Diagnosis and Management of Uric Acid Nephrolithiasis

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Objective: - The aim is to provide an account of the diagnosis & management of uric acid stones. Material & methods: A search was made on the topic of uric acid stones with regard to the diagnosis & management of uric acid stones. Results: The incidence of uric acid stones varies between countries and account for 5% to 40% of all urinary calculi. Uric acid stone cannot be seen on x-ray. Intravenous urography, CT scan or sonography is required for their diagnosis. This is the only stone that can be reliably dissolved by urinary alkalization with alkali (Bicarbonates, citrate). This medical treatment is highly effective resulting in dissolution of existing stones & prevention of stones. Extracorporeal shock wave lithotripsy and percutaneous nephrolithotripsy can be used successfully for uric acid stones. Open surgery is still performed especially for large complicated staghorn stones. Conclusion: Medical management with urinary alkalization for uric acid stone dissolution and prevention of recurrence is effective.

Key Words: - Uric acid stones, Diagnosis and Management.

The formation of stones in the urinary tract is an ancient disease in the history of humanity.1-3. It achieved importance not only by virtue of its antiquity but also due to its frequency throughout the world.4 The incidence of stone has been estimated to be as high as 12%.5 Pakistan falls in high stone belt area. Urolithiasis is a common ailment in our country. In 1930 Mccarrison cited by Khan6 published his data on the incidence of stone disease in India. He showed that high incidence was in Dera Ghazi Khan followed by Hyderabad & Sukkur. It is believed that highest incidence is in lower Punjab and Northern Sindh7. It is well established that people living in a hot climate have a higher incidence of urolithiasis8.9. It has been partly attributed to low urinary out put (dehydration), hormonal effects (Vitamin D) induce by ultraviolet light and super saturation of calcium salts10.11.12.13. The incidence of calculi in the urinary tract is quite variable in different regions. This result from geographical difference, ethnic variation, the standard of living, diet and employment. There are more cases from the urban as compared to the rural population. Upper urinary tract stone disease in Pakistan occurs at all ages with the peak incidence among 16-20 years and has a high rate of recurrence14.

Kidney stones are formed from crystals of one or other molecules. It may be formed of combinations of elements or rarely protein matrix15. Matrix component of urinary stones varies ranging from 2 to 10% by weight.16 It may serve as a nidus for crystal aggregation and co precipitate in the process of stone formation.17

Uric acid is a common component of urinary stones. It may contribute to calcium oxalate stone formation.19 Gout disease & its association with uric acid has long been recognized. 10 to 20% of the patients with gout are associated with uric acid stones20. Uric acid stones prevalence in patients with ileostomy vary from 50 to 70%.21 These patients tend to pass low volume acidic urine due to losses of fluid and bicarbonates from the gastrointestinal tract.22 Uric acid over production in patients with myeloproliferative disorder, leukemia and hemolytic anemia may be associated with uric acid stones23. Uric acid is an end product of purine metabolism. It is formed in the body from three sources:1) de novo synthesis, 2) diet and 3) tissue metabolism24-25.

Uric acid stones comprise 5 to 8% of all cases of stone disease in western countries26. The frequency of uric acid stones has worldwide variation. Generally, these stones occur in an older population compared with other stone types27. Urate stones have been reported in Pakistan and Iran. The majority of these stones are ammonium and urate28. Uric acid stones are the most common cause of radiolucent stones of urinary tract29.

Three factors are known for uric acid stone formation: acidic urine, hyperuricuria, and decreased urine volume30.31.32.33. The dissociation constant pKa of uric acid is 5.725.34 Thus the solubility of uric acid is pH dependent. Uric acid crystals are relatively insoluble and can precipitate when urinary pH is low.35 All conditions that lead to hyperuricuria, dehydration or low urinary volume will increase uric acid supersaturation and risk of stone formation36

DIAGNOSIS

Symptoms and signs at presentation Pain is the main symptom at presentation. Other manifestation of uric acid stone presentation may be hematuria, urinary tract infection (fever, nausea, vomiting) or renal failure.36 Uric acid stone may be discovered incidentally when patient is evaluated for disease other than urinary tract disease. Detailed medical history is important to identify factors associated with hyperuricuria: Familial Gout, uricosuric medicine, myeloproliferative disorders,37 Lesch Nyhan disease, Polycythemia, Hemolysis, Purine disorder, inflammatory bowel disease, dehydration, renal insufficiency or dietary induced hyperuricuria 

Physical findings
1. No physical finding is sensitive or specific for uric acid stone.
2. Patients with malignancy may have finding such as lymphadenopathy, hepatosplenomegally.
3. Tophi may be present.10

Laboratory Studies
Stone analysis should be obtained. Basic laboratory tests include urinalysis, serum electrolytes, uric acid, creatinine, blood urea nitrogen & calcium. A consistently low urinary pH < 5.5 indicate further evaluation for uric acid stone. An initial 24-hours urine sample collection for analysis of hypercalciuria, hyperuricuria, hyperoxaluria, hypocitraturia, sodium and volume. A spot urine pH should be obtained.16,41,42

Imaging studies:
Uric Acid stone cannot be seen on x-ray. Both xanthine and 2,8-dihydroxyadenine are also radiolucent.43 Patient may present with a radiopaque stone if uric acid is mixed with calcium oxalate or calcium phosphate.44 Renal ultrasonography is effective in identifying the stones. It is painless, noninvasive & patient is not exposed to radiation or contrast. It often is not a good test when stone is in the ureter. However in this case ureter is abnormally dilated.

Computed Tomography (CT scan)
Non contrast computed tomography scanning enhanced is the most sensitive to detect urinary stones.35 It is more sensitive than ultrasound or x-ray. It is performed by placing the patient in x-ray tube. It creates several imaging of kidneys, ureter and bladder. It can detect both calcium and non-calcium stones. In a recent study the mean density of 17 uric acid stones (344±152 hoursfield units) was significantly different compared with 82 calcium oxalate stones (652±490 hoursfield units).46 Uric acid stones appear as a dense image on CT. It can better differentiate uric acid stone from other radiolucent lesion like transitional cell carcinoma, fungal bezoars. Since it scans many organs, it can sometimes detect non-stone causes of pain. Non contrast enhanced CT scan fails to detect indinavir radiolucent stones.47

Intravenous Urography (I.V.U)
It is useful to detect stones in the ureter. A stone appears as a filling defect on imaging.

Retrograde Pyelography
Retrograde pyelography may be necessary to localize stone. It also defines upper urinary tract anatomy.

Treatment
a) Medical treatment
The goal of medical treatment is to dissolve formed stones & prevent new stone formation.42 Medical therapy can be divided into three parts:

1. Urinary alkalinization
2. Decrease urinary uric acid
3. Urinary volume should be >1.5 L in 24 hours.

I. Urinary alkalinization
The goal of urinary alkalinization is to achieve a pH of 6 to 6.5.48,49 Oral alkalinizing agents include sodium or potassium bicarbonate and potassium citrate.50 Citrate is metabolized to bicarbonate. Polycitra contain potassium and sodium citrate and citric acid. Bicitra contains only sodium citrate and citric acid.

Potassium citrate is used in dose of 60 meq in 3 or 4 divided doses. It is available in liquid, tablets and crystal form. It must be mixed with fluid. It should be avoided in patients susceptible to hyperkalemia. The sodium alkali are also used to alkalinize urine.51 Extra care should be taken in prescribing sodium alkali in patients susceptible to fluid overload.58 The sodium load may initiate calcium oxalate stone formation by increasing urinary excretion of sodium & calcium.52 A combination of sodium bicarbonate & acetazolamide proved to be successful in minimizing side effects.53 Orange juice and commercial baking soda can be used. A dose of 1 to 2 tsp thrice a day is generally effective.54

Intravenous alkalinization with one-sixth molar sodium lactate is also effective. Sodium lactate in the solution is metabolized into bicarbonate in one to two hours. Intravenous alkalinization through a percutaneous nephrostomy tube was a common practice in the past. Sodium bicarbonate 2-4 ampoules in one liter of normal saline (pH 7.0 to 9.0) are used for irrigation. Other agents include tromethamine-E and tromethamine (pH 8.0-10.5).55 These procedures require prolong hospitalization and endoscopic manipulation.56

Higher pH values may result in calcium phosphate stones formation and should be avoided.58 Increase fluid intake is recommended in chronically dehydrated patients.59

Decrease urinary uric acid
A diet rich in purines (red meat, fish & poultry) is most common cause of hyperuricosuria. To lower purine intake from food one should avoid liver, kidney, beans, meat, yeast extract and red wine. Also avoid large meal & plan day on three meals i.e. Break fast, lunch, dinner.

Uric acid lowering agents used to decrease the production of uric acid. Allopurinol is a xanthine-oxidase inhibitor. It decreases the production of uric acid & reduce both the serum & urinary levels of uric acid.58 Adult dose is 100-300mg/day. Allopurinol is generally well tolerated, best when taken after meals. Documented hypersensitivity is absolute contraindication. Minor side effects include skin rashes, gastrointestinal irritation, and altered liver function. Safety for use in pregnancy has not been established.41

b) Surgical treatment
Not all urinary tract uric acid stones pass spontaneously. They may not respond to systemic alkalinization. Stones not responding to systemic alkalinization are best managed by extra-corporeal shock wave lithotripsy (ESWL).60 This type of procedure depends on stone size. All lithotripsy modalities are effective in stone fragmentation. Despite the risk of cyanide production from Holmium:YAG lithotripsy of uric acid stone, no evidence of cyanide toxicity was observed.60 Fragmentation of uric
acid stones after ESWL improve oral chemolysis by increasing the stone surface. For the larger stones, both Percutaneous Nephrolithotripsy (PCNL) and ESWL is successful. Open surgery is still reserved for large complicated staghorn calculi.

Conclusion
Medical management with urinary alkalization and simple diet restriction is effective for stone dissolution and prevention. Small stones should be treated with ESWL. Large stones require ESWL, PCNL and open surgery in alone or in combination.

References
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