中文題目：Rasburicase 用於治療在發紺性心臟病併發之頑固型痛風關節炎《患者》

英文題目：Rasburicase for treatment of severe tophaceous gout in a congenital cyanotic heart disease patient

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Abstract

Hyperuricemia is one of long term complications in cyanotic heart disease patient. In most case, conventional urate-lowering agents may effective enough for control hyperuricemia. However, in some patient, who refractory to conventional therapy and with chronic renal insufficiency may limit the treatment effect. We present a 38 years old male, who refractory to several antigout medication and had multiple tophi deposition in bilateral hand and spinal joint, suffered from recurrent gouty arthritis. A therapy of rasburicase was started, after 3 consecutive monthly infusion, serum uric acid level decreased from 7-8 mg/dl to 3-4mg/dl, and his frequency of gouty arthritis was also decreased. No obvious allergic reaction or side effect was noted. Rasburicase appear to be a possible therapy for severe gout in such cyanotic heart disease patient.

Case presentation

A 38 years old male had suffered from severe tophaceous gout, which was induce by hyperuricemia due to cyanotic heart disease (Tetralogy of Fallot). He also had history of 1.Chronic kidney disease, stage IIIA 2. Infective endocarditis history complicated with severe aortic regurgitation. Physical exam show grade 4-5 systolic murmur over apex and grade 3-4 diastolic murmur over right upper sternal border, bilateral rales breathing sound. Multiple tophi deposition in bilateral wrist, elbow and lumbar and sacral spine facet joint (Figure1.2). He received several antigout medication, including cholchicine, uricosuric agents (benzbromarone) and xanthine oxidase inhibitors (allopurinol, febuxostat) in past several years, however, the patient seem refractory to conventional treatment and hyperuricemia was still noted. His serum uric acid (UA) level under aggressive antigout medication was around 7.1-11.1mg/dl. The frequency of his gouty arthritis was about every weeks. And his pain score by visual analogue scale was around 6-8 under those treatment. He also received several times tophi excision for symptom relief, even left index and right little finger amputation due to severe bone erosion and osteomyelitis. Due to hard to control his hyperuricemia, we decided to prescribe Rasburicase (7.5mg; 0.15mg/kg) for him. Patient was premedicated with methylpredinisolone 40mg and diphenhydramine 30mg IVD for prevent allergic reaction. After we used Rasburicase, his serum UA level was decreasing form 7.1 mg/dl to 3.6 mg/dl in first 2 weeks. His gouty arthritis was improving and pain score was decreasing form 6-8 to 3-4. However, his serum UA level was return to 6.3 mg/dl in following 1 months. Then, he received secondary and third Rasburicase treatment and his serum UA level was decreasing to 3.5 mg/dl. During this period, his tophi amount and mass was no obvious decreasing. However, the frequency of his gouty arthritis was decreasing form every week to month. After 3 times Rasburicase used in 3 months, his serum uric acid level was around 3-4 mg/dl in following 3 months without gouty arthritis attack (Figure 3).

Discussion

Rasburicase, a recombinant form of an enzyme, urate oxidase which converts hypoxanthine and xanthine into allantoin. And allantoin, which is soluble molecule, easily cleared by kidney. Rasburicase was approved by FDA for treatment and prophylaxis acute hyperuricemia in tumor lysis syndrome. (1) Besides, Rasburicase was also been successful used in treatment severe tophaceous gout in some case report (2.3) And a retrospective study (n=10) revealed 6 monthly infusions of rasburicase can significant decrease serum UA level and 40% patient decrease tophus area in patient is unresponsive or intolerance to allopurinol therapy (4). The major side effect of Rasburicase were allergenicity (urticaria, bronchospasm, and hypoxemia) and the development of antibodies which compromise their effectiveness.(1) Other Uricase, like Pegloticase was recommend by EULAR in treating refractory gout, who was poor response to conventional treatment (5). However, Pegloticase was not avalible in our country (Taiwan).

Tetralogy of Fallot (TOF) is one of most common cyanotic congenital heart disease (CHD). It accounts for up to 10 percent of all forms of CHD (6). Cyanotic heart disease patients induces secondary erythrocytosis to adapt long term hypoxia condition. Secondary erythrocytosis can increased turnover of red blood cells and lead to high purine metabolism and uric acid production (7). On the other hand, in chronic cyanosis, the renal glomeruli are abnormal, frequently hypercellular, and congested and eventually become sclerotic which will impair renal function (8). Impair renal function will cause abnormal urate clearance which will worsen hyperuricemia condition. In cyanotic patients who develop gout, allopurinol or colchicine is preferred, nonsteroidal anti-inflammatory drugs should be avoided due to may impair renal function.

In our patient, conventional urate-lowering agents (allopurinal, febuxostat) was not effective to lower serum uric acid level, and the patient suffer from recurrent gouty arthritis and tophi deposition complicated with bone erosion and osteomyelitis even received amputation surgery. Due to the patient also had chronic renal insufficiency, which limited our usage of allopurinol and benzbromarone, in this consideration, urate oxidase is an alternative choice to treat his hyperuricemia. Fortunately, our patient didn’t show obvious allergic reaction and the effect of lowering serum UA level was good. Although the patient didn’t reveal obviously decrease tophus area, but the frequency of gouty arthritis was decrease. Through systematic review of PubMed and Cochrane Library databases, there were no case report about urate oxidase used in cyanotic heart patient. We report this unique case of cyanotic heart disease patient who suffer from hyperuricemia and refractory to conventional antigout medication and safety treat by rasburicase.