PERSPECTIVE

The crystalline nephropathy syndrome

Jeneth Aquino, Kim Annis

Aquino J, Annis K, The crystalline nephropathy syndrome. J Kidney Treat Diagn. 2022; 5(6):66-67.

ABSTRACT

A distinct type of kidney disease known as crystalline nephropathies is characterized by intrarenal crystal accumulation. Crystal precipitation and deposition within the tubular lumens are caused by the intrinsic properties of some molecules and ions in conjunction with an advantageous tubular fluid physiology. Through tubular blockage and both direct and indirect cytotoxicities, crystal deposition facilitates kidney damage. These crystals cause inflammation, which leads to more kidney damage. Clinically, the crystalline nephropathies are connected to tubulopathies, Acute Kidney Injury (AKI), chronic kidney disease, and abnormal urinalysis and urine sediment results (CKD). Examining the urine for sediment can sometimes assist clinicians recognize the likelihood of kidney damage caused by crystals. Clinicians screen patients for medication-related kidney damage, dysproteinemia-related malignancies, and specific hereditary illnesses when pathologists find crystals in the kidneys during a biopsy. The clinical and pathologic characteristics of these three types of crystalline nephropathies will be the main emphasis of this review.

INTRODUCTION

Crystalline nephropathies are a significant yet underappreciated cause of kidney disease. The histologic observation of intrarenal crystal deposition, especially affecting the tubulointerstitium, is what distinguishes this condition. Clinically, patients have urine abnormalities include proteinuria, crystalluria, and cylinduria, but they may also develop tubulopathies, AKI, and CKD. The presence of numerous pathologic crystals and/or casts including crystals in urine under a microscope suggests that crystalline nephropathy may exist. When kidney crystals are found during a biopsy, crystalline nephropathy is unquestionably diagnosed, and an investigation into the underlying etiology is required. The discussion of crystalline nephropathies of relevance to clinicians and pathologists, such as those caused by drugs, dysproteinemias, and genetic illnesses, follows a brief review of the pathophysiology of crystal-related kidney injury. The high concentration of ions and molecules passing through the tubules, which increases the possibility of substrate supersaturation and crystal nucleation, is the main cause of intrarenal crystal deposition. Due to some intrinsic qualities, crystals precipitate outside and settle within the kidneys. They are 3-dimensional organized structures made of molecules or ions that collect at predetermined, symmetrical distances. The crystals aggregate and grow as more ions or molecules are added after their supersaturation and nucleation. Crystal deposition is initiated by the development of damaged cell membranes in conjunction with urine supersaturation of chemicals with crystal-forming potential. A local environment that is favorable for crystal nucleation and adhesion is created by cellular surface chemicals that are upregulated by damaged cells, and this environment serves as the nidus for subsequent crystal formation. Crystallization causes tubular blockage and both direct and indirect kidney damage from the crystals. Crystals that have been phagocytosed cause lysosomes to become unstable and expel their contents, which causes cellular stress and autophagic cell death. When different ingested crystals damage lysosomes/phagolysosomes and release cathepsin-B, which cleaves important cell death pathway regulators *RIPK3* and pseudokinase *MLKL*, renal tubular cells undergo necroptosis. In addition, danger-associated molecular patterns, histones, double-stranded DNA, mitochondrial DNA, demethylated DNA and RNA, adenosine triphosphate, and uric acid are released into the extracellular compartment as a result of crystal-triggered cellular necrosis. One or more of these activate the surrounding cells death receptors, accelerating cell necrosis. The ensuing

Editorial Office, Journal of Kidney Treatment and Diagnosis, Windsor, Berkshire, England

Correspondence: Kim Annis, Editorial Office, Journal of Kidney Treatment and Diagnosis, Windsor, Berkshire, England, e-mail kidney@eclinicalsci.org

Received: 05-November-2022, Manuscript No. puljktd-22-5652; Editor assigned: 07-November-2022, PreQC No. puljktd-22-5652 (PQ); Reviewed: 14-November-2022, QC No. puljktd-22-5652 (Q); Revised: 17-November-2022, Manuscript No. puljktd-22-5652 (R); Published: 24-November-2022, DOI: 10.37532/puljktd.22.5(6).66-7

OPEN ACCESS

This open-access article is distributed under the terms of the Creative Commons Attribution Non-Commercial License (CC BY-NC) (http://creativecommons.org/licenses/by-nc/4.0/), which permits reuse, distribution and reproduction of the article, provided that the original work is properly cited and the reuse is restricted to noncommercial purposes. For commercial reuse, contact reprints@pulsus.com

inflammatory process that takes place in crystal-related kidney injury is a crucial additional step. Kidney injury is facilitated by inflammatory cell damage and necroinflammation, which is the inflammatory reaction to necrotic cell death. Toll-like receptor activation contributes to inflammatory injury in the kidneys, but complement activation and leukocyte invasion are the main causes of detrimental inflammation after crystal-related tubular cell destruction. Intrarenal inflammation is also exacerbated by the activation of the *NLRP3* inflammasome in kidney phagocytes and interleukin-1 release, which interact via the interleukin-1 receptor. In a mouse model of calcium oxalate crystalline nephropathy, increased production of long noncoding *RNA-H19* led to tubular cell damage as well. By competitively binding microRNA-216b, up-regulated long non-coding RNA-H19 triggers inflammatory damage. This in turn activates the danger-associated molecular pattern, high-mobility group box 1, which binds to Toll-like receptor 4 and triggers the *NF-kB* pathway. The transcription and expression of a number of proinflammatory cytokines and chemokines that cause tubular cell damage are ultimately increased by this crystal-stimulated pathway. Sorting of lipids on the cell surface and tyrosine protein kinase activation is another mechanism of harmful intrarenal inflammation that stimulates B-cells. Crystal-related *NLRP3* inflammasome synthesis may also play an indirect role in the development of pyroptotic cell death, which results from inflammation-induced cell lysis. Additionally, crystal-stimulated release of inflammatory cytokines such as tumor necrosis factor and others may encourage renal tubular cell necroptosis. In the numerous crystalline nephropathies, all of these crystal-related mechanisms probably contribute to harmful inflammation and cell death. Through the production of urinary blockage, it was believed that the deposition of intratubular crystals was the main cause of AKI (plugging of the tubular lumens). Acute tubular damage, which was frequently seen on biopsy specimens, was also believed to contribute to AKI. Though it is now believed to play a substantial role in the development of kidney injury, strong inflammation within the tubulointerstitium caused by the crystals through the previously discussed routes is still a major factor. Tubulointerstitial inflammation and tubular damage probably play the two biggest roles in developing AKI, even though it is impossible to determine exactly how much of each causes AKI. Crystalluria and crystalline nephropathy are linked to several clinically used medicines. To ensure accurate diagnosis and therapy, physicians and pathologists must be aware of the offending substances, their clinical presentation, and their histologic characteristics. Crystal deposition is primarily caused by increased drug supersaturation in the urine and the renal route of drug/metabolite excretion. Volume depletion, which lowers urine flow rates, and high medication dosage, which raises urinary drug concentrations, are the two factors that cause intratubular supersaturation of medicines. The pH of the urine can also increase crystal supersaturation, depending on the drug's pK after administration. The risk of medication-induced crystalline nephropathy may be significantly increased in the presence of underlying acute or chronic renal disease.