Hereditary chondrocalcinosis in an Ashkenazi Jewish family

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Abstract

A hereditary chondrocalcinosis is described for the first time in an Ashkenazi Jewish kindred. Of 34 family members in five generations, seven had medical history suggesting the disease. Five of 25 members of generations III-V had direct evidence for their disease. Characteristically, symptoms started at a fairly early age (third decade) while radiological evidence of chondrocalcinosis was delayed to the fourth decade. Joints commonly affected were knees, wrists, and elbows. The course was chronic with acute, exercise induced exacerbations.

Calcium pyrophosphate dihydrate (CPPD) crystal arthropathy is a disease characterised by the deposition of these crystals in the joint cartilage.¹ The exact factors responsible for such deposition are still unknown. Three main forms of disease may be defined: (a) a hereditary form; (b) a form associated with endocrine or metabolic disorders; and (c) a sporadic form, by far the most common.

Several hereditary series have been reported to date.³⁻¹³ The series differ in many aspects, including the presumed genetic transmission, though autosomal dominant inheritance was suggested in most.¹² Sporadic chondrocalcinosis in a Jewish home for the aged has been described in 27.6% of the residents¹⁴; no hereditary CPPD deposition was reported in this ethnic group, however. We report here for the first time a Jewish kindred with a clustering of chondrocalcinosis.

Materials and methods

The family of the proband (fig 1, IV-4) was studied. It included 34 members in five generations, 25 of whom (generations III-V) were available for direct examination. Radiographs of knees, wrists, hands, and cervical spine were performed in symptomatic subjects. In one patient (the proband) an elective arthrocentesis was done on a visit to Philadelphia and the fluid studied by routine analysis, compensated polarised microscope, and alizarin red S staining.

Routine laboratory tests from symptomatic subjects included blood count, fasting blood sugar, calcium, phosphorus, alkaline phosphatase, uric acid, free thyroxine concentrations, rheumatoid factor, and antinuclear antibodies. A more detailed laboratory study is presented in the case report.

Results

A family of Ashkenazi Jewish origin including 34 members in five generations was studied (fig 1). The family had lived in West Prussia and migrated to Berlin at the time of the first world war and to Israel between 1930 and 1940. Data before 1860 are unavailable. Medical history for generations I and II was collected from living relatives. Two sisters (II-1, II-5) had had significant joint symptoms affecting their knees and other non-specified joints before the age of 30, and in the absence of more data are considered as suspected chondrocalcinosis.

Twenty five family members of generations III-V were available for questioning and examination, five of whom were found to have been affected from a mean age of 24 years (range 19-30). The table contains their clinical and radiological data. The above mentioned laboratory tests were normal in all five living subjects. In six additional asymptomatic members (III-4, III-6, IV-2, IV-6, V-4, V-8) various x rays taken for unrelated reasons (trauma, low back pain, medical investigations) were traced. Joints included in the films were not found to have chondrocalcinosis. Patient No IV-4 is reported in detail.

Case report

A 43 year old doctor was referred for our observation because of protracted pain in his knees. The patient's father had gout and he had other relatives with hyperuricaemia. The patient was well and very fit until the age of 23 when he started to experience knee pain induced by exercise, sometimes accompanied by local swelling. At the age of 28 a right meniscectomy was performed at another centre where 'diffuse osteochondritis' was described. Calcium and routine laboratory results were normal. During the following 12 years he experienced exacerbations and remissions with gradual progression of both the severity and frequency of his symptoms, extending to the elbows, proximal and distal interphalangeal joints, and cervical spine. In 1986 arthroscopy of the left knee disclosed degenerative changes which were more prominent in the medial meniscus and the patellofemoral joint.

On general physical examination the patient was well. His cervical range was moderately limited. Heberden nodes were evident. The knees had 10° flexion contractures, weakened quadriceps muscles, and well preserved stability. Effusion was present on some occasions. Other joints were normal.

Figure 1: Genealogical tree of a Jewish family with hereditary chondrocalcinosis. Numbers I-V represent generations. Solid figures represent affected members. Squares represent men, circles—women. Diagonal line represents deceased member. Examined subjects are indicated by horizontal bars. — represents married without children. Arrow points to the proband. * = died accidentally at the age of 28. Note: the age range of generation V is between 4 and 23 years. Information on generations I-II was recovered by family history.

Serial x rays (fig 2) showed progressive osteoarthritis of medial, lateral, and patello-femoral compartments of both knees with chondrocalcinosis of both meniscal and articular hyaline cartilage. Osteoarthritis of the cervical spine with multiple subluxations and suspected congenital fusion of C3 to C4 were also evident. The intervertebral discs did not show calcification. Hands and wrists seemed normal.

Serum calcium was slightly raised on a single occasion, but repeated determinations, as well as phosphorus, magnesium, and alkaline phosphatase, were normal. Further laboratory tests were normal and included uric acid, creatinine, creatinine clearance, 24 hours cyclic AMP, serum iron and total iron binding capacity, caeruloplasmin, free thyroxine, parathyroid hormone, growth hormone, insulin, urine free cortisol, rheumatoid factor, and antinuclear antibodies. Knee joint fluid examined by one of us (HRS) during a quiescent phase, using polarised microscopy and alizarin red S screen stain, disclosed clear viscous fluid with 0.2×10^9 white blood cells/l, small positively birefringent CPPD-like crystals in synovial fluid cells, and occasional clumps of alizarin red S positive material suggestive of apatites.

Figure 2: x Ray films of the knees of the proband. Note the progression of chondrocalcinosis and osteoarthritic changes from 1969 (A) to 1984 (B) and 1986 (C).

The patient found partial relief with aspirin or piroxicam. During the past 12 months colchicine 0.5 mg three times a day has reduced the rate of his relapses and also the baseline daily pain.

Clinical and radiological data on five symptomatic members in a kindred with familial chondrocalcinosis

Family member	Sex	Age	Age of onset (years)	Joints affected (C=clinically; R=radiologically)										Osteo-arthritis on x ray	Course			
				Knee		Wrist		MCP*		Spine		Elbow			Shoulder	Other	Acute episodes	Chronic pain
				C	R	C	R	C	R	C	R	C	R		C			
III-2	F	78	19	+	+	+	—	+	+	+	—	—	—	+	—			
III-5	F	80†	28	+	+	+	+	+	+	+	+	—	+	—		Hips PIP*	+	+
																+	—	
IV-4	M	43	23	+	+	+	+	+	—	+	+	+	—	—	ND	PIP	+	—
IV-5	F	46	30	+	+	+	—	+	—	+	—	+	—	—	ND		—	+
V-12	M	23	22	+	—	—	ND*	—	ND	—	ND	+	—	—	ND		—	+
																	+	±

*MCP=metacarpophalangeal joints; PIP=proximal interphalangeal joints; ND=not determined.
†=deceased, medical notes and x rays available.

Discussion

This report is the first description of familial chondrocalcinosis in an Ashkenazi Jewish kindred. Sporadic chondrocalcinosis was observed radiographically in 27.6% of volunteer subjects in a Jewish home for the aged.¹⁴ In our survey five family members had a strong clinical history and findings suggestive of CPPD crystal deposition disease. In the patient who underwent joint aspiration CPPD-like crystals were found. Four had radiographic evidence of chondrocalcinosis. The fifth subject, without such evidence, is only 23 years old. Radiographic chondrocalcinosis appeared years after joint pain started in the propositus (fig 2).

Onset of symptoms occurred early during the third decade of life in all affected patients. The clinical course in our patients is characterised by recurrent attacks, commonly triggered by exercise, superimposed on moderate chronic arthralgia. The knee was the most affected joint, followed by the wrist, and showed degenerative changes beginning at age 30. Although meniscectomy may accelerate degenerative changes and CPPD deposition,^{15 16} the unilateral procedure in our patient cannot explain bilateral involvement. No metabolic abnormality was detected among the symptomatic family members. Laboratory tests were not carried out in asymptomatic subjects.

Familial or hereditary CPPD disease has been reported from various geographical regions and ethnic groups. Since the original description of Hungarian familial chondrocalcinosis by Zitnan and Sitaj in 1963,¹⁷ ten series, none of them Jewish, have been published from the Netherlands,⁷ France,⁸ Spain,⁹ Sweden,¹² Canada,¹¹ Chile,⁶ Germany,⁵ the United States of America,^{4 10} and Japan.¹³ No further studies have been reported during the past six years.

Tracing the exact origins of the present Jewish Ashkenazi family is hampered by historical events and the emigration to Israel. The oldest known members lived in West Prussia during the 19th century. Our patients when

compared with previously published series show clinical similarity to the Hungarian group.³

The inheritance pattern seems to be dominant with varying expressivity. Without a systematic radiological study of all family members, however, a firm conclusion on the inheritance pattern cannot be reached. Because this family, as in the Hungarian series,³ does not show man to man transmission, an autosomal versus sex-linked transmission cannot be excluded.

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