Nephrolithiasis: Pre-stone and Stone stages

A Krikun, I Vishnevsky

Citation

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Abstract

Poor practical return from the knowledge accumulated so far on etiology and pathogenesis of nephrolithiasis (NS) in the authors' opinion could be explained by lack of researcher's attention to the tubular intracellular processes in this disorder, or rather by lumping them up with those occurring in urine and overestimating the latter. Intracellular tubular acidosis probably is the key factor of matrix-forming events, i.e. of the first or Pre-stone stage of the disease . In most cases the matrix/microlith will be removed unnoticed, or as a sediment, with or without colic. The second or Stone stage requires presence of well known urinary chemistry factors like abnormal mucoproteins, inhibiting deficiency, retention and so on. Recognition of two stages of the NS, and correspondingly two groups of etiological factors as well as the role of tubular acidosis in pre-stone stage provide a rationale for new diagnostic and therapeutic ideas.

Dear Editor,

Poor practical return from the knowledge accumulated so far on etiology and pathogenesis of nephrolithiasis (NS) in our opinion could be explained by lack of researcher's attention to the tubular intracellular processes in this disorder, or rather by lumping them up with those occurring in urine and overestimating the latter. Meanwhile evidence obtained through numerous pathology studies including pioneering by Randall A. [1], Carr J. [2] indicate that the primary tangible event in calculogenesis - forming of so-called microlith- takes place within the epithelial cell of the nephron. Moreover, pathology data imply that mitochondria- the most important energy supply membrane structure of the tubular cell is subject to the first step damage [3, 4]

Prime regulatory role of kidneys impose high requirements to their energy homeostasis. Two main groups of causes change it:

1. Renal tissue hypoxia due to abnormalities of renal circulation of biological liquids (functional and organic).

2. The gap between request for active transport (functional overload by lithogenic substances) and cell power resources.

To maintain power supply of the active transport in these conditions, especially for calcium, the biochemistry of epithelial cell shifts towards activation of anaerobic pathway providing it with power independently of renal oxygenation. However glycolisis is far less efficient, thus leading to intracellular acidosis. This metabolic impairment finally may result in renal tubular acidosis (RTA), incomplete or even complete.

Alteration of cell membrane permeability in acidosis and failure to maintain normal cell-extracellular gradient for calcium do build a basis of microlith. The other word, RTA starting at a cell level becomes a key factor of “pre-stone” stage of NS.

Is it possible to diagnose NS at this stage? Urinary enzyme markers, particularly glycolisis enzymes show increased activity in patients with NS providing indirect evidence of cellular acidosis-mediated derangement, and proved useful in clinical setting [5].

Being the universal biological phenomenon related to the cell death tubular acidosis emerges as a consolidating point for variety of described hitherto factors, intrinsic or exogenous irrespectively. After all, tubular cells homeostasis directly influences lithogenic chemistry of the urine triggering the second - “stone” stage.

In absence of the stage 2 factors (abnormal mucoproteins, inhibiting deficiency, retention and so on) the matrix/microlith will be removed unnoticed, or as a sediment, with or without colic. If stage 2 factors are present they produce stone formation.

Recognition of two stages of the NS, and correspondingly two groups of etiological factors as well as the role of

tubular acidosis in pre-stone stage provide a rationale basis for new diagnostic and therapeutic ideas. Evidently each stage requires it's specific approach. For instance, measures to improve cell oxygenation and substrate supply will probably be beneficial in stage 1.

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Author Information

Andrew S. Krikun, Ph.D.
Chair of Urology, National Medical Academy Of Postgraduate Training

Igor O. Vishnevsky, Ph.D.
Department of Urology, Drohobych City hospital