



Early-Onset Gout: What is behind this Pathology?

Marta González Fernández, Paula García Escudero, Elena Barahona García, Alberto Alonso Ruiz and Fernando Pérez Ruiz*

Hospital Universitario Cruces e Instituto de Investigación Biomédica Biocruces, Spain

Keywords

Hyperuricemia; Gout; Chronic Kidney Disease (CKD); Autosomal Dominant Tubule-Interstitial Kidney Disease (ADTKD); Uromodulin (UMOD) Mutations

Background

Gout is a chronic disease which conditions inflammatory arthritis secondary to Monosodium Urate (MSU) crystal deposition due to persistent hyperuricemia. Among other comorbidities, gout is directly related to Chronic Kidney Disease (CKD), which becomes more frequent after the seventh decade of life, in relation to Hypertension (HT), diabetes mellitus or use of nephrotoxic agents, such as Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), angiotensin-converting-enzyme inhibitors or diuretics. Less common causes of CKD involve glomerulonephritis, tubule-interstitial nephritis or inherited disorders, which should be suspected in young patients, with renal impairment and/or positive familiar history of CKD, who present with hyperuricemia and gout.

Autosomal Dominant Tubule-Interstitial Kidney Disease due to Uromodulin Mutations (ADTKD-UMOD) is one of these unusual and under diagnosed inherited conditions that lead to CKD, with eventual renal failure, along with precocious hyperuricemia and gout.

Here, we report a 36-year-old male, with renal insufficiency and gout, index case of a family affected by ADTKD-UMOD.

Case Presentation

A 36-year-old Caucasian male, with personal history of HT, Hyperlipidemia, and CKD stage 3A since adolescence without any acknowledged cause, in chronic treatment with losartan 100 mg qd, manidipine 10 mg qd and pravastatin 20 mg qd. He was referred from Primary Care Attention to Rheumatology consultations because of early-onset gout, with first episode at age 22, poorly controlled despite Urate-Lowering Therapy (ULT) with allopurinol 100 mg qd.

Reduced renal function with an estimated Glomerular Filtration Rate (eGFR) of 45 mL/min/1.73 m² and serum creatinine ranging from 1.5 mg/dL to 1.7 mg/dL, and hyperuricemia, present for more than 10 years, with persistent serum Uric Acid (sUA) levels >7 mg/dL, were registered in electronic file data, with no other abnormalities found in previously performed complementary laboratory tests (including serum electrolytes, acute phase reactants, complete blood count, proteinogram, autoimmunity tests and urinalysis). Diseases coursing with hematuria or proteinuria, such as glomerulonephritis, were discarded.

The patient denied previous or present consumption of NSAIDs or use of any other nephrotoxic agents. Further studies showed a slightly reduced fractional excretion of uric acid in 24-h urine collection. Musculoskeletal Ultrasonography (US) evidenced specific findings of MSU deposit ("double contour" sign in the left knee, and hyperechoic, heterogeneous images with undefined contours in the fibular collateral ligament of the left knee and first metatarsophalangeal of the right foot, compatible with tophi). Abdominal and renal US showed normal kidneys, both in size and form, ruling out renal arteries stenosis or cysts presence related to polycystic kidney disease.

Family history revealed CKD in the father, who was in hemodialysis, attributed to abusive consumption of NSAIDs secondary to recurrent and frequent gout episodes. Also, the paternal grandmother and aunt suffered from CKD, having received the last one a kidney transplant.

An Autosomal-Dominant (AD) inheritance pattern of CKD was identified. Genetic tests confirmed a heterozygous pathogenic mutation in the UMOD gene, that conditioned a nucleotide exchange (guanine → cytosine) at position 665 (665 G>C), resulting in an arginine for proline final swap (p.Arg222Pro). ADTKD-UMOD diagnosis was confirmed.

OPEN ACCESS

*Correspondence:

Fernando Pérez Ruiz, Hospital Universitario Cruces e Instituto de Investigación Biomédica Biocruces, Spain,
E-mail: fperezruiz@telefonica.net

Received Date: 04 Mar 2020

Accepted Date: 26 Mar 2020

Published Date: 30 Mar 2020

Citation:

Fernández MG, Escudero PG, García EB, Ruiz AA, Ruiz FP. Early-Onset Gout: What is behind this Pathology?. *Am J Arthritis*. 2020; 4(1): 1016.

Copyright © 2020 Fernando Pérez Ruiz. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

During the diagnostic process, ULT was escalated [from allopurinol 100 mg qd to allopurinol 300 mg qd (adjusted-dose for eGFR: 600 mg/dL per day of eGFR) and afterwards to febuxostat 80 mg qd] due to inadequate control of sUA levels. Currently, the patient remains asymptomatic, with stable eGFR and maintained sUA <6 mg/dL.

Discussion

Gout is a common disease which seems to be linked closely to CKD, especially in the last decades of life. Exhaustive medical history must be performed in order to determine the aetiology behind these pathologies.

Due to widespread use of NSAIDs by general population and particularly in gout patients who use them to treat flares, its abusive consumption must be ruled out. Hereditary disorders should be suspected if there is a positive familiar history of CKD. In case of an AD-CKD pattern, mutations in the UMOD gene, conditioning ADTKD-UMOD, as in our case, must be ruled out.

Family history of CKD and use of nephrotoxic agents should always be taken into account, especially in young individuals. ADTKD-UMOD is an under diagnosed AD inherited disease that leads to CKD, between the fourth and fifth decades of life, as well as hyperuricemia and gout in the teenage years.

Although abnormalities in laboratory tests may vary between affected families, ADTKD-UMOD usually shows a pattern of altered eGFR with increased sUA levels and reduced fractional excretion of uric acid in urine. Urinalysis and renal US are typically normal. Genetic tests are necessary to confirm the diagnosis.

Control of eGFR and sUA with intensive ULT, adjusted to eGFR, to slow CKD progression are fundamental in this pathology management.

References

1. Bleyer AJ, Hart PS, Knoch S. Hereditary interstitial kidney disease. *Semin Nephrol.* 2010;30(4):366-73.
2. Bleyer AJ, Hart PS, Knoch S. Autosomal Dominant Tubulointerstitial Kidney Disease, UMOD-Related. 2007 Jan 12 [Updated 2016 Jun 30]. In: Adam MP, Ardinger HH, Pagon RA, editors. *GeneReviews*[®] [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2018.
3. Lucas GNC, Leitão ACC, Alencar RL, Xavier RMF, Daher EF, Silva Jr GBD. Pathophysiological aspects of nephropathy caused by non-steroidal anti-inflammatory drugs. *J Bras Nefrol.* 2019;41(1):124-30.
4. Williams SE, Reed AA, Galvanovskis J. Uromodulin mutations causing familial juvenile hyperuricaemic nephropathy lead to protein maturation defects and retention in the endoplasmic reticulum. *Hum Mol Genet.* 2009;18(16):2963-74.