Asymptomatic elevation of creatine kinase (CK) was first reported by Rowland, who proposed to call the condition "high serum enzymes, cause undetermined." In 1980, Rowland et al. coined the term "idiopathic hyperCKemia" to describe patients with serum creatine kinase levels that were consistently higher than normal despite lack of symptomatic weakness or other abnormality on neurological examination, electromyography, or muscle biopsy. Additional criteria for the diagnosis of idiopathic hyperCKemia were proposed in 1988 by Brewster and de Visser. These included absence of signs of hyperthyroidism, family history of neuromuscular disease, intake of medications that produce hyperCKemia, and intramuscular injections. No critical levels of serum creatine kinase activity were set to define the condition, and there was no follow-up of patients to determine their outcome.

With increasing concern about malignant hyperthermia and with the inclusion of creatine kinase determination in the automated blood chemistry profile performed upon hospital admission or as part of health screening, the number of patients with unexplained rise in creatine kinase has increased.

A literature search for patients with idiopathic hyperCKemia yielded a total of 55 patients, of whom only seven are children. Reports in the literature on idiopathic hyperCKemia reflect a male preponderance. Of reported patients, 78% of cases of all ages and 71% of childhood cases are male. Reported serum creatine kinase values vary from < 5-fold above the normal value up to an increase of 170-fold over normal. The majority have serum creatine kinase values between 5- and 10-fold above normal. No relationship between magnitude of serum creatine kinase elevation and age has been reported. None of the reported patients had weakness on initial examination, and about one third reported muscle-related symptoms, including myalgias, fatigability, cramps, and stiffness. Electromyographic (EMG) abnormalities are described in 41% of reported patients and in 50% of childhood cases. The commonest EMG abnormalities are a myopathic pattern, short duration potentials alone or with positive sharp waves, and fibrillations. Abnormalities in muscle biopsy specimens are reported in 56% of patients. Variations in fiber size, necrotic and regenerating fibers, and inflammatory myopathy are the most frequently reported findings. The family history of reported patients is usually normal with occasional reports of prominent calves.

The duration of follow-up in reported cases varies from 1 to 12 years; the majority were followed for 4 years. Clinical and/or histopathological evidence of a neuromuscular disorder developed between 1 and 7 years after detection of hyperCKemia in one third of the cases. These include distal myopathy, myoadenylate deaminase deficiency, polymyositis, mitochondrial myopathy, sarcoid myopathy, McArdle's disease, central core disease, multicore disease, inclusion body myopathy, and a carrier of Duchenne muscular dystrophy. A muscle biopsy was needed for the diagnosis in the majority of cases. Thus, without a muscle biopsy, the diagnosis of idiopathic hyperCKemia remains uncertain. There are no clues at the onset of hyperCKemia to help predict the outcome.

The subsequent development of neuromuscular disorders in patients who present with idiopathic hyperCKemia calls for vigilant follow-up especially in those patients with electromyographic and/or muscle biopsy abnormalities. Furthermore, the detection of carrier state for dystrophinopathy in female patients with idiopathic hyperCKemia in Tachi's report, and in one of our patients, suggests that tests for carrier state of a dystrophinopathy be done on all patients with idiopathic hyperCKemia, and that absence of dystrophinopathy be added to the criteria proposed by Rowland and Brewster and de Visser for the diagnosis of idiopathic hyperCKemia.
References


