รายงานผู้ป่วย

Rhabdomyolysis - induced acute renal failure in polymyositis

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Although patients with polymyositis frequently have rhabdomyolysis, rhabdomyolysis-induced acute renal failure is a rare manifestation of this disease. Herein, we report a case of a 48 year old Thai female presented with proximal muscle weakness, myalgia, and oliguria. Rhabdomyolysis-induced acute renal failure was diagnosed by the markedly elevated levels of serum muscle enzymes, high serum uric acid, a rising of serum creatinine out of proportion to blood urea nitrogen, low serum calcium and a high serum phosphate level. Electromyography and a muscle biopsy revealed the characteristic features of polymyositis. A renal biopsy demonstrated a widespread area of tubular necrosis and a certain degree of interstitial inflammation. The patient underwent hemodialysis until her renal function recovered. High dose corticosteroid was given and she recovered normal muscle power after 2 weeks of treatment. Because of the salubrious response to the appropriate treatment, polymyositis should be sought as a possible underlying disease in patients with rhabdomyolysis-induced acute renal failure.

Key words : *Polymyositis, Rhabdomyolysis, Acute renal failure.*

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ธนันดา ตระการวนิช, สมชาย เอี่ยมอ่อง, เสาวณีย์ เย็นฤดี, มาโนช เตชะโชควิวัฒน์, ชาญ โพชนุกูล, วิศิษฏ์ สิตปรีชา. ภาวะไตวายเฉียบพลันจากกล้ามเนื้อสลายในโพลีไมโอไซติส : รายงานผู้ป่วย 1 ราย. จุฬาลงกรณ์เวชสาร 2538 ตุลาคม; 39(10): 751-759

ถ้าแม้ว่าผู้ป่วยโรค polymyositis จะเกิดกล้ามเนื้อสลาย (rhabdomyolysis) ได้บ่อย แต่พบการเกิดไตวายเฉียบพลันในภาวะนี้ได้ไม่บ่อยนัก ได้รายงานผู้ป่วยหญิงอายุ 48 ปี มาพบแพทย์ด้วยอาการกล้ามเนื้อส่วนต้นอ่อนแรง ปวดกล้ามเนื้อ และปัสสาวะน้อย ได้ให้การวินิจฉัยว่าเป็นภาวะไตวายเฉียบพลันจากกล้ามเนื้อสลาย เนื่องจากผลการตรวจทางห้องปฏิบัติการพบระดับยูริคสูง, ระดับครีอะตินีนในเลือดสูงเป็นสัดส่วนมากกว่ายูเรียไนโตรเจน, ระดับแคลเซียมที่ต่ำและฟอสเฟตที่สูง ร่วมกับการตรวจอิเลคโตรโมโอกราฟี และชิ้นเนื้อของกล้ามเนื้อทางพยาธิวิทยาเข้าได้กับภาวะ polymyositis รวมทั้งการเจาะไตพบการตายของท่อไต (acute tubular necrosis) ผู้ป่วยรายนี้ได้รับการรักษาด้วยการฟอกเลือด และคอร์ติโคสเตียรอยด์ พบว่าการทำงานของไตและของกล้ามเนื้อดีขึ้นเรื่อย ๆ จนสามารถลดระดับคอร์ติโคสเตียรอยด์ลงได้ จึงควรนึกถึงภาวะไตวายเฉียบพลันจาก polymyositis ไว้ด้วย เพราะสามารถให้การรักษาที่จำเพาะได้

Polymyositis is an autoimmune-mediated inflammatory myopathy of unknown cause.[1] Renal involvement in this disorder is uncommon. Although patients with polymyositis frequently develop rhabdomyolysis, acute renal failure caused by rhabdomyolysis is a rare renal manifestation of the disease.[2] Here, we describe a case proven to be polymyositis which developed rhabdomyolysis-induced acute renal failure. Following supportive hemodialysis and corticosteroid treatment, the patient's renal function and muscle power resumed normal status.

Case report

A 48 year old woman who was in generally good health developed abnormal vaginal bleeding four months prior to admission. Initially she did not seek medical advice.

One month prior to admission she experienced progressive muscular weakness with increasing muscle pain. Three weeks later when she saw the local hospital doctor, oliguria had developed with dark urine and shortness of breath. The patient was referred to Chulalongkorn Hospital in April, 1994. On physical examination, she was found to be mildly pale, had tachypnea, and mild pitting edema on both legs. Her vital signs included a blood pressure of 140/80 mmHg, body temperature of 37.3° C, respiratory rate of 26 times/min, and heart rate of 90 beats/min. There was evidence of pulmonary congestion. A neurological examination revealed proximal muscle weakness grade III/V and muscle that was tender on palpatation. Deep tendon reflexes were symmetrically decreased. There were neither swelling nor limitations of motion of peripheral joints. There were no skin lesions. The remaining examination was unremarkable.

Laboratory investigations on admission revealed white blood count 13,000/ul, hemoglobin 10.2 g/dL, hematocrit 32%, platelet 30.0 x 10^4/ul, sodium 138 mEq/L, potassium 5.16 mEq/L, chloride 108.2 mEq/L, and bicarbonate 16 mEq/L.

Blood chemistry included blood urea nitrogen 126 mg/dl, creatinine 16.7 mg/dl, uric acid 20.2 mg/dl, calcium 6.5 mg/dl, inorganic phosphate 15.4 mg/dl, and albumin 2.2 mg/dl. There were marked increases in the levels of muscle enzymes, including lactate rogenase dehyd (LDH) 1528 u/ml, creatine phosphokinase (CPK) 3660 u/ml with the MB fraction of 11% (normal range less than 25%) at the end of first week. Urine examination, taken while the patient was on foley's catheter, showed mild proteinuria with 40-50 red blood cells/high power field. Morphological studies of these erythrocytes were normal, indicating that they were occurred from foley's cathe terization.

Upon admission, she was in oligoanuria with urine output of less than 100 cc/day. Hemodialysis was performed daily in the first week of her admission. The patient underwent a computer tomography of the abdomen which revealed normal size kidneys with no evidence of obstruction. Ultrasonography of the uterus showed myoma uteri which could explain her abnormal uterine bleeding.

Additional laboratory results included a erythrocyte sedimentation rate of 121 mm/hr, negative serum antinuclear antibody and anti-ds D NA antibody. Myoglobin in the blood and urine were not performed. An electromyography (EMG) was performed and revealed characteristic features of inflammatory myopathy. The electromyographic pattern included early recruitment with positive sharp waves, low amplitude

of muscle action potential, and short duration with high frequency discharge (Fig. 1). A muscle biopsy was undertaken and showed atrophic fibers with inflammatory cell infiltrations indicating the existence of inflammatory myopathy (Fig. 2). The diagnosis of polymyositis was made and corticosteroid at the dose of 1 mg/kg/day was given. Two weeks later her renal function and muscle power were vastly improved with blood urea nitrogen level of 38 mg/dl and creatinine level of 3.4 mg/dl. At that time, urine output was around 1,500-2,000 cc per day. Six weeks after admission she was discharged with normal renal function and normal muscle enzyme levels. A kidneybiopsy performed one week before discharge revealed distinct areas of tubular necrosis (Fig. 3). The epithelial lining of the tubules was flattened due to the process of regeneration. The tubular lumen was plugged with necrotic tubular cell debris. Several segmented neutrophils were also noted in some tubular lumen. Hemoglobin casts were not demonstrated. The mesangial cellularity was normal in all glomeruli and the capillary walls appeared normal.

One month after discharge from the hospital the patient continued to feel well. Prednisolone therapy was tapered off according to her clinical condition. Blood urea nitrogen, serum creatinine, and muscle enzymes were in the normal range. The muscle power was strong enough to allow the patient to return to work.

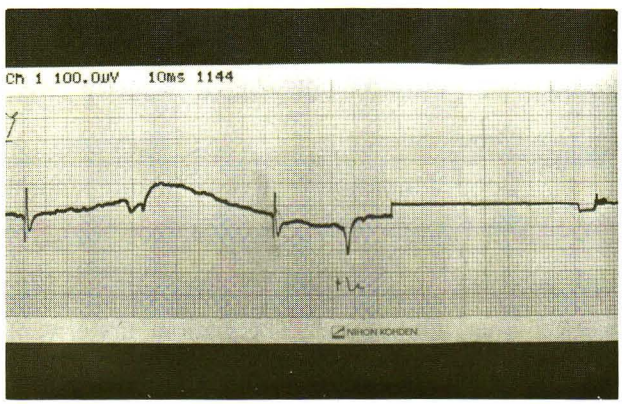

Figure 1. Electromyography of deltoid muscle. This figure depicts small amplitude of muscle action potential. Positive sharp wave is noted.

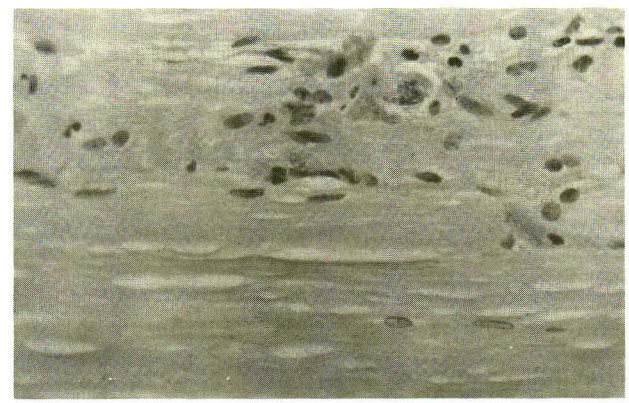

Figure 2. Muscle biopsy of the patient. This figure shows areas of fibrosis and mononuclear cell in the interstitum. Hematoxylin and eosin staining x 400.

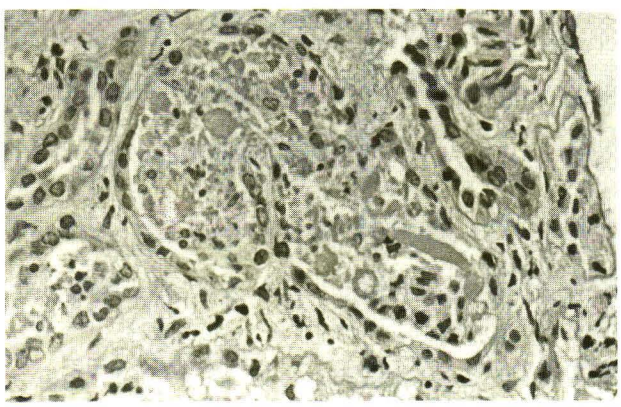

Figure 3. Kidney biopsy. The tubules are dilated with flattened, regenerating tubular epithelial cells. There are some mononuclear cells infiltrated in the interstitium. The tubular lumens are filled with necrotic epithelial cells. All findings are consistent with acute tubular necrosis.

Discussion

Rhabdomyolysis may be associated with myoglobinuria and acute renal failure.[2,3] The etiologies of rhabdomyolsis include trauma or non-traumatic conditions such as congenital myopathies, infections, electrolyte disturbances, hyperpyrexia, toxin exposure, increased muscle exertion, and inflammatory myopathies.[4,5] A case of rhabdomyolysis-induced acute renal failure in polymyositis is presented due to its uncommon occurrence.

Polymyositis is an inflammatory myopathy, the likely underlying of which is autoimmunity.[6,7] Renal involvement in polymyositis is not usually recognized but various forms of glomerulonephritis have occasionally been reported. These include focal or diffuse mesan gial proliferative glomerulonephritis, membranous glomerulonephritis, crescentic glomerulonephritis, focal segmental glomerulonephritis, and lipoid nephrosis.[8,9] Mesangial proliferation is the most common glomerular lesion encountered. Patients who have glomerular involvement usually have proteinuria and/or microscopic hematuria. The pathogenesis was thought to be due to immune complex-mediated tissue damage.[10] These renal diseases respond promptly to corticosteroid therapy.

Acute renal failure, the pathology of which is acute tubular necrosis, is not common in patients with polymyositis. The first two such cases were described in 1924 by Gunther and by Paul[11] but less than twenty reported cases can be found in the a literature review (Table 1). Theoretically, immunologic mechanisms associated with lymphocyte dysfunction is likely the proximate cause of acute renal failure. Following studies have shown that this acute alteration in renal function is related to rhabdomyolysis and myoglobinuria.[15] Indeed, previous studies have demonstrated that patients with dermatomyositis and polymyositis could frequently develop myoglobinemia and myoglobinuria.[13] No relation between the detection of these two parameters and age or sex has been found. Myoglobinemia appears to be more common in patients with dermatomyositis than in those with polymyositis. After the institution of steroid therapy, the occurrence of myoglobinemia declines.[14] Thus, myoglobinemia is a sensititve index of disease activity in polymyositis.

The evidence of rhabdomyolysis-induced acute renal failure in this reported case included elevated muscle enzymes, high levels of serum creatinine out of proportion to blood urea nitrogen, low serum calcium, and high serum phosphate levels. No other causes of acute renal failure could be found in this patient. The underlying disease was proven to be polymyositis according to the electromyography and muscle biopsy. The renal biopsy results were similar to previous reports which showed widespread areas of tubular necrosis with some degree of inflammatory cell infiltration in the interstitium. Myoglobin casts in the renal tissue, however, was absent in this case. This may be due to the long interval between the onset of the illness and the time of the renal biopsy procedure.

The pathogenesis of myoglobinuric acute renal failure remains unestablished.[21-23] Myoglobin can enhance vasoconstriction by inhibiting the production of endothelial relaxing factor.[24]

Table 1. Review of the literature : Myositis-induced acute renal failure.

Author	Diagnosis	Age(sex)	Outcome	BUN (mg per 100 ml)
Gunther and Paul[11]	P	54(M)	---	---
Gunther and Paul[11]	D	42(F)	---	---
Walton and Adams[12]	P	27(F)	Death from ARF	200
Walton and Adams[12]	P	47(F)	Death from ARF and respiratory figures	---
Kagen[13]	D	47(F)	Transient ARF with recovery	141
Kagen[13]	D	47(M)	Transient ARF with recovery	---
Kessler[11]	D	30(F)	Transient ARF, death from respiratory failure	88
Skrabal et al[12]	D	27(F)	Transient ARF with recovery	110
Johnson[15]	P	---	--- ---	
Pirovino[12]	P	33(F)	Transient ARF with recovery	61
Sloan[16]	P	56(M)	Transient ARF with recovery	205
Kreitzer[17]	P	69(M)	Transient ARF with recovery	80
Swainson[18]	P	38(M)	Transient ARF with recovery	101
Misra[19]	P	32(M)	Death from progressive azotemia and overwhelming infection	50
Caccamo[20]	D	25(M)	Death from ARF and respiratory failure	---
Trakarnvanich et al (The present case)	P	48(F)	Transient ARF with recovery	126

--- = No data

P = Polymyositis ; D = Dermatomyositis ; ARF = Acute renal failure

F = Female, M = Male

number in parenthesis following the name of the authors indicates reference number.

Myoglobin itself appears to be non-toxic in animal models, but it becomes highly toxic when dehydration and/or acidemia exist.[25] At or below a urine pH 5.6, myoglobin dissociates into ferrihemate which can depress tubular transport and thus can cause tubular damage from imbalance between the oxygen supply and continued oxygen demand thus resulting in inefficient transport[24]

Previous works have shown that the persistent reduction in glomerular filtration rate (GFR) caused by the decrease in glomerular permeability is mediated by angiotensin II and vasopressin, and by the increase in renal vasoconstriction caused by reduced prostaglandin synthesis. The backleakage of filtrate and obstruction of tubules by cellular debris and pigmented casts also contribute to this persistent reduced GFR.

Previous studies have demonstrated some predictive factors whether or not acute renal failure would develop following rhabdomyolysis. These include the degree of elevation in serum creatine kinase, serum potassium, and serum phosphorus. Other parameters include the depression of serum albumin, dehydration, and sepsis. The high serum creatine kinase and low serum albumin levels observed in our case might be the predisposing factors in developing renal failure.

Treatments of rhabdomyolysis-induced acute renal failure are generally similar to other types of acute renal failure. These include supportive therapy and dialysis when indicated. Treatment of the underlying disease, however, is most important since this can abrogate the process of rhabdomyolysis. Patients with polymyositis, including our patient, have salubrious responses following corticosteroid therapy. Previous study has shown that there is about an 80% 5-year survival rate of patients with polymyositis.[26] Adverse prognostic factors include the long duration of the disease and the severity of muscle weakness at the starting time of treatment.[27]

In conclusion, rhabdomyolysis-induced acute renal failure is an uncommon renal manifestation in polymyositis. The acute deterioration in renal frunction is reversed following appropriate supportive management while the severity of the polymyositis is effectively controlled by corticosteroid. As such, it is suggested that polymyositis should be considered and sought as a potential underlying cause of acute renal failure following rhabdomyolysis.

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