Acute Interstitial Nephritis in a Patient with High Aluminum Blood Levels: A Case Report

Abstract

A known case of hypertension and recent onset diabetes presented to our neurological clinic with symptoms of ataxia, rigidity, and tremors. His symptoms were of relatively recent onset. He gave no history of any renal disease in past. The magnetic resonance imaging of the brain done by the neurologist was suggestive of demyelinating pathology. His renal functions showed progressive deterioration (Cr 1.4 mg/dl about 3 months back to 2.2 mg/dl at present) along with the onset of his neurological illness. An extensive work up for autoimmune encephalitis and paraneoplastic syndrome was noncontributory. A toxicology screen revealed high levels of aluminum in the blood. A renal biopsy showed features of interstitial nephritis and predominant vacuolar injury of the proximal tubule (suggestive of toxic injury.) On further questioning, the patient gave history of using an over the counter native medication. The medication was stopped and weekly desferrioxime chelation advised. A short course of steroids (0.5 mg/kg/day tapering dose for 6 weeks) was also given. The creatinine stabilized to 1.3 mg/dl on follow-up after 3 months. The neurological symptoms also resolved completely.

Keywords: *Acute interstitial nephritis, acute tubular injury, aluminum toxicity*

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Introduction

Aluminum toxicity is rare after universal use of water purification in patients with normal renal functions. The toxicity of this metal is usually seen in patients on dialysis. Studies of occasional aluminum toxicity is noted in patients on parenteral nutrition.[1] We report a case of acute kidney injury and neurological symptoms who was using over the counter native medications.

Case Report

A 67-year-old male with known case of hypertension for 10 years on Losartan and recent onset type 2 diabetes mellitus on Metformin with reasonable blood pressure and sugar control presented with history of loss of appetite, slowness of movements, decreased memory, frequent falls, and swaying to either side while walking for the last 3 months. He also gave a history of loss of appetite associated with nausea, occasional vomiting, and easy fatiguability. For his symptoms, he was taking over the counter indigenous medication for the last 6 months. He was evaluated by a neurologist, who did not notice any significant findings on examination. His cardiovascular, respiratory, and abdominal examination was noncontributory. Neurological examination revealed the presence of ataxia, dysmetria, dysdiadokokinesia, tremors, bradycardia, and mild rigidity. A neurological diagnosis of early Parkinsonson's disease was made and a magnetic resonance imaging (MRI) of the brain was done, which was suggestive of a encepaholapathy. There was no evidence of ischemic changes secondary to age, hypertension, and diabetes mellitus in the MRI [Figure 1]. His paraneoplastic panel and autoimmune markers were not contributory. (autoimmune encephalitis mosaic antibodies and paraneoplastic neuronal antibodies were all negative.)

His initial laboratory investigations showed normal hematological parameters, normal liver function tests, normocalcemia, normal electrolytes, and normal ammonia levels. His serum creatinine was high (2.2 mg/dl). The serum creatinine done 6 months back before starting the over the counter medications was normal at 1.4 mg/dl (normal range for the lab 0.9–1.5 mg/dl). Because of his worsening renal function he was evaluated by a nephrologist also. His

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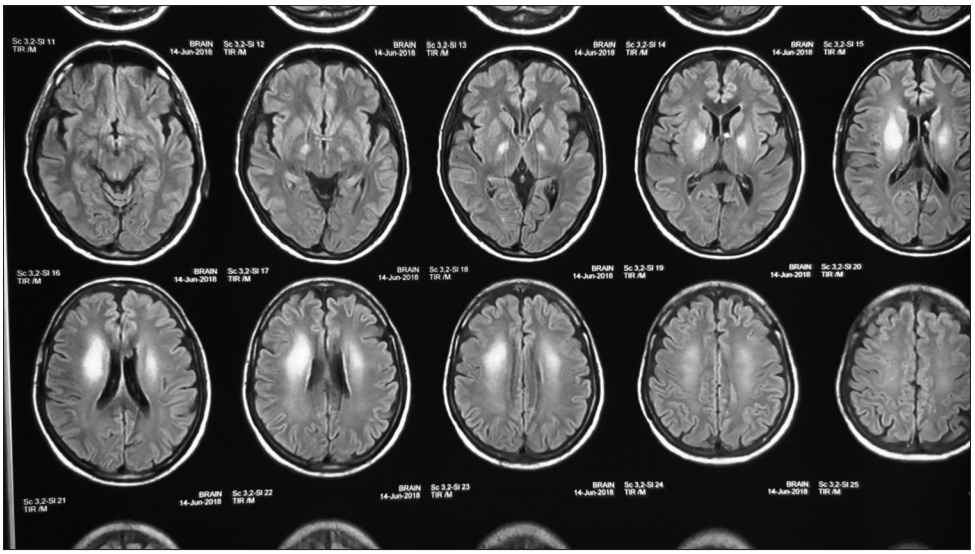

Figure 1: MRI brain showing symmetrical T2/FLAIR hyperintensities are noted in bilateral cerebral peduncles along the cortico- spinal tract, mid pons, bilateral cerebellar peduncles, bilateral cerebellar parenchyma with subtle diffusion restriction predominantly in the pons and centrum semiovale

urine examination was normal and his protein creatinine ratio was within normal range (0.12). His ultrasound of the abdomen revealed normal sized kidneys. He underwent a renal biopsy for unexplained renal dysfunction, which showed normal glomeruli with dense interstitial infiltrate consisting of mononuclear cells and eosinophils [Figure 2]. The electron microscopic examination revealed toxic vacuolation of the proximal tubules [Figure 3]. A diagnosis of interstitial nephritis with toxic proximal tubular injury was made and as the MRI was suggestive of a toxic/metabolic encepahalopathy, investigations were done to find a putative cause. As the basic metabolic evaluation did not reveal any plausible cause, a toxicology screen was asked for. The aluminum levels were above normal in the toxicology screen [Table 1]. Treatment with desferroxime chelation was advised and the indigenous medicine was stopped. One month later the aluminum levels had reduced to 29.4 μg/l and the chelation was continued for another 4 weeks. A course of 6 weeks of low dose steroids (0.5 mg/kg/day) was also given for the interstitial inflammation. Currently, the patient has a normal serum creatinine (1.3 mg/dl) with complete resolution of the neurological symptoms. The cause of cerebral symptoms were believed to be because of aluminum toxicity as the symptoms resolved completely with aluminum chelation and it is speculated that the toxic proximal tubular injury can also be attributed to aluminum.

This patient developed neurological manifestations after 3 months of starting over the counter medications. His creatinine was only checked after 6 months of continuation of the medications. The complete resolution of his neurological and kidney injury simultaneously with the reduced aluminum levels (temporal association) suggests a putative role of aluminum in this patient's illness.

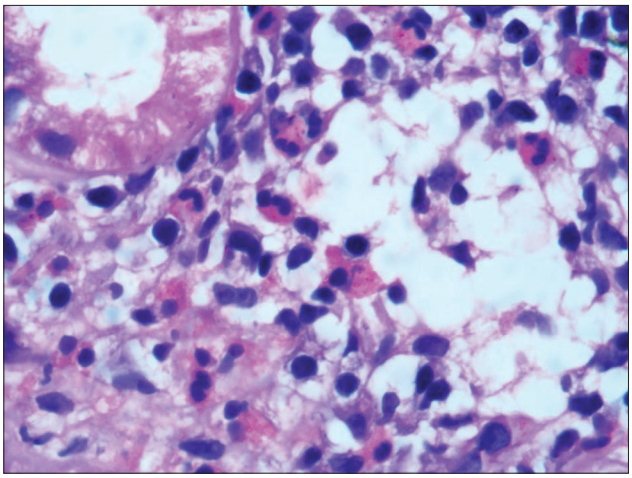

Figure 2: Renal biopsy showing prominent interstitial infiltrate of mononuclear cells and eosinophils

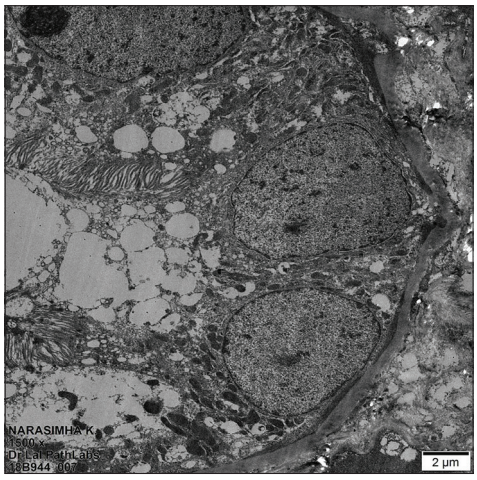

Figure 3: Electron microscopy showing prominent proximal tubular vacuolation

Table 1: Toxicology screening

Laboratory parameter	Observed value	Reference value
Lead (whole blood) µg/dl	2.92	0-9
Chromium µg/L	1.33	0.7-28
Arsenic µg/L	0.89	0.4-11.9
Aluminium µg/L	35.91	<10
Zinc µg/dl	109.54	54-151
Nickel µg/L	0.98	0.14-1.0
Selenium µg/L	79.14	74-90
Mercury µg/L	0.2	0.46-7.5
Copper µg/dl	112.66	74-130
Cadmium µg/L	0.9	0.0-5.0
Cobalt µg/L	0.69	0.01-0.91
Ceruloplasmin mg/dl	25.8	15-35

Discussion

Aluminum is one of the most abundant metal on earth surface and dietary aluminum is ubiquitous. It has no role in physiological process, but being highly reactive, it is a competitive inhibitor of physiological reactions involving iron, calcium, and magnesium.[2] Toxic levels of aluminum usually accumulate in brain, bone, liver, heart, spleen, and muscle. Accumulation usually happens in situations when aluminum bypasses the gut (parenteral nutrition, vaccines, etc), the gut barrier is impeached or when it's renal excretion is impaired. In clinical situations, it accumulates when aluminum containing antacids are used as phosphate binders in chronic kidney disease patients.[3] The majority of reports of aluminum toxicity were seen in patients with renal failure on dilaysis.[4] Aluminum toxicity was commonly observed in dialysis patients secondary to the aluminum in dialysate.[5] With reverse osmosis aluminum toxicity is very rare currently. The classic clinical symptoms of aluminum toxicity included anemia, bone disease, and encephalopathy.[6-8] The mechanisms of aluminum encephalopathy are being studied extensively,[9] but there is no literature of aluminum induced renal injury in the form of interstitial nephritis/tubular injury. We believe the indigenous medication use had a major role to play in the development of interstitial nephritis, but the resolution of renal failure on chelation and subsequent reduction in aluminum levels suggest a putative role of high aluminum levels in acute kidney injury (AKI) in this patient. However, it is important to note that 6 weeks of steroids also might have contributed to the renal recovery. The return of serum creatinine to baseline occurred only after more than 2 months of chelation.

An attempt was made to request the village practitioner to prepare the concoction for laboratory testing. The practitioner declined to provide us with the sample. Hence, this report only highlights the association of development of neurological symptoms and AKI on ingesting a native medication and does not attempt to prove causality. Extensive search for the cause of the acute onset cerebrorenal symptoms revealed a high blood level of aluminum. Significantly, the symptoms resolved on use of chelation.

Further studies are required to understand the role of aluminum in various physiological processes in the kidney to determine whether toxic levels can cause renal damage.

Conclusion

Our patient presented with acute onset neurological and renal dysfunction and had high aluminum levels in blood. With appropriate therapy, both the renal and neurological issues resolved suggesting a putative toxic role of aluminum in the development of acute kidney injury.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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