Use of Newly Available Febuxostat in a Case of Chronic Tophaceous Gout Contraindicated to Allopurinol and Probenecid

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SUMMARY

Urate lowering therapy in this country has mainly been achieved by the use of allopurinol and probenecid. A new xanthine oxidase inhibitor called febuxostat has been approved in 2009 for treatment of hyperuricaemia in gout. In this report, we describe the management of a patient with chronic tophaceous gout using febuxostat. The reduction in serum uric acid to target levels was rapid, and the tophi size had also reduced significantly while on therapy. There was no unwanted side effect observed during the therapy. Therefore, febuxostat would be a useful alternative drug in the treatment of hyperuricaemia in gout patients who have contraindications to allopurinol and probenecid.

INTRODUCTION

Chronic tophaceous gout is a spectrum of gout that requires urate lowering therapy. Allopurinol and probenecid have been the only drugs used to treat such condition in Malaysia. The use of both drugs is not without risks. Allopurinol is commonly associated with allergy which can be life threatening. It should be used with caution in patients with renal impairment which can occur quite commonly in patient with gout. Probenecid, on the other hand, is contraindicated in the presence of renal calculi which is also a consequence of gout. In this report, we describe a patient with chronic tophaceous gout who was started on febuxostat therapy since he had contraindications to the use of both allopurinol and probenecid.

CASE REPORT

Mr CR, a 59-year old lecturer with 25 years history of gout, presented to the rheumatology clinic, Selayang Hospital for further management of his gout in view of his allergy to allopurinol. He has had intermittent acute attack of gout over the years with the last episode occurring 3 weeks prior to presentation. The pain was mainly affecting his left ankle and left knee, causing him to require daily use of non steroidal anti-inflammatory drugs (NSAIDs). He had been receiving treatment from various private general practitioners for the past 20 years and took alternative treatments for many years e.g. homeopathy and direct selling products. Besides that he also sought cupping and leech therapy regularly (Figure 1).

He developed rashes when he was started on allopurinol 12 years ago which recurred when he was re-challenged. He presented with bladder and renal calculi about 10 years ago, and subsequently underwent lithotripsy. Recently, he still noticed calculi which were being passed intermittently in the urine. He does not have any other medical problem.

On examination, he was alert but in mild residual pain. His blood pressure was 160/90, pulse rate 70 beats/min, and body temperature was 37°C. Musculoskeletal examination revealed arthritis of the left ankle and left knee. Tophi were noted over his left elbow and the left second metacarpophalangeal joint. Examination of other systems was normal.

Investigation showed the following: white blood cell 10.0 x 103/µL, haemoglobin 15.2 g/dL, platelets 375 x 10^3/µL, urea 6.5 mmol/L, creatinine 110 µmol/L, creatinine clearance 67 mls/min, uric acid 505 mmol/L, fasting blood glucose 4.4 mmol/L. Urine studies were normal. Plain radiography of the kidney, ureter and bladder system was normal. Kidney ultrasound showed left renal calculus measuring 1.7 cm, however, there was no hydronephrosis.

He was admitted to the ward for further management and observation in view of starting febuxostat. Low dose colchicine adjusted to his creatinine clearance was given to prevent acute flare during initiation of Febuxostat.

Febuxostat 40 mg once a day was started and 3 weeks later his uric acid level decreased from 505 µmol/L to 265 µmol/L which is about 47% reduction hence achieving the target level of less than 360 µmol/L. He also mentioned that the size of the tophi has decreased significantly while on febuxostat (Figure 2). His blood pressure was controlled with Losartan 50mg once daily which was later changed to Amlodipine 5 mg once daily due to worsening renal impairment. He was referred to Urology for his renal calculi and later underwent extracorporeal shock wave lithotripsy (ESWL).

On follow up review, he remained well and tolerated febuxostat without any side effects clinically and biochemically.

DISCUSSION

The 2008 Malaysian CPG on the management of gout clearly outlines the conditions which require urate lowering

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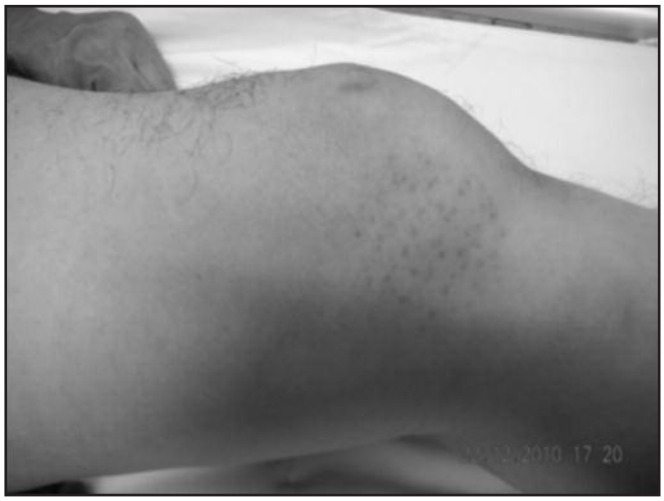

Fig. 1: Cupping and leech marks seen at the medial and anterior sides of the left knee respectively.

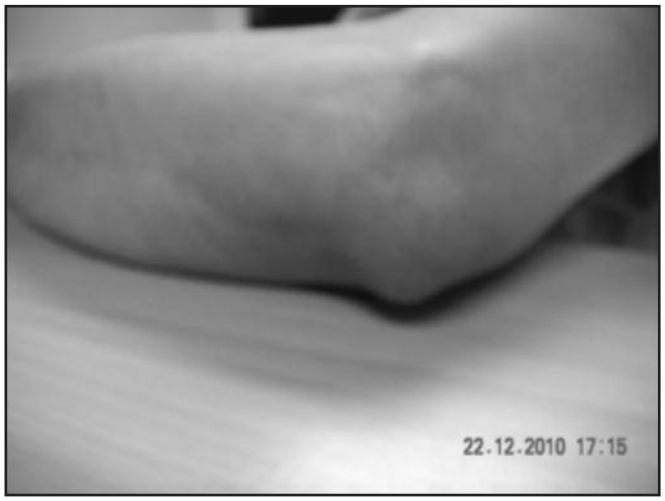

Fig. 2: Tophi at the left elbow.

therapy[1]. Two conditions present in our patient were chronic tophaceous gout and urate nephrolithiasis. The target uric acid level should be less than 360 micromol/L following therapy.

In Malaysia, allopurinol and probenecid have been the only drugs available to lower uric acid levels. Allopurinol, a xanthine oxidase inhibitor, is probably more superior for such purpose[1], however, target uric acid level of less than 360 micromol/L is only achieved in less than 50% of patients taking standard doses of allopurinol[2].

Febuxostat, a new xanthine oxidase inhibitor has been approved for use in gout in 2009. Unlike allopurinol, it is not purine based and is safe to use in patients with renal impairment. Febuxostat 40 mg/day i.e. the lowest starting dose produces a reduction in uric acid levels that is roughly equivalent to that seen in patients treated with allopurinol 300 mg/day[3]. A phase 3 double-blinded controlled trial comparing between febuxostat at doses of 80 mg/day, 120 mg/day and allopurinol 300 mg/day showed that febuxostat was more effective in reducing uric acid level at 3 months[4].

Due to his allopurinol allergy, he has not been on urate lowering drug for the past 13 years. In view that probenecid is contraindicated in this patient as he had mild renal impairment with nephrolithiasis, febuxostat is the only option for him. In a study comparing between febuxostat 40 mg/day, 80 mg/day and allopurinol 300 mg/day, in which 65 percent of subjects in each of the treatment group had mild or moderate renal impairment, febuxostat at either dose was shown to be more effective than allopurinol in reducing the uric acid level to target[3]. Safety was comparable across all treatment groups.

CONCLUSION

Febuxostat, a newly available urate lowering agent should be considered in patients with gout who are contraindicated to allopurinol or probenecid.

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