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Case Report

Acute interstitial nephritis induced by *Solanum nigrum*

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Abstract

Acute interstitial nephritis (AIN) is an important cause of reversible acute kidney injury and pathologically characterized by inflammatory infiltrate in the renal interstitium. *Solanum nigrum* (*S. nigrum*) is a medicinal plant member of the Solanaceae family. Although *S. nigrum* has been traditionally used to treat various ailments such as pain, inflammation, and fever, it has also been reported to have a toxic effect, resulting in anticholinergic symptoms. However, there have been no reports of AIN caused by *S. nigrum*. Here, we report the first case of biopsy-confirmed AIN after ingestion of *S. nigrum*. The patient was successfully treated using corticosteroid therapy.

Introduction

Acute interstitial nephritis (AIN) is an important cause of reversible acute kidney injury and pathologically characterized by inflammatory infiltrate in the renal interstitium [1,2]. AIN occurs in approximately 1% of renal biopsies on evaluation of hematuria and proteinuria. In some studies of patients with acute renal failure, approximately 5–15% demonstrated AIN [2]. Although the pathogenesis of AIN is not fully understood, AIN is likely due to immune allergic disequilibrium, mainly cell-mediated immunity [3], the exact mechanism of which is still unknown. Furthermore, some medications and infections have been reported to trigger such pathologic immune reactions.

Solanum nigrum (*S. nigrum*), of the Solanaceae family, is a weed commonly found in wastelands, old fields, and ditches and traditionally used in Asia to manage and control diabetes [4]. However, it has dose-dependent toxic effects due to solanine, resulting in nausea, vomiting, diarrhea, headache, dizziness, loss of speech, mental confusion, coma, and death [5–7]. However, there have been no case reports of AIN caused by *S. nigrum*.

Here, we report the first case of biopsy-confirmed AIN after ingestion of *S. nigrum*. The patient was successfully treated using corticosteroid therapy.

Case report

A 72-year-old Korean man visited our outpatient clinic for evaluation of generalized edema. He had a 5-year history of hypertension and was taking an angiotensin receptor blocker and diltiazem. He had a 7-year history of diabetes and was taking gliclazide. He had ingested a raw extract of *S. nigrum* as a traditional remedy by mouth at least 2 times/d during the 2 months before admission (Fig. 1). He denied the use of any other medication of supplements except for *S. nigrum*. On admission, his blood pressure was 150/80 mmHg, and body temperature was 37.4°C. His lower extremities demonstrated grade 3 pretibial pitting edema.

Chest radiographs revealed pleural effusion in both lungs. Both kidneys demonstrated elevated renal parenchymal

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echogenicity and were slightly smaller than normal (right kidney, 9.7 cm × 5.3 cm and left kidney, 9.9 cm × 5.9 cm). His blood urea nitrogen and serum creatinine concentrations were 35 mmol/L (reference, 2.8–7.1 mmol/L) and 0.28 mmol/L (reference, 0.05–0.11 mmol/L), respectively. Two months earlier, his serum creatinine concentration was 0.13 mmol/L, and urinalysis showed 1+ proteinuria by a dipstick test, 1–3 red blood cells per high power field, and no cast. The patient's urinary protein excretion was 9.85 g/d on admission. His hemoglobin concentration was 6.7 mmol/L. A complete blood count revealed a leukocytosis of 12,300 /mm^3 (71% neutrophils) and an elevated absolute eosinophil count of 861 /mm^3 (range, 0–450/mm^3). His serum protein level was 4.3 g/dL. The serum concentration of C-reactive protein was 0.64 mg/dL (range, < 0.3 mg/dL). Serological tests indicated that levels of antineutrophil cytoplasmic antibody, antinuclear antibody, complements, and double-stranded DNA were within normal ranges.

Under the clinical impression of acute kidney injury due to AIN, the patient was provided with supportive care. However, renal function did not improve, and urine volume decreased from 2,000 mL/d on admission to 200 mL/d on day 8. In addition, the patient complained of dyspnea. Therefore, hemodialysis was initiated, and we planned a renal biopsy; however, we did not perform the biopsy because of generalized edema.

On day 16, a percutaneous renal biopsy was performed. The biopsy revealed features of AIN, with diffuse interstitial infiltrate of lymphocytes and eosinophils, some of which had invaded the tubular cells (Fig. 2). Some tubular atrophy and interstitial fibrosis were also observed but were not characteristic. There were no specific findings on electron microscopy or immunofluorescence examination. Oral administration of prednisolone (30 mg) was initiated on day 20 on the basis of the biopsy findings. After steroid therapy, serum creatinine level and proteinuria decreased to 0.14 mmol/L and 1.3 g/d, respectively, on day 27 (Fig. 3). The dose of corticosteroid was reduced to 5 mg/d over the next 3 months. At the 3-month follow-up, the patient's serum creatinine level was 0.13 mmol/L.

Discussion

We report the first case of biopsy-confirmed AIN after ingestion of *S. nigrum*, for which renal replacement therapy was required. After corticosteroid therapy, the patient's serum creatinine level and proteinuria returned to baseline levels.

Figure 1. A sample of *Solanum nigrum* ingested by the patient.

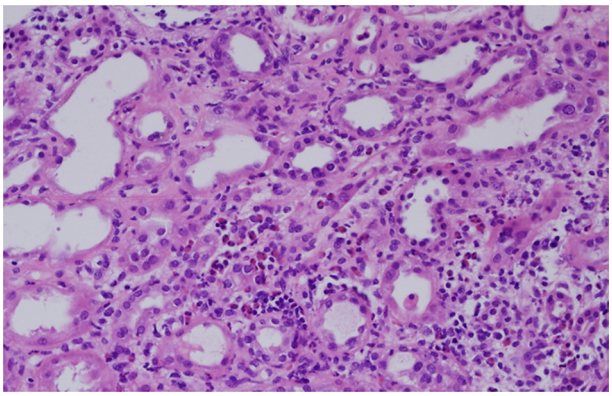

Figure 2. Renal biopsy finding. Interstitial inflammation was composed of eosinophil, lymphocytes and neutrophil infiltration (hematoxyline eosin stain, original magnification ×200).

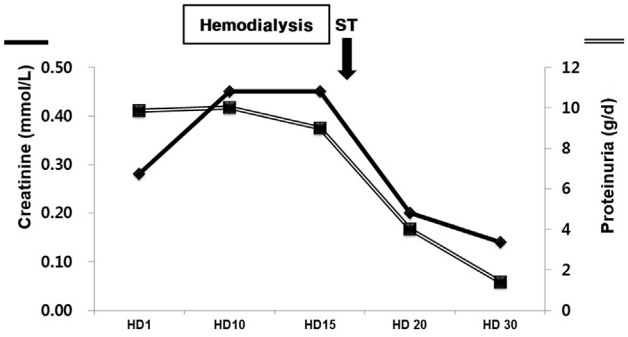

Figure 3. Clinical course of the patient. After immunosuppressive therapy, serum creatinine and proteinuria returned to the baseline levels. HD, hospital day; ST, steroid therapy.

S. nigrum, commonly known as Makoi or black nightshade, grows as a weed in a variety of environments, including dry, stony, shallow, and deep soils [4,5]. Although the exact mechanism of action remains unclear, *S. nigrum* is widely used in many traditional medicine systems for the treatment of various diseases [6,8]. However, *S. nigrum* has not received attention for modern therapeutic use, and toxic side effects of *S. nigrum* have been reported. The toxicity is primarily due to the presence of solanine and may result in anticholinergic effects, seizure, and coma [5–7]. However, there have been no previous case reports of AIN as a result of *S. nigrum*. To our knowledge, this is the first case of biopsy-confirmed AIN after ingestion of *S. nigrum*.

Symptoms and signs of AIN may be nonspecific and are often absent unless symptoms and signs of renal failure develop [2]. Although it was difficult to relate AIN to ingestion of *S. nigrum* in this case, the association was strongly suspected on the basis of the temporal relationship between kidney injury and *S. nigrum* ingestion. In addition, clinical and laboratory features, such as fever, eosinophilia, and renal biopsy findings provided clues to the cause of AIN. Therefore, we think that the possible mechanism of AIN induced by *S. nigrum* could be associated with immune-mediated mechanism, which is believed to play a significant role in drug-induced AIN.

The mainstay of therapy for drug-induced AIN is discontinuation of the causative agent [9]. The benefit of

corticosteroids in the treatment of AIN remains unproven, and there are no guidelines for the precise dose or duration of corticosteroid use in patients with drug-induced AIN. However, small case reports and studies have demonstrated rapid diuresis, clinical improvement, and return of normal renal function within 72 hours of initial steroid treatment [10]. In this case, we administered oral steroids because renal function of the patient did not recover in spite of supportive care. The response to steroid therapy was dramatic. The patient's serum creatinine and proteinuria improved within 7 days of initial steroid treatment. Therefore, we believe that steroid therapy may be beneficial for the treatment of AIN induced by *S. nigrum.*

In this case, we did not initially perform a kidney biopsy and provided the patient with supportive care. However, renal function worsened, and the patient underwent hemodialysis. The patient underwent kidney biopsy on day 16 after his edema had been controlled via hemodialysis, and he received steroid treatment on day 20. We believe that the patient may have improved more quickly if we had performed kidney biopsy earlier and thus initiated steroid treatment sooner. Therefore, we think that prompt kidney biopsy and steroid therapy should be considered if *S. nigrum* is the suspected cause of AIN.

In summary, we report the first case of biopsy-proven AIN due to *S. nigrum* requiring hemodialysis, in which we successfully treated AIN with corticosteroid therapy.

Conflicts of interest

All authors have no conflicts of interest to declare.

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