# Idiopathic hyperuricosuria, hypercalciuria and infantile renal stone disease: new association and therapeutic approach

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**Background:** Urolithiasis in association with idiopathic hypercalciuria (IHC) plus idiopathic hyperuricosuria (IHU) has been reported in older children and adult patients only. IHU plus IHC in association with progressive infantile bilateral renal stone disease has not been previously reported during the first year of life. **Aim:** The aim of this paper is to report the novel association of IHU, IHC and progressive infantile bilateral renal stone disease and also to report our therapeutic approach for this new association, combining traditional treatments of hyperuricosuria (HU) and hypercalciuria (HC) with recently used essential oil terpenes in the management of childhood and infantile urolithiasis. **Patients & methods:** An 8.5-month old boy was referred with bilateral multiple stone disease. He initially presented with excessive crying and irritability since early infancy. The first renal stone was detected using ultrasound and intravenous pyelogram (IVP) at the age of 4 months. On referral, he showed signs of colic with excessive crying. Renal ultrasound showed bilateral multiple stones. 24-h urine examination revealed concomitant significant HU (1.7 g/day) and HC (15 mg/kg/day). 24-h urine oxalate excretion was also mildly elevated (2.9 mg/kg/day). Due to the serious nature of infantile progressive stone disease, the boy was treated with triple therapy consisting of hypocalciuric diuretics, allopurinol and essential oil terpenes with the aim of achieving a stone-free state and preventing renal damage. **Results:** Early symptomatic relief was achieved during the first week of therapy. A stone-free state was achieved after 3 months of treatment without the occurrence of any side effects. **Discussion & conclusion:** IHC and IHU have rarely been association with progressive infantile bilateral renal stone disease. Therapy for this new association with a combination of the traditional treatments of HU and HC with essential oil terpenes may be beneficial.

**Keywords:** idiopathic hypercalciuria, idiopathic hyperuricosuria, infantile stone disease, therapeutic approach

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Idiopathic hyperuricosuria (IHU) and associated idiopathic hypercalciuria (IHC) commonly presents in children with hematuria, and are symptoms suggestive of crystalluria (dysuria and/or recurrent abdominal or flank pain in participants with a family history of urolithiasis). Urolithiasis in association with IHU plus IHC has been reported in older children and adult patients only. In the largest study carried out to date of patients (41) with hypercalciuria (HC) plus hyperuricosuria (HU), a family history of nephrolithiasis was found in 78%. Calculi (>3 mm in diameter) were present in less than 10% of the patients. IHU has previously been reported in only a limited number of children with hematuria. The concomitance of IHC in patients with IHU was associated with significantly less frequent microscopic hematuria but with no difference in prevalence in other clinical or sonographic signs [1–4]. The aim of this paper is to report the novel association of IHU, IHC and progressive infantile bilateral renal stone disease, and also to report our therapeutic approach for this new association, combining traditional treatments of IHU and IHC with recently used essential oil terpenes in the management of childhood and infantile urolithiasis.

## Patients & methods

An 8.5-month old boy (weighing 8.5 kg) was referred with bilateral multiple stone disease. He initially presented with excessive crying and irritability since early infancy. The first renal stone was detected by ultrasound (US) and intravenous pyelogram (IVP) at the age of 4 months. On referral, he showed signs of colic with excessive crying. Renal US showed bilateral multiple stones. There were three stones in the right kidney (RK). One was 10 mm in diameter in the middle pole, and two stones were 5 mm in diameter each and were located in the lower pole. Multiple tiny stones less than 3 mm were detected in

the left kidney. A 24-h urine examination revealed concomitant HU (1.7 g/day, 212.5 mg/kg/day) and HC (15 mg/kg/day). At the 24-h urine analysis, urine volume was 860 ml, calcium was 127 mg, uric acid was 1.7 g and oxalate was 0.025 g. Cyanide niroprusside and monospot tests for cystinuria were both negative. 24-h urine oxalate excretion was also mildly elevated (2.9 mg/kg/day) and urine PH was 5.5. Serum uric acid was 216 µmol/l and serum calcium was 1.16 mmol/l. Due to the serious nature of infantile progressive stone disease, the boy was treated with triple therapy consisting of hypocalciuric diuretic hydrochlothiazide and amiloride HCl as a quarter tablet of Moduretic (Merck & Co.; hydrochlothiazide 25 mg and amiloride 2.5 mg) daily. Allopuriniol 25 mg daily and an essential oil terpene capsule (initially one capsule twice daily for 1 month and than two capsules twice daily) were administered. In addition, essential oil preparations of the terpenic type currently available are shown in **Table 1** [5,6].

The gelatin oily capsules were divided and their contents expressed and administered with sugar before meals. The aim of treatment was to reach a stone-free state and prevent renal damage.

## Results

Early symptomatic relief was achieved during the first week of therapy. A stone-free state was achieved after 3 months of treatment without the occurrence of any side effects. Treatment was associated with a lowering of urinary calcium and uric acid and oxalate 24-h urine analysis after disappearance of all stones showed urine volumes of 685 ml, calcium 83 mg, uric acid 1.3 g and oxalate 0.018 g.

## Discussion

Childhood urolithiasis is generally attributed to metabolic disorders that are associated with recurrence and/or the progression to nephrocalcinosis [7,8]. Surgery and lithotripsy have no effect on these underlying metabolic disorders, either in preventing the recurrence of stone disease or the progression to nephrocalcinosis. Physicians managing children with stones must be conservative with these new techniques and be able to use a variety of methods to provide the most appropriate therapy for a particular situation [9].

Therapeutic experience with this novel association of IHU, IHC and progressive infantile bilateral renal stone disease does not exist at present. However, this case report describes the successful treatment of a patient using a novel regimen consisting of traditional therapies of the underlying metabolic disorders of IHU and IHC with recently used essential oil terpenes in the management of childhood and infantile urolithiasis [10].

Essential oil terpenes, the terpenes contained in the essential oils of many different plants, are a large group of cyclic and noncyclic hydrocarbons with the general formula $(C_5 H_8)_n$. Cyclic terpenes – general formula $(C_{10}H_{16})n$, where n = 2 – are the group commonly used as therapeutics. Enatin was the first essential oil preparation introduced for the treatment of urolithiasis during the 1930s. Essential oil terpene preparations containing monocyclic terpenes (cineol and anethol) and bicyclic terpenes (pinene, camphene, fenchone and borneol) have been registered for use in the treatment of urolithiasis in 50 countries, including developed industrialized countries such as the UK, Italy and Japan [5,6,11,12].

**Table 1. Composition of essential oil preparations of the terpenic type.**

| Preparation | Composition | % |
|---|---|---|
| Pinene | 2,6,6-trimethyl-bicyclo-(3.1.1)-heptane-(2) | 31% |
| Camphene | 2,2-dimethyl-3-mehtylene-bicyclo-(2.2.1)-heptane | 15% |
| Borneol | 1,7,7-trimethyl-bicyclo-(2.2.2)-heptanol | 10% |
| Anethol | 4-methoxy-1-ropenylbenzol | 4% |
| Fenchone | D-1–3,3-trimethyl-bicyclo-(2.2.19-heptanone-(2) | 4% |
| Cineol | 1,8-oxide-*p*-methane | 3% |
| Olive oil | ad | 100% |

## Expert commentary

In this report, a stone-free state was achieved in multiple bilateral stone disease, including one large stone 10 mm in diameter, associated with a complex underlying metabolic abnormality. Spontaneous passage of urinary stones can be expected in 8–80% of children [13]. However, Spontaneous disappearance of multiple bilateral stone diseases associated with a complex underlying metabolic abnormality has rarely been reported in the literature.

## Outlook

IHC and IHU can rarely be association with progressive infantile bilateral renal stone disease. Therapy for this new association with a combination of the traditional treatments of HU and HC with essential oil terpenes may be beneficial.

**Highlights**

- Childhood urolithiasis is generally attributed to metabolic disorders that are associated with recurrence and/or the progression to nephrocalcinosis.
- Surgery and lithotripsy have no effect on these underlying metabolic disorders – they neither prevent the recurrence of stone disease or the progression to nephrocalcinosis.
- Urolithiasis in association with idiopathic hyperuricosuria (IHU) plus idiopathic hypercalciuria (IHC) has been reported in older children and adult patients only.
- Essential oil terpenes have recently been used in the management of childhood and infantile urolithiasis.
- A stone-free state was achieved in multiple bilateral stone disease, including one large stone 10 mm in diameter, associated with a complex underlying metabolic abnormality.

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