5%, but 0.5% of the total cases) were diagnosed with definite (eight patients) or probable (six patients) CPPD-CDD. Different clinical presentations, including that of acute monoarthritis (that is, pseudogout), premature generalised osteoarthritis, and polyarticular rheumatoid-like presentations, were seen in different patients. Overlap with true gout, with the additional presence of monosodium urate crystals in the joint aspirate, was seen in two patients. **Conclusion**—The present report shows that CPPD-CDD may not be uncommon among Arabs in the Gulf region. A high degree of clinical awareness and routine examination of joint aspirates with careful analysis for crystals may make it a more common diagnosis in this part of the world. In this regard it is interesting to note that cases and case series including

familial cases have been reported from North Africa, especially Tunisia, indicating that the disease has been well described in Arabs of other geographical regions. (Ann Rheum Dis 2001;60:416–419)

Calcium pyrophosphate dihydrate crystal deposition disease (CPPD-CDD) is the second most common form of the crystal deposition disease.¹ However, because of the marked heterogeneity in clinical syndromes associated with CPPD-CDD, its prevalence and incidence are difficult to define.¹ Most epidemiological studies are small and have relied upon necropsies or radiological findings of chondrocalcinosis.^{2 3}

A Medline search and search of reviews showed a paucity of reports on CPPD-CDD from developing countries. Only one centre from Tunisia has reported cases and families of CPPD-CDD (cited by Reginato and Hamza *et al*⁴). In addition to reports from this centre, only one series from Thailand and one case report from Qatar in the Gulf region has been published in the past 20 years.^{5 6} In two earlier reports from this institution some interesting observations relating to hyperuricaemia and gout were highlighted.⁷ This report describes our experience with CPPD-CDD in a large teaching hospital in Kuwait.

Subjects and methods

The study included a prospective radiological survey of the knee joints in 100 consecutive patients presenting to the rheumatology service of this institution with knee arthritis during 1997. In addition, the study also included all patients diagnosed as CPPD-CDD by the rheumatology service of this institution over a period of five years (middle of May 1994 to the middle of 1999).

The diagnostic criteria of Ryan and McCarty⁸ were used for diagnosing definite and probable CPPD-CDD.

A standard technique of polarised light microscopy was used to show the presence of crystals in synovial fluid,⁹ modified by using a kit for producing polarised light (for the identification of gout or pseudogout crystal manufactured by M/S Crystal Diagnostics, Division of J & G Manufacturing Co, Midlothian, Virginia, USA). To improve the sensitivity of the technique lightly centrifuged samples were also examined under oil-oil immersion microscopy.⁹

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Results

The 100 consecutive patients presenting with knee pain comprised 70 men and 30 women, with a median age of 50 (range 45–80). The age distribution of the patients was as follows: 39 patients aged 45–49, 44 aged 50–59, 12 aged 60–69, 2 aged 70–79, and 1 aged >80. All the patients were of Middle-Eastern Arab stock, the majority being Kuwaiti (82). Two male Kuwaiti patients aged 50 and 75, respectively, were found to have chondrocalcinosis in the knee.

Of a total of 2726 patients seen by the rheumatology service over the period of the study, 85 had crystal arthritis—69 had gout, 14 had CPPD-CDD, and there were two others.

Definite CPPD-CDD was seen in eight patients (six men) aged 50–94. In seven of these patients the diagnosis was delayed by 10–20 years. In three patients the diagnosis was made during an acute attack of knee arthritis at ages 45, 55, and 94, respectively. In two of these eight patients examination of the joint fluid showed the presence of CPPD as well as monosodium urate crystals.

Probable CPPD-CDD disease was seen in six Kuwaiti patients (four men, aged 42–86), with joint symptoms associated with typical chondrocalcinosis. In four of them the diagnosis was delayed by three to 10 years and in two the diagnosis was made at the first attack of acute arthritis.

Figure 1 (A) Lumbar spine: calcification of the annulus is seen at all the levels with small marginal osteophytes from L2–S1. Note the degenerative changes in the sacroiliac joints. (B) Both knees—weightbearing anteroposterior view: chondrocalcinosis and periarticular calcification are seen bilaterally. Degenerative changes with marked narrowing of the medial and lateral compartments of both knees, and marginal osteophyte formation, are present. (C) Right ankle—lateral view: calcification of the Achilles tendon and plantar fascia is seen. Degenerative changes are present in the talocalcaneal and calcaneocuboid joint. Note the degenerative cyst in the cuboid bone.

Chronic CPPD-CDD with characteristic structural abnormalities of osteoarthritis (OA) was the presentation in five patients. Premature aggressive, destructive OA of the knee was seen in two patients. In both of them the disease started earlier than 50 years of age. Both required knee replacement within 10 years of the onset of symptoms. Severe generalised OA with deformities and disability, interspersed with acute intermittent monarthritis in some of the large joints in the arms and legs, was the presentation in two patients. In one, a woman, the first symptoms of an insidious onset of non-inflammatory polyarthritis affecting small and large joints in the arms and legs started at the age of 38. Interspersed with this were episodes of acute arthritis in some of the joints—namely, knee, wrists, elbows. Extensive chondrocalcinosis in most of the peripheral and axial joints, with features of aggressive OA in joints not usually affected in primary osteoarthritis—namely, wrists and metacarpophalangeal (MCP) joints, was demonstrable on radiological examination (fig 1A-C). Synovial calcification was present in most of the MCP joints of both the hands and the first carpometacarpal joint on the left side, with capsular calcification of the second right proximal interphalangeal joint. No obvious underlying cause was detected on detailed investigations during her visit to the United Kingdom.

The second patient was a 75 year old Kuwaiti man who had had a renal transplant 10 years previously, with chronic pains and swellings in several peripheral large and small joints in the arms and legs, interspersed with acute attacks of fever, pain, and swelling in the knee joints since 1982, and in the elbow joints since 1997. He had been noted to be hyperuricaemic on several occasions in the past. Joint imaging showed advanced aggressive OA in the various large and small joints in the arms and legs, with chondrocalcinosis in the knee. Synovial fluid

showed large numbers of CPPD crystals in association with crystals of monosodium urate.

A 50 year old man had had RA-like extensive disease of small and large joints in his arms and legs, with ulnar deviation of the digits, since the age of 35 years. He also had low rheumatoid factor titres and high erythrocyte sedimentation rate and C reactive protein levels. However, the presence of typical hook-like drooping osteophytes on the radial aspects of the metacarpal heads with normal bone density (fig 2), other features of extensive aggressive OA at several other joints usually not affected in OA (wrists, MCP joints), and synovial fluid from the knee showing CPPD crystals, confirmed the diagnosis of CPPD-CDD. Haemochromatosis and other possible associated diseases were excluded clinically and by relevant investigations.

Acute arthritis of the knee was the presentation in three patients. Radiological examination showed typical destructive osteoarthritic changes with bilateral chondrocalcinosis in all of them. The synovial fluid was inflammatory and positive for CPPD crystals.

In five patients with probable CPPD-CDD the presentation was that of chondrocalcinosis with haemorrhagic acute knee arthritis. However, synovial fluid examination was negative for crystals as well as microbial cultures. An additional patient, a 75 year old man, had acute wrist arthritis with chondrocalcinosis of the knee. Aspirated fluid was negative for crystals. The microbial cultures were also negative. All the patients responded satisfactorily to non-steroidal anti-inflammatory drugs with intra-articular corticosteroid injections.

A search for a possible underlying cause for the disease in young patients included investigations for hypothyroidism, hyperparathyroidism, haemochromatosis, hypomagnesaemia, and hypophosphatasia. One patient, in whom the disease started at age 36, was studied more extensively during her visit to the United Kingdom. However, no underlying cause could be established in any of these patients.

Discussion

This study showed that 2% of the patients presenting to rheumatology clinic with knee arthritis showed chondrocalcinosis. When the younger age of the group studied is taken into account this figure was comparable with those found in studies from the UK and USA.^{10 11}

Among crystal deposition diseases, CPPD-CDD is the second most common disease after gout,¹ but there are many fewer reports of this disease than of gout. A search for CPPD-CDD from Asia showed only one series from Thailand and a single case report from Qatar, in the Gulf Region.^{5 6} The reasons for this paucity of reports on CPPD-CDD are not obvious. Our study re-emphasised some of the main features of this disease. Thus it showed that the disease does occur among Arabs and that its presentation is similar to that described from Western countries.^{1 8 12} The study also confirmed the occurrence of this disease among Arabs from North Africa, especially Tunisia,

Figure 2 Radiographs of the wrists and hands: osteoarthritis of the distal interphalangeal, proximal interphalangeal, and metacarpophalangeal joints with calcium pyrophosphate dihydrate deposition disease (CPPD-CDD). The hook-like drooping osteophytes on the radial aspects of the heads of the metacarpal joints and ulnar bones, destructive symmetrical bilateral arthritis of the wrists with scapholunate advanced collapse, radiocarpal joint space narrowing, and subchondral sclerosis are all characteristic features of CPPD-CDD.

from where cases, case series, and familial cases have been described (cited by Reginato and Hamza *et al*^{2,4}).

Radiological changes in CPPD-CDD are characterised by features of aggressive destructive OA (massive osteophytes, subchondral bony sclerosis) in the affected joints.¹³ In addition, besides involvement of joints commonly affected in OA—namely, hip, knee, distal interphalangeal joint, the disease prominently affects joints not usually involved in primary OA, such as the wrists and MCP joints.¹⁴ Patients presented in this report showed these features, including aggressive destructive OA and OA affecting joints that would be considered unusual for primary OA.

The main lessons learnt from this study were, firstly, that CPPD-CDD does occur among Middle-Eastern Arabs, possibly as frequently as reported from North Africa and Western countries. Secondly, this disease must be considered as a differential diagnosis of acute monarthritis in adults, especially if the knee is the affected joint and also among those presenting with arthritis resembling generalised primary OA but, at a relatively younger age, with the involvement of joints considered unusual for OA. Such patients must be carefully examined for chondrocalcinosis and CPPD crystals in the joint aspirates.

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