Gout and neurological abnormalities associated with cardiomypathy in a young man

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Abstract

A 21 year old man with a family history of gout and neurological deficits, developed severe idiopathic congestive cardiomypathy after a long history of typical gouty attacks and neurological abnormalities. Clinical and laboratory evaluations showed borderline mental retardation, ataxia, sensorineural deafness, marked hyperuricaemia, and excessive uric acid excretion in the presence of impaired renal function. None of the known causes of cardiomypathy was found. Even though red cell hypoxanthine guanine phosphoribosyltransferase enzyme activity was normal, this case probably represents an inborn error of purine metabolism. The association of cardiomypathy with gout is very unusual. Previously it has been only once described in a single case.

The description of symptoms and metabolic delineation of the Lesch-Nyhan syndrome has established an association with hyperuricaemia and neurological disease. In men only a complete or partial hypoxanthine guanine phosphoribosyltransferase (HGPRT) enzyme deficiency leads to different degrees of the syndrome, characterised by mental retardation, self mutilation, choreothetosis, gouty arthritis, and gouty nephropathy. As far as we know cardiomypathy has not been found in association with any primary, secondary, or idiopathic gout, except in a single case reported by Rosenberg et al.6

A further case is described here of a young man with a family history of hyperuricaemia and neurological deficits who presented with severe cardiomypathy, gouty arthritis, impaired renal function, ataxia, sensorineural deafness, and borderline mental retardation. Red cell HGPRT enzyme levels were normal.

Case report

In July 1988 a 21 year old Greek man was referred to Alexandra Hospital for evaluation of a progressive dyspnoea on exertion, which had started six months earlier. Previous medical history included: several episodes of typical gouty attacks in the last six years, treated with colchicine-allopurinol, and a hearing loss registered progressively in the last three years without any evidence of acoustic trauma. The diagnosis of gout was based on the past typical clinical picture of attacks of acute arthritis of the metatarsophalangeal joints of the great toes. In addition, polarised microscopy showed needle shaped, strongly negative birefringent urate crystals free and within leucocytes in aspirated synovial fluid from the left metatarsophalangeal joint and the right knee. The knee was not severely inflamed but he had had an acute attack during his hospital care. During the 11 months before admission he had intermittent diplopia and a short episode of weakness in his right hand and foot, with slight slurring of speech. His family history showed that his mother, aged 41, and her brother, aged 38, had a long history of gout. In addition, at the age of 31 his mother also had diplopia and weakness in hands and feet; these symptoms responded well to a steroid treatment. There were no other children in the family and his father and his uncles had no remarkable medical history.

The patient denied significant smoking and alcohol consumption. Clinical examination showed tachycardia, gallop rhythm, and rales at the bases of both lungs. There was no clinical evidence of previous valvulitis, recent infection, arterial hypertension, or any signs or symptoms of congenital heart disease. Neurological findings included mild tremor of both hands, hyperactive deep tendon reflexes, marked ataxia on finger-nose-finger testing, and a positive Romberg test. He appeared mildly retarded and compulsively bit his lips and fingernails.

Laboratory results showed normal complete blood count, electrolytes, cholesterol, aldolase, serum protein and lipid electrophoresis, and immunoelectrophoresis. Urine analysis showed acicity of the urine and uric acid crystalluria. Blood urea concentrations ranged from 17-8 to 23-2 mmol/l and, the creatinine clearance was 35 ml/min. Serum uric acid concentrations ranged from 595 to 773 mmol/l and the urinary uric acid excretion was over 800 mg/24 hours. All investigations for autoimmune connective tissue diseases, thyroid disease, amyloidosis, toxoplasmosis, syphilis, AIDS, and other viral infections were negative. The activity of HGPRT was measured in dialysed erythrocyte lysates by the method of Kelley et al and found to be 79-6 nmol/mg of protein for each hour of incubation with hypoxanthine as the substrate (normal value, mean (SD) 90 (11) nmol/mg protein/h). Erythrocyte phosphoribosyl pyrophosphate (PRPP) synthase activity was determined in addition with Becker's modification9 of the two step method of Hershko et al in dialysed erythrocyte lysates and found to be 63-3 nmol/mg protein/h (normal value, mean (SD) 52 (9)).

Radiography of the chest showed cardiomegaly and hilar congestion. Electrocardiography showed 150° axis deviation, left posterior hemiblock, and left ventricular hypertrophy. The
Gout and neurological abnormalities associated with cardiomyopathy

The aggregate of clinical abnormalities in our patient was important. The differential diagnosis included several rare syndromes such as: Alport's syndrome (progressive renal failure, sensorineural deafness),\(^5\) Herrmann's syndrome (nephritis, sensorineural deafness, mental retardation),\(^6\) von Gierke's disease (hyperuricaemia, cardiac disease),\(^7\) Friedreich's ataxia (neurological disease, cardiomyopathy),\(^8\) and some other genetically determined enzymatic abnormalities, which might also have justified the cardiac disease.\(^9\) None of these conditions was compatible with the whole clinical picture and laboratory data described above.

In 1970 Rosenberg et al reported a case of a whole family with a syndrome characterised by hyperuricaemia, ataxia, decreased renal function, and sensorineural deafness; erythrocyte HGPRT activities were normal.\(^6\) Five members of this kindred had the complete syndrome, and only one of them at the age of 22 has developed congestive heart failure, due to cardiomyopathy.

Obviously our patient has striking similarities with Rosenberg's case, including normal HGPRT activity, but with the difference that our patient had a typical gouty arthritis, mental retardation, and excessive uric acid excretion despite the impaired renal function. Rosenberg's patient in contrast had hyperuricaemia without hyperuricosuria and a normal mental state,\(^6\) with cardiomyopathy, which was not evident in 21 other members of the kindred.\(^6\)

In conclusion, although the mechanisms responsible for the metabolic, otological, neurological, and cardiac findings described in our patient are not clear, the normal HGPRT and PRPP synthetase enzyme activities, the excessive amount of uric acid excreted, in association with neurological dysfunction and his family history, suggest the presence of an inborn error of purine metabolism. We believe that the above case may be included in the Lesch-Nyhan syndrome variants or phenocopies, in which further cases with an intact HGPRT pathway are included.\(^16\)

Discussion

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