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CASE REPORT

Extensive prostatic calculi in alkaptonuria: An unusual manifestation of rare disease

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Abstract Extensive prostatic calculi in a young man should always elicit the suspicion of alkaptonuria. Although prostatic calculi are seen in chronic prostatitis, chronic pelvic pain syndrome and benign prostate hyperplasia, none of these have prostatic calculi or calcification as extensive as in alkaptonuria. A 36 years young man who had severed obstructive lower urinary tract symptoms with extensive prostatic calculi was found to be alkaptonuric on further evaluation.

1. Introduction

Alkaptonuria is a rare hereditary disease due to inborn error of metabolism in homogentisate 1,2-dioxygenase (HGD) enzyme.This enzyme is involved in the metabolism of the tyrosine. Deficiency in HGD leads to deposition of homogentisic acid and its oxidized product benzoquinone acetic acid (BQA) in the various tissues called as ochronosis. Ochronosis leads to renal and prostatic calculi, sialolithiasis, cholelithiasis, pigmentation of the skin, musculoskeletal abnormalities, and cardiac valve calcification. We present a case of 36 years man who presented with bothersome lower urinary tract symptoms (LUTS) and was found to be alkaptonuric on further evaluation.

2. Case

A 36 years man presented with severe obstructive LUTS. On digital rectal examination prostate was hard and nodular. Flow was a Q_{max} of 2 mL/s for a voided volume of 130 mL and post void residual urine volume of 380 mL. Prostate specific antigen (PSA) was 0.393 ng/mL, while X-ray of pelvis showed punctate calcification in the region of pubic symphysis (Fig. 1), computerized tomography scan of pelvis showed extensive and well calcified areas into the prostatic

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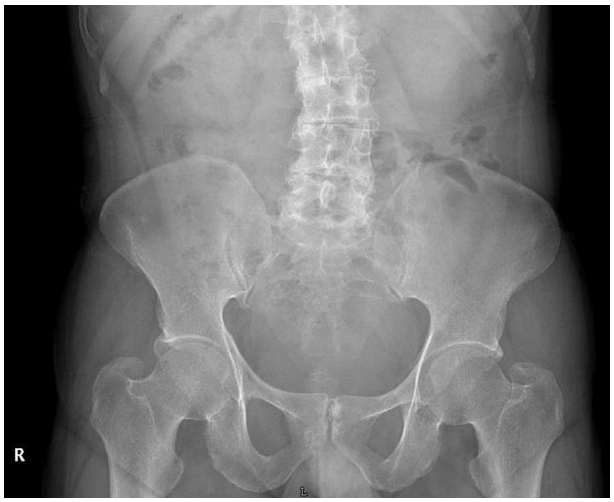

Figure 1 Punctate calcification in the region of pubic symphysis by X-ray of pelvis.

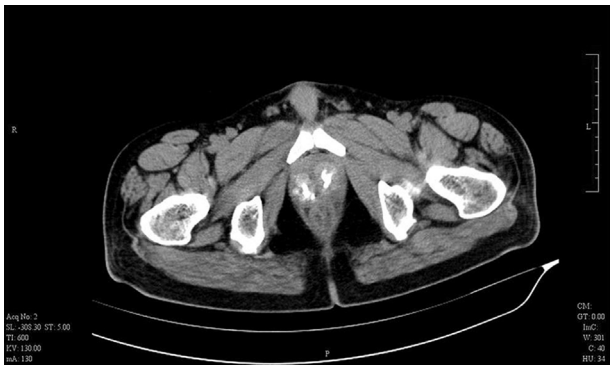

Figure 2 Extensive prostatic calcification by computerized tomography.

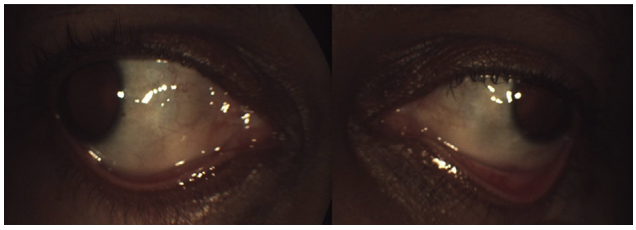

Figure 3 Osler's sign.

parenchyma (Fig. 2). On further evaluation, he gave history of passage of dark colored urine and chronic low back ache. He was short statured with kyphotic spine. Osler's sign (bluish discolouration of sclera) was present (Fig. 3). Biochemical analysis of urine showed the presence of homogentisic acid. These findings confirmed the diagnosis of alkaptonuria. He underwent transurethtral clearance of prostatic calculi which revealed multiple blackish calculi in prostatic urethra and in prostatic fossa (Fig. 4) and clearance of calculi. On biochemical analysis, calculi were composed of calcium oxalate and uric acid.

3. Discussion

Hard prostate is a common manifestation of carcinoma of prostate, but in presence of extensive prostatic calculi and normal PSA level in a young man carcinoma of a prostate should not be serious diagnostic consideration. Prostatic calculi are common with incidence varying from 7.35% [1] to 71% [2] but usually they are asymptomatic and are discovered incidentally. Conditions associated with prostatic calculi are chronic prostatitis, chronic pelvic pain syndrome and benign prostate hyperplasia but none of these have prostatic calculi or calcification as extensive as alkaptonuria. Patients with alkaptonuria have tendency to form stones, because homogentisic acid may act as a chemical irritant, causing inflammation or it is also possible that HGA physically binds to connective tissue and alters the structure and interactions of the macromolecules [3]. In alkaptonuria calculi are also formed in kidney, gall bladder, and salivary glands. Although intraprostatic reflux of urine containing high levels homogentisic acid may be responsible for extensive calcification in prostate, the exact mechanism is not known. Prostatic calculi is one of the manifestations of alkaptonuria and is reported in two reports [4,5] but they were incidental findings and asymptomatic. There is only one report in which patient with alkaptonuria had a hard prostate clinically mimicking a carcinoma, secondary to the diffuse deposition of calculi [6]. In a report by Decramer et al. [7], an alkaptonuric patient had prostatic calculi leading to chronic prostatitis. A thorough search of literature revealed only one case report [8] where patient with alkaptonuria had bothersome LUTS and underwent transurethtral clearance of prostatic calculi but in this report patient was 50 years old.

No treatment modality has been unequivocally demonstrated to reduce the complications of alkaptonuria. Main treatment attempts have focused on preventing ochronosis

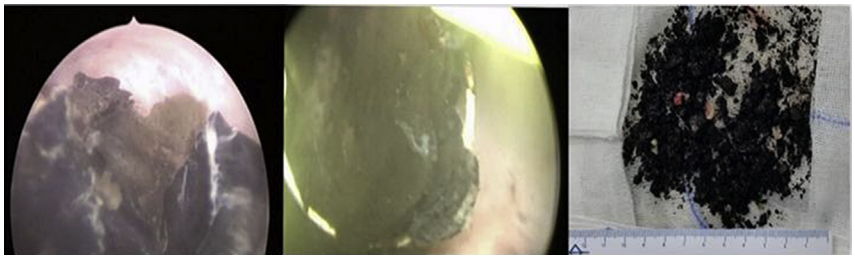

Figure 4 Cystoscopic view of prostatic urethra contaning calculi and postprocedure extracted calculi.

through the reduction of accumulating homogentisic acid. Such commonly recommended treatments include large doses of ascorbic acid (vitamin C) or dietary restriction of amino acids phenylalanine and tyrosine. However, neither vitamin C treatment nor protein restriction (which can be difficult to adhere to) has not shown to be effective in clinical studies [9]. A potential disease modifying drug, Nitisinone, inhibits 4-hydroxy-phenyl-pyruvate-dioxygenase and decreases formation of HGA and could prevent or slow the progression of disease in alkaptonuria [9], but its efficacy is yet to be proved. So treatment of alkaptonuria is symptomatic and palliative in early stages with surveillance for cardiac, renal, and prostate complications. This case of alkaptonuria is unique for its presentation with extensive prostatic calcification. Strong clinical suspicion is required to diagnose alkaptonuria. Although, alkaptonuria (also known as black urine disease, black bone disease) is rare disease with incidence of 1 in 250,000 to 1,000,000 of general population [10] thorough history with physical examination is necessary so that this condition would not remain unnoticed. The paucity of published cases could be due to the fact that many cases would have gone unnoticed or not reported.

Conflicts of interest

The authors declare no conflict of interest.

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