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## Acute renal failure due to henna stone ingestion as a remedy of diabetes

### Fallo renal agudo debido a la ingestión de cálculos de henna en el tratamiento de la diabetes

Dear Editor,

In developing countries; traditional, herbal or alternative medicine has huge impacts on patients with chronic diseases. The easy and promised illusion of these products catches attention and drives patients using them. Henna is used traditionally for hair dying and temporary tattooing in Turkey, and many other countries; henna stone also known as German stone is a kind of solid material in which crushed powder form can be used as henna and contains a high amount of *p*-phenylenediamine (PPD)<sup>1</sup> Toxicity of this compound has two

phases in human; first allergic reaction with angioedema and the second systemic phenomena occurs with intravascular hemolysis, rhabdomyolysis, and acute kidney injury. Herein, we presented a case of an elderly woman who ingests henna stone in the hope of treating diabetes and had acute kidney failure requiring hemodialysis treatment without the initial allergic phase.

A 73-year-old woman was brought to the emergency room of Hakkari State Hospital with a one-day history of feeling bad, skeletal muscle pain, dizziness, and disorientation. Two days prior to admission, an herbalist advised her to drink crushed henna stone powder in water for her uncontrolled diabetes and to quit insulins. After she did this, symptoms appeared gradually.

Her examination revealed that she was afebrile, oriented and able to communicate. Her blood pressure was 150/80 mmHg with a heart rate of 104 bpm. There were no

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**Table 1 – Laboratory data of the patient through follow-up.**

	Day 0	Day 1	Day 7	Day 14	Day 20	Day 30
Hb, g/dl	10.8	10.7	11.0	11.9	12.0	11.9
PLT, ×10 <sup>9</sup> /L	190	187	220	250	218	235
LDH, U/L	1315	2470	1900	412	166	198
CK, IU/L	46,903	78,135	8189	988	422	112
Total bilirubin, mg/dL	0.99	0.98	0.66	0.72	0.84	0.69
ALT, IU/L	719	1420	225	131	28	32

signs of allergic reactions or a shortage of breath with oxygen saturation of 95% in room air. In the investigations, hemoglobin was 10.8 g/dL, no leukocytosis and a high C-reactive protein level were measured. The other biochemical tests were creatinine kinase 46903 IU/L, AST 719 IU/L, LDH 1315 IU/L, blood glucose 334 mg/dL, urea 38.4 mg/dL and creatinine 0.75 mg/dL. Although there was no chest pain (diabetes may hide), cardiac markers were high. Chest X-ray, electrocardiogram and echocardiography were totally normal. Urine analysis was mildly positive for protein and blood. Renal ultrasound revealed large kidneys with edema. The patient was hospitalized with the diagnosis of rhabdomyolysis. There were no schistocytes in the peripheral smear, serum total and direct bilirubin levels were normal, Coombs tests were negative; detailed serologies including Brucella and Leptospira and other virologic markers were also negative, an upper abdominal ultrasound revealed the only hepatosteatosis. Normoacidemia with limiting bicarbonate level was found in the arterial blood gas analysis. Cardiac markers were decreased in repeated measures.

We started appropriate intravenous fluids with bicarbonate infusion just from the emergency room to alkalize the urine. At first, she did not have an indication for hemodialysis with normal pH, no electrolyte disturbances or any other clinic situation. But reddish-brown urine and oliguria occurred within 24 h; edema and renal failure increased gradually. We started hemodialysis treatment with a femoral catheter on the third day of hospitalization. 24-h proteinuria was 170 mg/day and urinary sediment was showed one to two white blood cells, one to three red blood cells. Taken into account the most probable diagnosis of rhabdomyolysis, non-severe proteinuria (below 1 g/day), age of patient and harmful side-effects of immunosuppressive treatment, we did not make a renal biopsy or give a corticosteroid. Alternating-day hemodialysis and ultrafiltration provided volume control and after the 7th session of dialysis/ultrafiltration, the patient started to have polyuria, a decrease in CK, LDH and transaminases and also clinical symptoms were relieved. On the 14th day of hospitalization, we withdrew the catheter and she was discharged on 20th day with normal urine output and kidney function. First-month control after discharge, the patient was in a good situation with clinical and laboratory parameters. Initial and follow-up laboratory parameters are shown in Table 1.

In the literature, there are several case reports about PPD toxicity after topical use or suicide attempt. But toxicity occurring after using as a medicine to a specific disease is lesser. Khine YY was reported a man who drank boiled henna leaves for having an unhealthy feeling and Qurashi et al. notified a 32-year-old male had also boiled henna for dyspepsia.<sup>2,3</sup> This is the first case using henna or henna leaf as a cure for diabetes.

The tirade for PPD intoxication includes exposure to PPD (local or systemic), early signs of angioneurotic edema and later acute renal failure. A cohort study from Sudan demonstrated that affected patients were more female, of 83.7% were a suicidal attempt and 53.3% had angioneurotic edema. The need for renal replacement therapy as hemodialysis was 86.7%, fortunately, all patients had full recovery.<sup>4</sup> It should be kept in mind allergic reaction of the upper respiratory system is not a must as seen in our case but life-treating. It may be about the amount of ingested PPD dose. Higher amounts are associated with higher morbidity and mortality rates. The outcome of renal damage is good with early hemodialysis. There is no antidote for PPD, conservative treatment is only the choice in particularly for rhabdomyolysis.

Hemolysis may be a part of the disease and contribute the renal damage. Henna leaf as known *Lawsonia alba* may induce hemolytic crisis in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency.<sup>5</sup> Hyperbilirubinemia, increased LDH and reticulocyte count should be listed in the differential diagnosis. In the case, the patient had dark brown urine and normal serum bilirubin levels led us to rhabdomyolysis rather than hemolysis. We do not have a chance to measure the G6PD level after recovery to certainly exclude.

To conclude, refined henna/henna leaf or a henna stone has a wide-spread usage area, and intoxication may occur in a topical or systemic implementation. Physicians should recognize the material, be aware of the lethality and prognosis. Public knowledge about traditional herbal medicine should be risen immediately to decrease this kind of herb-induced acute kidney injury.

### Informed consent

Written informed consent was taken.

### Conflict of interest

Authors declare no conflict of interest.

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## Etanercept in the treatment of ankylosing spondylitis and nephrotic syndrome in the context of AA amyloidosis: A 48-month follow-up

### Etanercept en el tratamiento de la espondilitis anquilosante y el síndrome nefrótico en el contexto de la amiloidosis aa: un seguimiento de 48 meses

Dear Editor,

Amyloidosis represents a family of diseases characterized by the deposition of proteinaceous material in the extracellular space that, by forming insoluble clusters on various tissues and organs, affects its function.<sup>1</sup> Amyloidosis can be classified as systemic or localized, acquired or hereditary and according to their constitutive proteins.<sup>3</sup> Systemic subtypes consist of primary AL amyloidosis, secondary amyloid A (AA), familial amyloidosis and  $\beta$ 2-microglobulin-related amyloidosis.<sup>1,4</sup> AA amyloidosis is classically associated with chronic infections (essentially in developing countries), inflammatory chronic diseases (such as spondyloarthritis, inflammatory bowel disease and rheumatoid arthritis), periodic fever syndromes, among other examples.<sup>1–4</sup> Clinical and laboratory manifestations depend on the type of amyloidosis and may include, for example, easy bruising, macroglossia, signs and symptoms of heart failure or arrhythmias, hepatomegaly, coagulation disorders or nephrotic proteinuria.<sup>1–3</sup>

We present a case of an older woman with nephrotic syndrome and a previously non clarified inflammatory peripheral arthropathy, with the latter becoming responsible for AA amyloidosis. This 48-month follow-up proves the need and effectiveness of properly treating the underlying disease.

O. G. D., a 78-year-old caucasian woman with a personal history of seronegative peripheral polyarthritis, poor thera-

peutic compliance and corticoid-induced diabetes mellitus, was admitted for etiological study of constitutional syndrome, inflammatory arthralgias, diarrhea and anasarca refractory to oral diuretics. Usual medication included methotrexate, deflazacorte, esomeprazole and tapentadol, folic acid, calcium carbonate plus cholecalciferol and insulin. Denied drug allergies.

The complementary study revealed anemia (normocytic, normochromic) of 9.2 g/dL, normal leukogram, thrombocytosis ( $720 \times 10^9/L$ ), pCr of 1.3 mg/dL, a 24-h proteinuria (Pu) of 10.4 g, severe hypoalbuminemia of 1.4 g/dL, mixed dyslipidemia as well as elevated sedimentation rate (117 mm/h) and C-reactive protein (77 mg/L). Urinary sediment also showed microscopic hematuria (+). Nephrotic syndrome was considered.

In this context, occult neoplasia was excluded. Viral and bacterial screening was negative, as well as autoimmunity. In relation to articular manifestations, there were mostly peripheral joint complaints. However, as it was a seronegative disease (rheumatoid factor and anti-citrulline protein antibodies) and the patient also described low back pain for a long time, this raised the hypothesis of spondyloarthritis, which was confirmed (bilateral radiographic sacroiliitis; antigen HLA-B27 positive) and a definitive diagnosis of ankylosing spondylitis (AS) was established. Intestinal mucosal and renal biopsies revealed amyloid AA deposits (amyloid A protein). Concerning the latter, light microscopy showed amorphous deposition in mesangium and invasion of the basement membrane (Fig. 1, panel A), and congo red evidenced amyloid deposits in glomeruli and small arteries (Fig. 1, panel B). IMF is also available (Fig. 1, panel C). Diffuse tubular atrophy was

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