Rasburicase for Treatment of Severe Tophaceous Gout in a Congenital Cyanotic Heart Disease Patient: A Case Report

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Abstract

Hyperuricemia is one of the long-term complications in patients with cyanotic heart disease. For most cases, conventional urate-lowering agents may be effective enough for hyperuricemia control. However, the treatment effect can be limited, due to chronic renal insufficiency, malignancy or congenital heart disease. We present a 38 year old male who suffered recurrent gouty arthritis with multiple tophi deposition in bilateral hand and spinal joints, but was refractory to several traditional antigout medications. After monthly infusion of Rasburicase for 3 months, serum uric acid level decreased from 7-8 mg/dl to 3-4 mg/dl with decreasing gouty arthritis attack frequency. No obvious allergic reaction or side effect was noted. Rasburicase appears to be a possible therapy for severe refractory gout in congenital cyanotic heart disease patients.

Keywords: severe tophaceous gout, congenital cyanotic heart disease, Rasburicase

Background

Hyperuricemia is frequently observed in congenital cyanotic heart disease.[1] Conventional urate-lowering agents are usually sufficient to lower serum uric acid level. However, some challenging cases may have renal insufficiency and may be refractory to traditional therapy.

Case presentation

This 38 years old male patient has past history of 1. Tetralogy of Fallot (ToF), 2. Chronic kidney disease, stage IIIA, and 3. Infective endocarditis history complicated with severe aortic regurgitation. Physical examination showed grade 4-5 systolic murmur over apex, and grade 3-4 diastolic murmur over right upper sternal border, bilateral basal lung rales on chest auscultation. Multiple tophi deposition was recorded in bilateral wrist, elbow (Figure 1) and lumbar and sacral spine facet joints. Tracing his history, the patient had received several antigout medications, including cholchicine, uricosuric

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agents (benzbromarone) and xanthine oxidase inhibitors (allopurinol, febuxostat) over several years but the disease had progressed and become refractory to conventional treatment. Even with aggressive antigout treatment, his serum uric acid (UA) level was around 7.1-11.1 mg/dl with recurrent gouty arthritis at weekly frequency. Pain score by visual analogue scale was around 6-8 with conventional antigout treatment. Tophi excision with left index and right little finger amputation was performed due to severe bone erosion and osteomyelitis. Considering his uncontrolled hyperuricemia, Rasburicase treatment was initiated (7.5 mg; 0.15 mg/kg). To prevent allergic reaction, methylprednisolone 40 mg and diphenhydramine 30 mg IVD was used prior to Rasburicase treatment.

Figure 1. The patient suffered multiple tophi deposition over bilateral hand joints and had received left index and right little finger amputation in previous osteomyolitis episode.

After Rasburicase treatment, serum UA level decreased from 7.1 mg/dl to 3.6 mg/dl in the first 2 weeks after Rasburicase initiation. Severity of gouty arthritis was improved with pain score decreasing from 6-8 to 3-4. However, serum UA level increased again to 6.3 mg/dl 1month post 1st Raburicase treatment, and secondary and third Rasburicase treatment rounds were started with serum UA level decreasing to 3.5 mg/dl 1 month post the 3rd treatment. There was no significant decrease in the tophi amount and volume during the Rasburicase treatment period. Improvement in gouty arthritis with frequency decreasing from weekly to monthly recurrence was noted. Serum uric acid level was around 3-4 mg/dl 3 months post 3rd Rasburicase treatment without gouty arthritis attack (Figure 2).

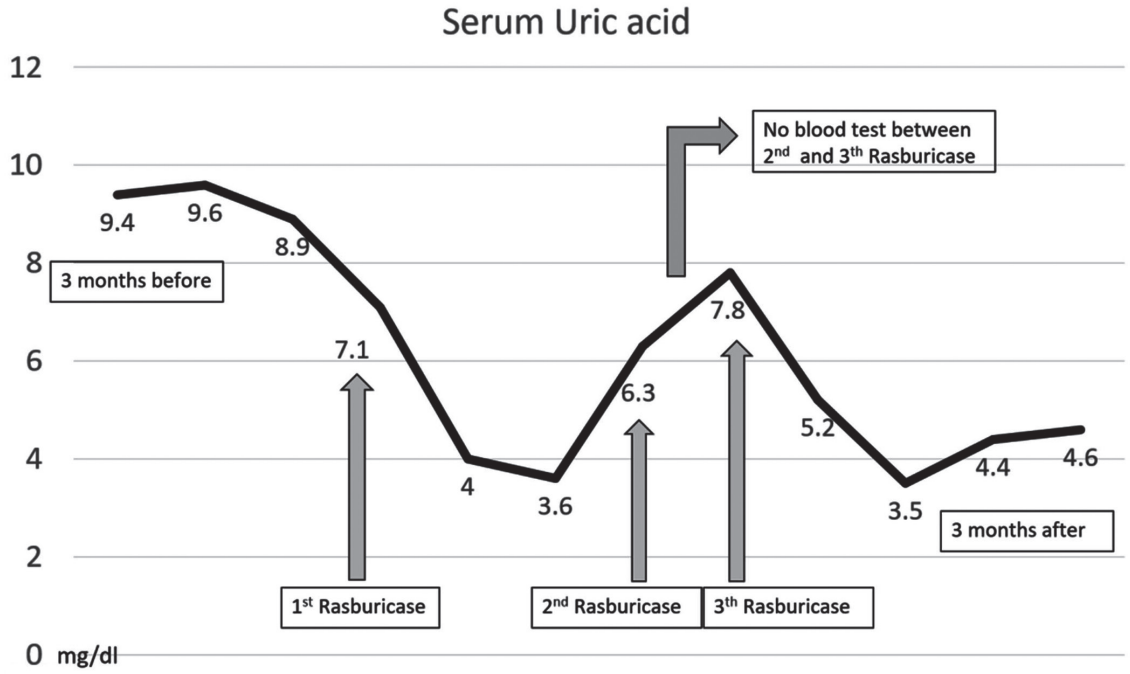

Figure 2. Serum uric acid level during Rasburicase therapy.

Discussion

Rasburicase is a recombinant form of the enzyme urate oxidase, which converts hypoxanthine and xanthine into allantoin. Allantoin is a soluble molecule, which is easily cleared by the kidney. Rasburicase was approved by the FDA for prophylaxis and treatment of acute hyperuricemia in tumor lysis syndrome.[2] Furthermore, successful outcome using Rasburicase to treat severe tophaceous gout has been reported in some case studies.[3,4] A retrospective study (n=10) targeting those unresponsive or intolerant to allopurinol therapy involved monthly Rasburicase infusions over a 6-month period and revealed significant decrease in serum UA levels with decreased tophus area observed in 40% of the study population.[5] The major side effect of Rasburicase is allergenicity (urticaria, bronchospasm, and hypoxemia) and the development of antibodies which compromise the treatment outcome.[2] Another uricase, namely Pegloticase has been recommended by EULAR for treating refractory gout which is non-responsive to conventional treatment.[6] However, Pegloticase is not available in Taiwan.

Tetralogy of Fallot (TOF) is one of the most common cyanotic congenital heart diseases (CHD). It accounts for up to 10 percent of all forms of CHD.[7] Cyanotic heart disease induces secondary erythrocytosis as an adaptation to long term hypoxia. Secondary erythrocytosis can increase the turnover of red blood cells and lead to high purine metabolism and uric acid production.[8] Simultaneously, in chronic cyanosis cases the renal glomeruli can be abnormal, frequently hypercellular and congested, which may eventually lead to sclerosis and ultimately renal function impairment.[9] Impaired renal function will cause abnormal urate clearance which will worsen the hyperuricemia condition. In cyanotic heart disease patients who develop gout, allopurinol or colchicine is preferred, and non-steroidal anti-inflammatory drugs should be avoided considering their impact on renal function.

Conventional urate-lowering agents (allopurinol, febuxostat) were not effective in lowering serum uric acid level in the current study case, and the patient suffered recurrent gouty arthritis with tophi deposition complicated with bone erosion and osteomyelitis. Due to chronic renal insufficiency, the dose titrations of allopurinol and benzbromarone were limited, and hence urate oxidase should be considered as an alternative choice to treat his hyperuricemia. In our case, there was no allergic reaction and a successful outcome with UA level decrease was achieved. Although there was no significant decrease in tophus area in the short period of time, significant decrease in the severity of gouty arthritis was observed. After systematic review of PubMed and Cochrane Library databases, no case report about urate oxidase used in a cyanotic heart patient was found. This report describes the unique case of a cyanotic heart disease patient who suffered hyperuricemia and was refractory to conventional antigout medication, but was treated successfully with Rasburicase, with ideal outcome.

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