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# Prostatic calculi: silent stones

*H. Köseoğlu[a,*], G. Aslan[b], B.H. Şen[c], B. Tuna[d], and K. Yörükoğlu[d]*

[a]*Department of Urology, Faculty of Medicine of the University of Başkent, Turkey*
[b]*Department of Urology, Faculty of Medicine of the University of Dokuz Eylul, Esmirna, Turkey*
[c]*Faculty of Dentistry, Ege University, Esmirna, Turkey*
[d]*Department of Pathology, Faculty of Medicine of the University of Dokuz Eylul, Esmirna, Turkey*

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A B S T R A C T

*Introduction and objectives:* Prostate stones are frequently encountered during transurethral resection of the prostate in urology practice. We aimed to demonstrate the physical and chemical properties of prostate stones. We also aimed to determine possible relationship between inflammation of prostate gland and prostate stones.
*Methods:* The consecutive patients (excluding subjects with PSA ≥ 4ng/ml and urolithiasis), who underwent TURP operation and who were observed to have prostatic calculi during TURP, were included in the study. The prostatic stones obtained from each patient during TURP were analysed for chemical composition and observed under electron microscopy (SEM) for structure and surface morphology. The pathological specimens were assessed by the uropathologist for the final diagnosis and existence and degree of inflammation.
*Results:* Five patients were included in the study. From each patient at least three (range 3-8) samples of stones (diameter varying from 1 mm up to 5 mm) were obtained. The stones were made of mixed composition of calcium phosphate and calcium carbonate. The stones were found to have lobular surface made up of small spheres under SEM. Histopathological examination of the TURP specimens revealed benign prostatic hyperplasia accompanied with inflammation of mild to severe degree.
*Conclusions:* Prostatic stones are concentrically precipitated calcium stones within the prostatic ductuli with granular grape-like morphology. Histopathological inflammation seems to be associated with these prostatic calculi.



## Litiasis prostática: cálculos silentes

*Palabras clave:*
Cálculos
Próstata
Hiperplasia prostática

R E S U M E N

*Introducción y objetivos:* En la práctica urológica se encuentran con frecuencia cálculos prostáticos durante la resección transuretral de la próstata. Nuestro objetivo era demostrar las propiedades físicas y químicas de los cálculos prostáticos, así como determinar la posible relación entre la inflamación de la próstata y los cálculos prostáticos.

*Author for correspondence.
E-mail: hikmet.koseoglu@gmail.com (H. Köseoğlu).

Resección transuretral
de la próstata
Microscopia electrónica
de barrido

*Métodos:* Se incluyó en el estudio a pacientes consecutivos (excluidos los sujetos con PSA ≥ 4 ng/ml y urolitiasis) sometidos a resección transuretral de la próstata (RTUP) en quienes se observaron cálculos prostáticos. Se analizó la composición química de los cálculos prostáticos obtenidos de cada paciente durante la RTUP, que se observaron también al microscopio electrónico (MEB) para determinar su estructura y morfología superficial. El uroanatomopatólogo valoró las muestras para emitir el diagnóstico definitivo y determinar la existencia y el grado de la inflamación.

*Resultados:* Se incluyó en el estudio a cinco pacientes. Se obtuvieron de cada paciente al menos tres (de 3-8) muestras de cálculos (con un diámetro de 1-5 mm). Los cálculos tenían una composición mixta de fosfato cálcico y carbonato cálcico. En la MEB se observó que los cálculos tenían una superficie lobular formada por pequeñas esferas. El examen histopatológico de las muestras de RTUP reveló hiperplasia prostática benigna acompañada de inflamación entre leve e intensa.

*Conclusiones:* Los cálculos prostáticos son cálculos de calcio precipitados concéntricamente situados dentro de los conductillos prostáticos con una morfología granular arracimada. Estos cálculos prostáticos parecen ir acompañados de inflamación histopatológica.



## Introduction

Small prostatic calculi are often found during transurethral resection of the prostate (TURP). These stones are generally considered to be clinically insignificant. Such calculi are more often seen with greater depths of resection, as a result of which they sometimes act as a limit to the prostate capsule during TURP. The studies carried out to date on prostatic stones point to the calcification of corpora amylacea as the basis for stone formation[1-3]. The proposed stone formation mechanism comprises urinary obstruction and stasis within the prostate glands, giving rise to calcification of the corpora amylacea and posterior crystal precipitation[1-3]. The importance of prostate stones and their relationship to inflammation have not been sufficiently investigated to date. However, a recent ultrasound study has suggested that larger-size prostate stones could be related to clinical prostatitis[4].

The present study analyzes the ultrastructure and chemical properties of the prostate stones obtained from patients subjected to TURP. In addition, we examine the possible relationship between inflammation and prostatic calculi in the light of current knowledge.

## Materials and methods

The study population consisted of consecutive patients subjected to TURP due to a lack of response to treatment with an alpha-blocker for lower urinary tract symptoms (LUTS) indicative of benign prostate hyperplasia (BPH). We included those patients found to have prostate stones during TURP. We excluded those patients presenting prostate specific antigen (PSA) levels of over 4 mg/ml, those with a history of urolithiasis, and those patients recently subjected to urethral instrumentation or prostate biopsy (in the 3 previous months).

The chemical composition of the stones obtained from each patient was analyzed, and a scanning electron microscope (SEM) study [JEOL JSM 5200 SEM] was carried out to assess their ultrastructure and surface morphology. Before SEM examination, the stones were immersed in 10% sodium hypochlorite for 60 minutes to eliminate the organic remains from the surface. After washing the stones with sterile distilled water, they were fixed on tin supports and placed in a dryer containing phosphorus pentoxide during 72 hours. After the dehydration process, the samples were coated with a gold film measuring approximately 200 Å in thickness. All the samples were examined under a JEOL JSM-5200 scanning electron microscope (Tokyo, Japan) operating at a voltage of 20 kV. Representative photographs were obtained of the stones under different magnifications. The chemical composition of the stones was evaluated by atomic absorption spectrophotometry (Analytikjena novAA 300).

A urological pathologist (KY) evaluated the samples for the diagnosis of the resected tissue and determination of the intensity of the chronic inflammatory process in these TURP specimens. Chronic inflammation was classified as mild, moderate or intense according to the ubiquity and prominence of the inflammatory cells and their location within the luminal space of a duct or gland, and the alterations in gland integrity.

## Results

We included 5 consecutive patients found to have prostate stones during TURP. At least three samples of stones were obtained from each patient (range 3-8, with a total of 24 different calculi). These small stones were randomly located, but were mainly obtained from the proximal region of the veru montanum. The stone diameter varied from 1-5 mm (fig. 1).

The composition of the stones was found to be a combination of calcium phosphate and calcium carbonate, and was the same in all the stones corresponding to the same patient. Under the SEM, the stones presented a lobulated surface composed of

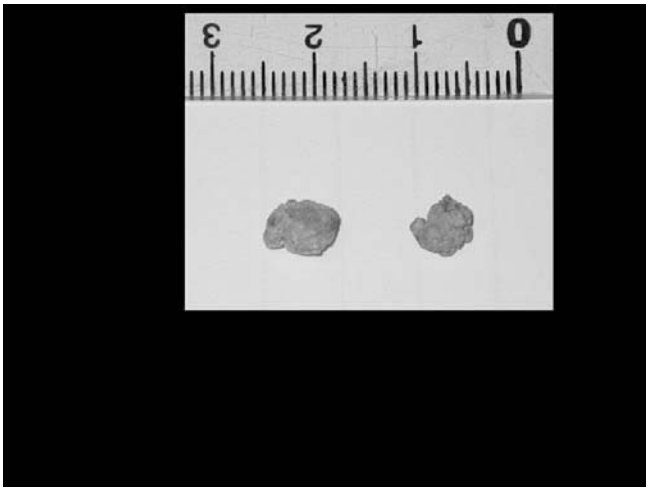

**Figure 1 – Macroscopic appearance of the prostate stones.**

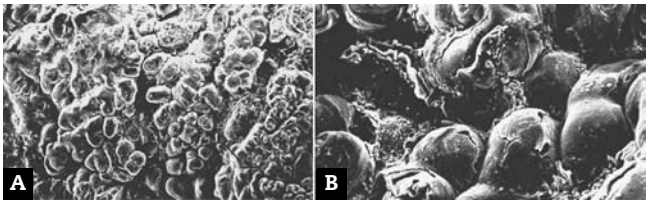


**Figure 2 – Prostate stone surface under the scanning electron microscope: A) ×15 magnification and; B) ×150 magnification.**

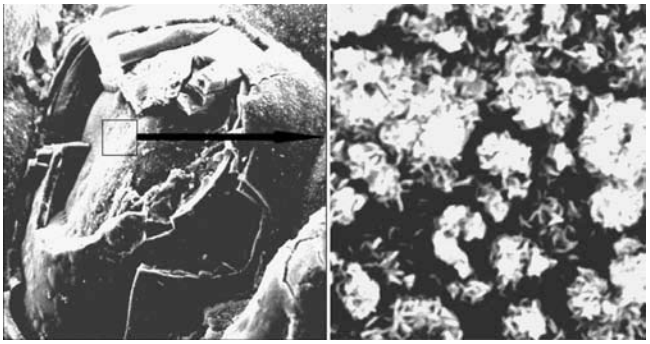

**Figure 3 – Stratified concentric calcification layers (left, ×350 magnification) and crystal formation on the surface (right, ×5000 magnification), seen under the scanning electron microscope.**

small spheres (fig. 2). The cross-sections of the stones under higher SEM magnification revealed crystallizations arranged in concentric calcification layers (fig. 3).

The histopathological study of the TURP samples revealed prostate hyperplasia with mild to intense inflammation (figs. 4, 5 and 6).

All patients with prostate stones underwent intravenous pyelography in search of urinary tract calculi, which proved negative in all cases. None of the patients had a prior diagnosis or history of clinical prostatitis. Likewise, none of

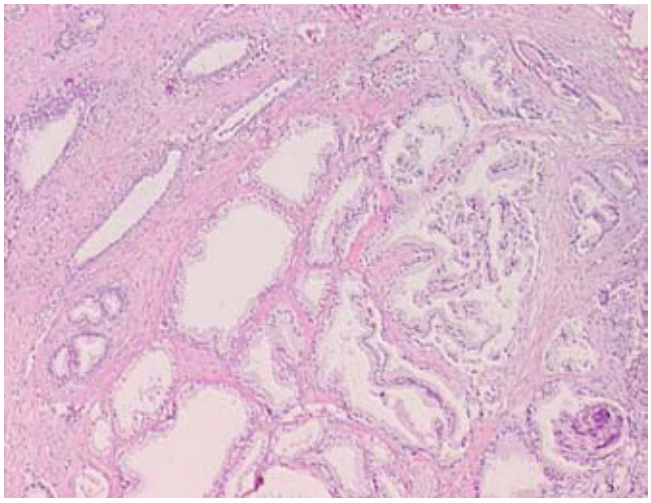

**Figure 4 – Mild inflammation in a TURP specimen (hematoxylin-eosin staining, ×100 original magnification).**

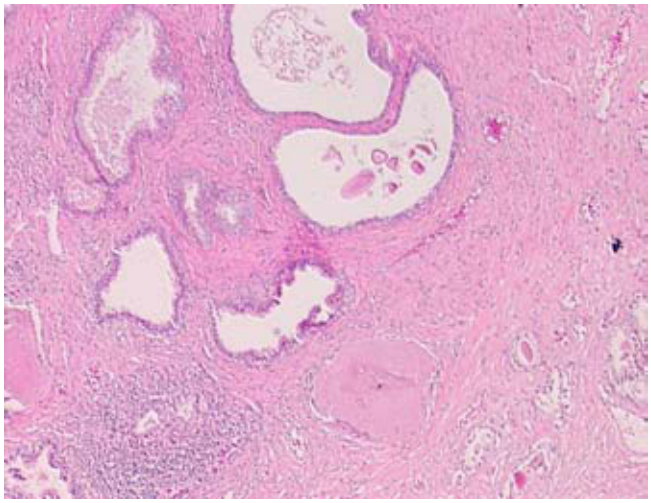

**Figure 5 – Moderate inflammation in a TURP specimen (hematoxylin-eosin staining, ×100 original magnification).**

the patients received antibiotic treatment before TURP. The urine tests revealed no anomalies of importance capable of contributing to stone formation.

## Comment

Although it is very common to find prostate zones during TURP, our knowledge of their physiopathology and of the relationship among inflammation, hyperplasia and prostate infection, is still limited. The present study is one of the few publications on the SEM ultrastructure of prostate calculi, and on their relationship with inflammation and prostate infection.

It has been suggested that these stones are formed as a result of the calcification of corpora amylacea[1-3]. With intraprostatic urine reflux, the depositing of hydroxyapatite

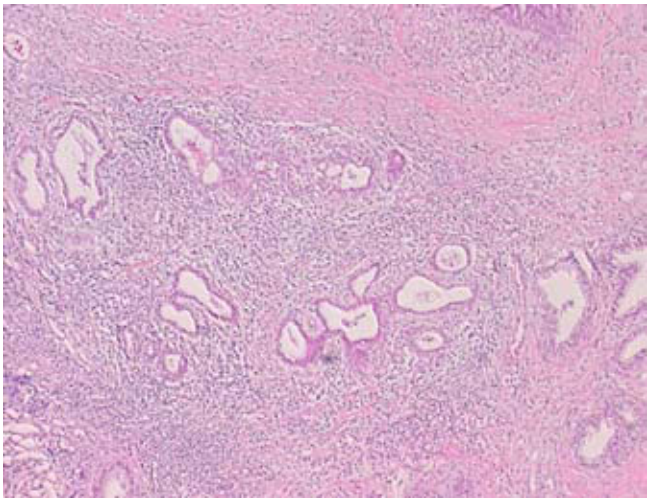

**Figure 6 – Intense inflammation in a TURP specimen (hematoxylin-eosin staining, ×100 original magnification).**

crystals in the corpora amylacea and the mineralization of these bodies with calcium would lead to formation of the prostate stones[3]. On the other hand, any pathological process capable of producing urinary calculi can also generate prostate stones[5,6].

Previous studies have shown that the main component of prostate stones is calcium phosphate or calcium oxalate, together with carbonate-apatite and hydroxyapatite[3,7]. In coincidence with these data, our chemical analyses revealed a combination of calcium phosphate and calcium carbonate. It is important to mention that there were no infected calculi in our series. The data available in the literature regarding the prevalence of prostate stones are inconclusive in this context. In a study of 100 necropsy cases involving microradiographic evaluations, intraprostatic calcifications were found to represent 71%[8]. In that study, the microradiographs revealed stratified concentric calcification layers, in coincidence with our own SEM findings (fig. 3).

Under the SEM, the stones presented a lobulated surface composed of small grape-like spheres (fig. 2). In a previous study, the morphology of prostate stones was divided into two types[9]. One such type corresponded to little stones with a lobulated surface composed of small spheres. The other morphological type corresponded to irregular stones with a rough surface[9]. In our study we also observed the concentric calcification layers within the small spheres of the calculi (fig. 3). Taking into account the proposed mechanism of formation of the stones, with urine obstruction and stasis within the prostate glands, giving rise to corpora amylacea calcification and posterior crystal precipitation, these concentric layers may represent the basis of such stone formation.

Prostate inflammation is a common finding in TURP samples. However, its relationship to benign prostate hyperplasia (BPH) has not been clearly established. In addition, no studies have been made on the overlapping of histopathological prostatitis and non-bacterial clinical prostatitis (NIH 3a-b, 4). It has been seen that the presence of prostate stones does not imply an increase in PSA levels, which do increase with inflammation — thus indirectly suggesting the absence of a relationship between the calculi and increased inflammation[10]. In the necropsy series, the prostatitis component was present in the prostate glands with and without stones, in similar proportions of 51% and 52%, respectively. In our series we likewise found all the samples to show mild to intense prostate inflammation. Intraprostatic reflux may also play a role in prostate inflammation associated to prostate stones[1]. However, it remains unclear whether inflammation is the cause or the result of stone formation. No concrete causal bacterial or viral agent has been found to be related to prostate inflammation. In a recent study using an antinanobacterial antibody, the size of the prostate zones was reported to decrease 50% at ultrasound, with a drop in the chronic prostatitis symptoms index (CPSI)[11]. However, no relationship was observed between the CPSI and the prostate stones or histological grade of prostate gland inflammation[11]. Likewise, none of our patients showed clinical prostatitis or antecedents of infectious episodes. However, our study showed prostate stones to be accompanied by histologically manifest prostate inflammation of variable intensity.

## Conclusion

Prostate stones are composed of concentric calcium precipitates, and are located within the prostate ducts, exhibiting a granular cluster-like morphology. Considering their chemical composition, these are not infectious calculi. Prostate stones appear to be accompanied by histologically manifest inflammation. Nevertheless, further studies are needed to establish the precise relationship between inflammation and prostate stones.

## Conflicts of interest

The authors declare no conflicts of interest.

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