39. ACUTE MONOARTHRITIS: LOOK BEYOND JUST AN ACUTE ATTACK

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Introduction: Calcium pyrophosphate disease (CPPD) or pseudogout is usually a disease of elderly. Common secondary causes include osteoarthritis, hyperparathyroidism, dialysis dependent renal failure, hypomagnesaemia. We describe a case of pseudogout in young lady who has persistent hypokalemia and was later found to have Gitelman syndrome. Recurrent pseudogout attacks can be due to secondary causes and may be the only clinical feature in this rare disease.

Case description: A 55 year old Afro-Caribbean lady presented to Emergency department with history of sudden onset, non-traumatic, right knee pain and swelling with inability to bear weight in October 2013. She had similar episode in the right ankle a few years previously. She also had a history of thyrotoxicosis and on thyroid supplements post thyroidectomy. She was extensively evaluated in the past for microcytic hypochromic anemia and found to have alpha thalassemia trait. There was no history of gout, diabetes, psoriasis, bleeding diathesis, use of long term diuretics or fever at that time. Family history was non-contributory. On examination, her heart rate was 78beats/min and BP was 94/55 mm Hg. She was afebrile. The right knee was swollen and tender without redness. She was unable to move the knee and passive movements were not possible due to pain. CRP was 35 and ESR was 28. Complete blood count, coagulation profile was normal. Aspirated synovial fluid showed rhomboid shaped positively birefringent crystals indicating calcium pyrophosphate crystals seen in pseudogout. There was no evidence of septic arthritis and cultures of synovial fluid were negative for growth of any microorganism. She was prescribed diclofenac and advised to follow up in rheumatology outpatient department. At rheumatology review she was noted to have previous biochemical evidence of hypokalemia. X-ray of knees and wrists showed chondrocalcinosis. A review in the metabolic clinic was advised in view of persistent hypokalemia and hypotension. Further evaluation revealed metabolic alkalosis with hypomagnesaemia, hypocalciuria and hypophosphaturia. Serum Renin level was 52 mU/L (12.9-33.7 mU/L in erect posture. Considering the synovial fluid report and imaging she was diagnosed to have CPPD crystal disease. In view of her metabolic abnormalities including elevated serum Renin level she was suspected to have Gitelman syndrome which was confirmed by genetic DNA sequencing for pathogenic mutations in a panel of genes known to cause Gitelman and the related Bartter syndrome; MLPA analysis of the SLC12A3 and CLCNKB gene was also completed to look for large scale deletions and duplications.Sequencing analysis of the SLC12A3 (a sodium ion transporter gene) detected the homozygous mutation c.2687G>A in exon 23 (abnormal protein p.Arg896Gln) previously reported in other patients with Gitelman syndrome. She was prescribed magnesium glycerophosphate and later magnesium aspartate for the metabolic correction of hypomagnesaemia, both of which she did not tolerate and developed diarrhea. She suffered two further attacks of pseudogout after the initial attack. She is currently taking Magnesium lactate SR (84 mg/3.5 mmol of magnesium per tablet) twice daily and thyroxine supplements. She has been advised to consume a high sodium and high potassium diet along with the magnesium supplements. There have been no further attacks of pseudogout after introduction of Magnesium lactate tablets.

Discussion: Pseudogout and its radiologic appearance, chondrocalcinosis, are commoner in the elderly. Acute pseudogout, asymptomatic chondrocalcinosis, pseudo-osteoarthritis, pseudo-rheumatoid arthritis, pseudo-polymyalgia rheumatica and pseudo-neuropathic arthropathy are all potentiallly presentations of CPPD. Acute pseudogout occurs in approximately 25% of patients with CPPD. The most common joint involved is the knee. The wrist, ankle, elbow, toe, shoulder and hip can also be involved. In most cases the cause is idiopathic. Wilson's disease, Hyperparathyroidism, Hemochromatosis, Haemophilia, Hypomagnesaemia, Hypophosphatemia, Hypothyroidism, Diabetes Mellitus, Acromegaly, Ochronosis and Gout are some of the known secondary causes. The association with Gitelman symdrome is less well known and may go unrecognized. In our case, patient was below the age of 60 at the time of presentation which prompted the search for secondary causes. Due to the presences of low blood pressure, hypokalemia, metabolic alkalosis, and hypomagnesaemia, the possibility of Gitelman syndrome was considered which was confirmed by genetic testing. It is necessary to think of such causes if patients are younger than expected to have pseudogout, especially when there is no evidence of osteoarthritis in the affected joint. In Gitelman syndrome hypomagnesaemia impair the relationship of calciotropic hormones like calciotriol, PTH with ionized calcium in blood. There is decreased sensitivity of bones to circulating PTH and impaired intestinal calcium transport in presence of normal calcitriol levels. Hence there is no hypercalcemia in Gitleman syndrome. The chondrocalcinosis seen in Gitelman syndrome is probably related to alteration in pyrophosphatase activity which promotes pyrophosphate salt crystallization in periarticular sites and lead to pseudogout. This is corrected by magnesium supplementation which is the treatment of pseudogout related with Gitelman syndrome as confirmed by absence of further attacks after magnesium supplementation in our case.