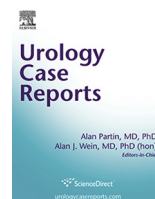


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## Urology Case Reports

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## Endourology

## A Case of Randall's Plugs Associated to Calcium Oxalate Dihydrate Calculi

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## ABSTRACT

A case of a patient who developed multiple calcium oxalate dihydrate calculi, some of them connected to intratubular calcifications (Randall's plugs), is presented. Randall's plugs were isolated and studied. The mechanism of Randall's plug development is also suggested.

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Randall's plugs

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## Introduction

Renal papillary calcifications may be observed during endoscopic intrarenal surgery for removal of renal stones. Such calcifications can result from two different mechanisms. One type of calcification is a subepithelial calcification (hydroxyapatite) of renal papillae that develops following a pre-existing injury. This calcification (Randall's plaque) is associated with the typical calcium oxalate monohydrate papillary calculi. The other type of calcification forms following occlusion of the openings of the ducts of Bellini by stone-forming crystals (Randall's plug). These calcifications are associated with calcium oxalate dihydrate (COD) calculi, although not all patients with COD calculi develop tubular calcifications. We report a patient who developed multiple COD calculi, some of them connected to Randall's plugs.

## Case presentation

The patient was a 57-year-old woman with a previous history of bilateral nephrolithiasis and spontaneous expulsion of COD calculi. After that, the patient required percutaneous nephrolithotomy (PNL). Her renal calculi and urine samples were obtained and renal

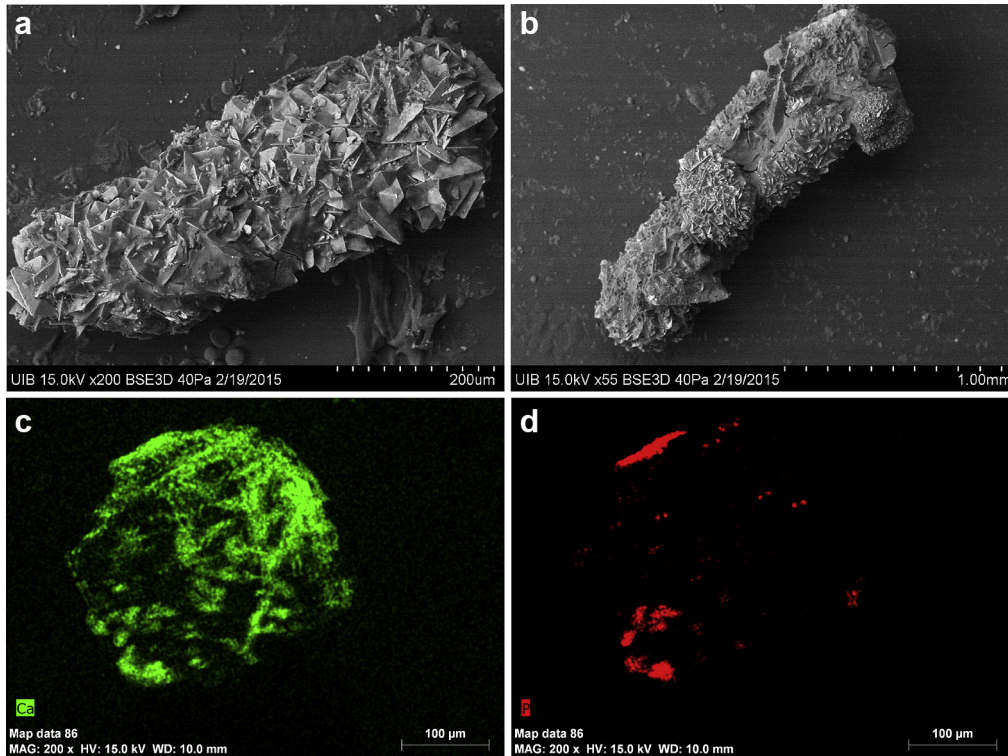
papillae were observed by flexible cystoscope Olympus 16 Ch. Urinary biochemical analysis indicated high concentrations of calcium (9.98 mM), phosphate (32.29 mM), oxalate (0.34 mM) and elevated urinary pH (pH = 6.8). During PNL several typical COD calculi were removed, containing small amounts of biological hydroxyapatite (BHAP). Some of these calculi were connected to the papillary tip, and had connections with the interior of the papilla with finger-like extensions in the collecting ducts. Several of these extensions were recovered as thin rods, predominantly consisting of inter-grown COD crystals of irregular size (30 – 100 μm) with approximately 5% BHAP and organic matter (Fig. 1). We also observed some large COD crystals. The distribution of phosphorus in the plugs was mostly uniform, although a few isolated regions had higher concentrations (Fig. 1). The diameter of rods was ~200 μm, corresponding to the mean diameter of the Bellini ducts. The openings of the Bellini ducts were deformed after stone removal. This study is a retrospective evaluation of clinical information from this patient. The patient provided written informed consent for publication of this information.

## Discussion

The patient had nephrocalcinosis due to the development of tubular plugs. The formation of these plugs in the Bellini ducts is associated with high urinary concentrations of calcium and phosphate and a high pH, as previously described.<sup>1,2</sup> These plugs develop

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**Figure 1.** Plugs blocking the Bellini's ducts, obtained by percutaneous nephrolithotomy (PNL). (a, b) scanning electron microscopy images of Randall's plugs. (c) calcium (green color) and (d) phosphorus (red color) distribution in a section of the plug of (a). Distribution of calcium and phosphorus in the plugs was determined by X-ray energy dispersion spectrometry.

in part as a consequence of the high supersaturation of calcium oxalate and calcium phosphate salts and they can be easily observed radiologically, but rarely have been isolated and observed by scanning electron microscopy, as in the present case. Considering the structure of the observed tubular plugs, it seems that tubular obstruction was not caused by single crystals, although there were some large COD crystals.

Moreover, as not all the Bellini's ducts of the patient were obstructed at the same time, this means that high supersaturation alone is not a determinant factor, and other circumstances should contribute to such obstruction, as for example the stenosis of the Bellini's ducts as a consequence of injuries caused by COD crystals. Such injuries will favor BHAP calcification and attached COD crystals development. Due to the high urinary calcium concentration, the patient also developed several COD calculi.

It is important to emphasize that, calcium oxalate monohydrate (COM) papillary calculi are associated to pre-existent papillary tissue injuries (mainly caused by oxidative stress), that generate subepithelial BHAP calcifications. These calcifications cause the disruption of the papillary epithelial layer by a BHAP plaque (Randall's plaque), that even in contact with urine with normal composition, becomes the nidus of a COM papillary calculus.<sup>3,4</sup> These plaques are initiated in thin-loop basement membranes, in basement membranes of collecting tubules and in vasa recta.<sup>5</sup> Conversely, the Randall's plugs are related to BHAP and COD crystals deposited into the Bellini ducts as a consequence of severe urinary alterations (hypercalciuria, high urinary pH). Randall's

plugs normally affect to both kidneys and are commonly associated to COD or mixed COD/hydroxyapatite renal calculi. Therefore, both Randall's plaques and Randall's plugs correspond to intrapapillary calcifications named nephrocalcinosis, but with a totally different etiology and formation mechanism and also associated to different calculi types.

#### Conflict of interest

The authors declare no conflict of interest.

#### Acknowledgment

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