Case Report

Acute renal failure with severe loin pain and patchy renal ischemia after anaerobic exercise caused by rapid resumption after prolonged detraining

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Background: We report a case of acute renal failure with loin pain and patchy renal ischemia after anaerobic exercise (ALPE) caused by sudden training resumption.

Case presentation: A 19-year-old Asian man who was a college American football player presented with severe back pain, headache, and malaise. He developed acute kidney injury without myoglobinuria. Based on the typical medical history and symptoms, we made a diagnosis of ALPE. Symptoms improved within a few days, and serum creatinine levels simproved after discharge. He resumed training, adjusting his load step by step.

Conclusion: During the coronavirus disease 2019 pandemic, many athletes were unable to undergo adequate training. Long-term de-training leads to decreased various organ function and reduces the anaerobic threshold. Rapid resumption after prolonged de-training may put individuals at risk of developing ALPE.

Key words: acute renal failure, ALPE, exercise-induced AKI

INTRODUCTION

ACUTE RENAL FAILURE with loin pain and patchy renal ischemia after anaerobic exercise (ALPE) is a subtype of acute kidney injury (AKI) induced by exercise but without myoglobinuria. The diagnosis of ALPE is mainly dependent on clinical manifestations including severe low back pain and general fatigue after anaerobic exercise such as short-distance sprinting, which are typically present in young males.[1]

The coronavirus disease 2019 (COVID-19) pandemic has led to lockdown in many countries, and athletes were unable to not only participate in competitions but also undergo adequate training. In Japan, a state of emergency was declared from April 7 to May 25, 2020, in the Tokyo area. Many university student athletes had restricted activities during the declaration. We experienced an ALPE case induced by practice after a long absence during the COVID-19 pandemic.

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CASE PRESENTATION

A 19-YEAR-OLD MAN presented to the emergency department in our hospital with a chief complaint of general malaise, headache, and low back pain. He was an American football player in a college team. His medical history was not significant except for minor head injury.

History taking revealed that, owing to the COVID-19 pandemic and nationwide emergency state in Japan, team practice had been suspended for 2 months. Two days before this visit, he finally resumed training including the repetitions of 50-m sprinting. He started to experience headache, back pain, and general fatigue the night after training. His symptoms did not improve, and he visited the emergency department in our hospital.

The vital signs were stable; however, he developed severe back pain and malaise. Table 1 shows his laboratory tests on first visit, which revealed a serum urea nitrogen level of 38.7 mg/dL (normal values: 8–22 mg/dL), creatinine level of 4.77 mg/dL (normal values: 0.61–1.04 mg/dL), and estimated glomerular filtration rate of 15 mL/min/1.73 m^2, indicating stage 3 AKI (Kidney Disease: Improving Global Outcomes or KDIGO).[2] Serum creatinine kinase levels were 259 U/L (normal values: 60–287 U/L). A urinalysis showed a 2+ result for protein and was negative for occult blood. Ultrasonography showed diffuse enlargement of both kidneys without stones or hydronephrosis.

Based on the typical medical history and symptoms, we made a diagnosis of ALPE. He was treated with infusion therapy for the first 3 days of hospitalization; on the fourth day, his back pain resolved. The creatinine level worsened until day 3 (5.73 mg/dL) but then improved, and it was 3.17 mg/dL on day 9. He was discharged on day 10. One month after discharge from the hospital, his creatinine level was 1.14 mg/dL, his serum uric acid level was 0.8 mg/dL, and his fractional excretion of uric acid was 48.5%, suggesting renal hypouricemia.

Although he was informed about the risk of recurrence and renal failure, he wanted to continue playing. He started with aerobic exercises such as jogging, making sure he did not have any symptoms, and then gradually increased the program to include anaerobic exercises. There has been no flare-up of symptoms and he has returned to competition.

DISCUSSION

THE DIAGNOSTIC CRITERIA for ALPE are as follows[3]:

1. Episodes of vigorous exercise (especially anaerobic exercise such as sprinting).
2. Severe loin pain often developing 1–48 h after exercise.
3. Serum creatine kinase levels were within the normal range, or only slightly elevated (no more than 9 times higher than the upper limit of normal).

In addition, renal hypouricemia is crucial for the diagnosis of ALPE. Fifty-one percent of ALPE cases have been reported to occur in patients with renal hypouricemia.[1] In Japan, 0.21% of men and 0.39% of women had hypouricemia.[4] ALPE with renal hypouricemia has normal or mildly elevated levels of serum uric acid during AKI and shows severe hypouricemia below 1.0 mg/dL after the recovery of renal function.[5,6] Patients with renal hypouricemia have a higher risk of development and recurrence of ALPE than those without hypouricemia.[7] If they wish to continue hard sports activity, adjusting the training load under medical advice is important.

In the present case, the athlete developed ALPE on the day he resumed practice after a long period of inactivity. Because of the pandemic, in many countries and regions, a state of emergency was declared, and lockdown orders were issued. Never before has an infectious disease pandemic prevented athletes around the world from practicing for an extended period. His college team suspended all activities, including

Table 1. Blood and urine tests

	Day 1	Day 2	Day 3	Day 5	Day 7	Day 9	Day 23	Day 40	Day 71	Day 162	Day 365
Parameters											
Uric acid (3.4–7.0 mg/dL)	3.9	4.1	3.4	2.9	2	1.9	1.1	0.8	0.9	0.5	0.7
Creatinine (0.61–1.04 mg/dL)	4.77	5.24	5.73	4.78	4.07	3.17	1.36	1.14	1.12	0.97	1.02
Estimated glomerular filtration rate (≧60 mL/min/1.73 m^2)	15	14	12	15	18	24	60	72	74	86	80
Total bilirubin (0.2–1.2 mg/dL)	0.85	1	1.21	0.46	0.5	0.35	0.82	0.55	0.81	0.64	0.37
White blood cell (3100–8400/μL)	11,000	9300	11,000	9200	8500	9900	6700	6300	6200	5100	6200
Proteinuria (–)	2+	+	+	±	–	–	–	–	–	–	–
Urine occult blood (–)	–	–	–	–	–	–	–	–	–	–	–
Urinalysis bilirubin (–)	–	–	–	–	–	–	–	–	–	–	–
Urinalysis pH (5.0–8.0)	6	6	6	6	6	5.5	6	6	6.5	6	6
Fractional excretion of sodium (<1.0%)				2.23	2.89		0.7	0.26	0.73	1.22	0.51
Fractional excretion of urea (5.5%–11.1%)				45.82	56.62	48.24	46.77	48.53	48.43	56.68	56.19

practice from April 7 to June 16, 2020. During this period, he spent almost the entire time at home without training.

As the name suggests, ALPE often occurs after anaerobic exercise. Although the pathogenesis of ALPE remains unclear, it may involve vasoconstriction of the renal arteries.[7] Renal hypouricemia is the most important risk factor for ALPE.[3] Diagnosis of renal hypouricemia is made based on the following three criteria[8]:

1. Hypouricemia with a serum uric acid level of less than 2.0 mg/dL
2. Increase in urinary uric acid excretion rate or uric acid clearance
3. Other hypouricemia can be ruled out.

Mutations in the etiologic genes of renal hypouricemia (*URAT1*/*SLC22A12* gene, *GLUT9*/*SLC2A9* gene), history of ALPE, and family history of renal hypouricemia are reference factors for diagnosis. As shown in Table 1, he had hypouricemia with a serum uric acid level of less than 2.0 mg/dL, and increased uric acid excretion at follow-up. Based on the medical history, we ruled out other diseases causing hypouricemia. With reference to this episode of ALPE, we clinically diagnosed him as having renal hypouricemia. Renal hypouricemia is caused by genetic mutations that lead to decreased function of uric acid reabsorption transporter and increased uric acid excretion. Although the causative genes (*URAT1*/*SLC22A12* gene, *GLUT9*/*SLC2A9* gene) were identified,[9,10] our patient was not tested for genetic mutations. In addition, renal hypouricemia is a congenital disease, and it often goes unnoticed due to the absence of symptoms and is often diagnosed with the onset of ALPE as in our patient.

He was an athlete and routinely engaged in high-intensity training, including anaerobic exercise. Prolonged de-training in athletes has been shown to lead to decreased functioning of the respiratory circulatory system, metabolism, endurance, and muscles. Long-term de-training reduces the anaerobic threshold.[11] A decrease in anaerobic threshold indicates that anaerobic metabolism is likely to occur at the same load of exercise. It is rare for athletes to be unable to train for long time. The sudden resumption of training after 2 months of reduced training may activate anaerobic metabolism to induce vasoconstriction of renal arteries, and develop ALPE. Hence, a gradual resumption of training may reduce the risk of developing the disease. When an athlete who has been off heavy exercise for a long time suddenly presents with renal failure upon resuming training, ALPE should be considered even if the athlete has had no problems with the same level of training in the past.

There is insufficient research on programs for a safe return to play. In order to prevent recurrence, we did the following. We presented information about ALPE to the patient and his family. He explained his disease to his teammates and coaches and asked for their understanding that he could not work on the same program with his teammates, and that he would gradually return to play. The use of nonsteroidal anti-inflammatory drugs and exercising with a cold have been reported to be risks for ALPE.[3] We instructed him to prevent dehydration, to avoid strenuous exercise when he had a cold, and not to use nonsteroidal anti-inflammatory drugs. Two months after the onset, he resumed exercise. He started with aerobic exercises such as jogging. Strength training and sprinting were gradually increased in frequency and volume. Four months after the onset, he returned to the regular exercise level.

CONCLUSION

EVEN FOR well-trained athletes, rapid return to exercise after a long period of de-training could be a risk for the development of ALPE. While resuming sporting activities, gradual resumption of exercise is desirable for particular populations with renal hypouricemia, to reduce the risk of developing ALPE. Athletes, sports coaches, schoolteachers, and primary physicians at emergency departments should be educated on this issue.

DISCLOSURE

Approval of the Research Protocol: N/A.
Informed Consent: Informed consent was obtained from the patient.
Registry and the Registration No. of the Study/Trial: N/A.
Animal Studies: N/A.
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AUTHOR CONTRIBUTIONS

KT: Conceptualization, writing—original draft **MM**, **KE**, **AM**, and **TS**: Writing—review and editing; **HF**: Writing—review and editing, supervision.

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