Acute Kidney Injury and Fanconi Syndrome in the Post-partum Period: A Complication of Over the Counter Use of Ayurvedic Medication

Sir,

In renal tubular acidosis (RTA), the kidney fails to regulate acid homeostasis of the body. This may result from reduced acid clearance from the tubules (distal or type 1 RTA) and decreased bicarbonate reabsorption (proximal or type 2 RTA).[1] Proximal RTA results in urinary bicarbonate wasting and hence an acidic state.[2]

A 22-year-old female, known case of psoriasis presented 8 days post-delivery of her first child, with psoriatic erythroderma. She had been in remission since the start of her pregnancy and had hence not consulted with her dermatologist but was taking off-label prescriptions from some Ayurvedic practitioner for her skin ailment. She had stopped using the topical steroids she was taking for her psoriasis prior to pregnancy out of concern for possible adverse effects on the pregnancy. She had been using the Ayurvedic medication for approximately 12 months. The details regarding the composition or the quantity of the Ayurvedic medication were not available.

Her pregnancy had been uneventful. On examination, her vitals were stable. There were features of dehydration in the form of delayed skin turgor and a dry tongue and oral mucosal surface. Systemic examination including neurological evaluation did not reveal any abnormalities. There was widespread silvery scale like lesions on her skin that involved her entire body surface area with the characteristic “auspitz” sign. She also had acute kidney injury, though she had no urinary complaints (serum creatinine 3.6 mg/dl, blood urea nitrogen of 90 mg/dl). Renal functions had been normal at the time of discharge post-delivery (serum creatinine-0.8 mg/dl, blood urea nitrogen-13 mg/dl). There was compensated metabolic acidosis on the blood gas analysis with a normal anion gap. On ultrasonography, kidney sizes were 10.4 × 4.6 cm on the left and 10.2 × 4.3 cm on the right with maintained cortico-medullary distinction. Urine analysis showed a pH of 4.0, with strongly positive tests for glucose (3+), proteins (3+), along with the presence of phosphates. There were no red blood cells or casts in the urine. 24-hour urinary protein was 1.9 g. Serum electrolyte panel on admission is listed [Table 1]. Urine anion gap was negative.

On giving an intravenous load of bicarbonate, the urine pH rose to 8.6. Uric acid levels were not done as the extensive psoriatic skin lesions were expected to confound results. There was no evidence of haemolysis on the peripheral blood smear. The laboratory features were suggestive of Fanconi syndrome and type 2 renal tubular acidosis.

For further evaluation of the proximal tubular dysfunction, we revisited the history. There was no obvious culprit drug or systemic illness. We decided on a heavy metal screen due to the history of consumption of unlabelled Ayurvedic medicines throughout her pregnancy. This returned positive for high levels of nickel (4.28 ug/L, NR-0.14-1.00), lead (26.39 ug/dL, NR-0-9) and aluminium (166.45 ug/ml, NR <10). We hypothesized heavy metal toxicity to be the cause of generalized proximal tubular dysfunction in this patient. The glycosuria and concomitant diuresis probably led to a volume depleted state and contributed to acute kidney injury in this patient. Another possibility entertained was acute tubulointerstitial nephritis due to the heavy metal toxicity. Her acute kidney injury resolved with supportive management alone in the form of intravenous crystalloids targeted to maintain a central venous pressure of 8-10 cm. Bicarbonate supplementation was started with oral sodium bicarbonate (2.5 g in three divided doses) with oral potassium citrate supplementation (120 mEq of potassium/day). Renal functions recovered by the ninth day of admission (serum creatinine-1.0 mg/dl, blood urea nitrogen-16 mg/dl). She was started on dexamethasone for her psoriasis and later switched to cyclosporine once her acute kidney injury resolved. She made a complete recovery from her flare of psoriasis over 3 weeks. At discharge, serum creatinine and blood urea nitrogen were 0.9 mg/dl and 14 mg/dl respectively. Unfortunately, there have been no follow up visits from her at our hospital.

Type 2 RTA may manifest as an isolated defect in proximal tubular bicarbonate reabsorption or more commonly as a generalized tubular dysfunction, resulting in loss of all substances normally reabsorbed by the proximal tubules. The latter, known as Fanconi syndrome, results in an acidic state along with normoglycemic glycosuria, bicarbonaturia, phosphaturia and aminoaciduria. Proximal RTA occurs in two phases. The first is characterised by transient bicarbonate loss from the proximal tubule which

| Table 1: Electrolytes and arterial blood gas on admission and at discharge |
|-----------------|-----------------|-----------------|
| On admission    | At discharge    |
| Na⁺             | 136 mEq/l       | 142.5 mEq/l     |
| K⁺              | 3.1 mEq/l       | 4.3 mEq/l       |
| Cl⁻             | 112 mEq/l       | 104 mEq/L       |
| HCO₃⁻           | 13.3 mEq/l      | 26.2 mEq/L      |
| pH              | 7.276           | 7.402           |
| iCa²⁺           | 4.3 mg/dl       | -               |
| PO₄³⁻           | 1.6 mg/dl       | -               |
| Spot Urine Na⁺  | 68.5 mEq/L      | -               |
| Spot Urine K⁺   | 16.2 mEq/L      | -               |
| Spot Urine Cl⁻  | 90 mEq/L        | -               |

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IRIS has been documented by renal biopsy as a cause of immune reconstitution inflammatory syndrome (IRIS). Pregnancy is a state of immune suppression and this might be a cause of acute tubulointerstitial nephritis in HIV infected patients. Our hypothesis is that IRIS might be a cause of acute tubulointerstitial nephritis in other conditions as well, such as the postpartum immune reconstitution. However, we did not find any literature regarding renal manifestations of postpartum IRIS. The lack of a renal biopsy limits our ability to assign a definite etiology to the acute kidney injury in our case.

Ayurvedic medicine has been popular for a number of ailments in India, given its traditional roots and a cultural aversion to the so-called artificial drugs used in modern medicine. There is, however, a dearth of quality control and oversight in the manufacturing process of alternative forms of medicine. Studies consistently show high heavy metal content in Ayurvedic medicines. Lead, arsenic and copper in herbal medicines have been documented to be the cause of heavy metal toxicity across multiple case series. Heavy metals in regulated doses are required by the human body but an overdose of the same results in systemic illnesses including RTA. Surveillance of these drugs in terms of their content, over the counter availability and their chronic consumption is pivotal.

Pregnancy is a state of immune shift, with a reversal of Th1:Th2 cells with the Th2 phenotype gaining predominance. This shift results in remission of most autoimmune diseases including psoriasis. This can cause patients of autoimmune diseases to be lulled into a false sense of security regarding their disease leading to non-compliance and resort to alternative forms of medicine. This stems from the fear of potential harm to the mother and the fetus from allopathic medicines.

The cause of acute kidney injury in this case was likely multifactorial. Pre-renal injury could have occurred due to persistent glycosuria and osmotic diuresis that had resulted in a volume depleted state. Acute tubulointerstitial nephritis as evidenced by the acute kidney injury with generalized proximal tubular dysfunction as a result of the heavy metal toxicity is another plausible hypothesis. Heavy metals have been documented to cause biopsy proven acute interstitial nephritis that responds to steroids and withdrawal of the offending agent. Our patient was started on injectable dexamethasone for her flare of psoriasis. The use of corticosteroids along with the withdrawal of the offending agents might have aided recovery from the acute tubulointerstitial nephritis. As already mentioned, pregnancy is a state of immune suppression and this immune function recovers post delivery, which results in flares of autoimmune disease like psoriasis. This is a form of immune reconstitution inflammatory syndrome (IRIS). IRIS has been documented by renal biopsy as a cause of acute tubulointerstitial nephritis across multiple reports.
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