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CASE REPORT

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A case with unexplained weight loss the underlying cause is aluminum toxicity

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Abstract

Aluminum, is the third most common element in the earth and has a significant toxic effects for humans. Although Al toxicity has been generally reported in dialysis population, it has been demonstrated elevated concentrations of Al was also toxic to non-dialyzed individuals, especially who is working in metal industry. Al toxicity mainly affects nervous system, musculoskeletal system, hematopoietic system and endocrine system. We presented a case who had severe weight loss, memory impairment and had a history of drinking well water. Complete blood count elicited normocytic anemia and other laboratory results proved low basal cortisol level. The toxicological analysis of water and patient's blood sample revealed high Al level, we started desferrioxamine chelation and hydrocortisone replacement. After six month-therapy, anemia ameliorated and cognitive dysfunction was improved. Al toxicity should be thought as a possible diagnosis when a patient presents with unexplained anemia, weight loss, early onset dementia or personality changes.

Keywords: Aluminum toxicity, adrenal insufficiency, weight loss, cognitive dysfunction, early onset dementia

Introduction

Aluminum (Al), as a toxic element is contained in cosmetic products, processed foods, food packaging, drinking water, some drugs such as antiacids and some vaccines [1]. Around 0.1% of orally ingested aluminum is absorbed from the gastrointestinal tract and is made bioavailable. Ingested Al is absorbed primarily from the duodenum and small intestine via passive diffusion, pinocytosis, and transferrin/vitamin D-dependent active transport. Intestinal Al absorption is also affected by Parathyroid hormone (PTH), which increases Al uptake by inducing renal synthesis of 1, 25-dihydroxycholecalciferol [2]. In addition, dietary factors that enhance Al uptake include citric and other organic acids [3]. Al interferes with Fe homeostasis and impairs essential enzymatic reactions, which results in increase labile Fe and rise in reactive oxygen species (ROS), that induces cytotoxicity [3,4]. Al also blocks the production of NADH via TCA cycle [5]. Some studies have shown that dysregulation of mitochondrial metabolism is the key site of the toxicological action of Al [5]. The cut off values for Al toxicity are in serum >5 ng/mL and in urine >15 ng/mL. Al toxicity has been mostly observed dialysis population, patients with chronic kidney disease who is taking Al containing phosphate binder drugs and individuals who is working in metal industry, printing press, automotive industry etc [6]. Seldomly, toxicity can be seen in individuals who is consuming Al contained drinking water and foods unintentionally.

Case

55 years old male patient was admitted to hospital with fatigue and weight loss. His profession was reverend and he stated he had lost weight nearly 40 kg in last 4 years. He had no comorbidity except hyperlipidemia and no history of smoking and alcohol consuming. Physical examination was completely normal, vital signs were as follows; fever: 36.2oC, blood pressure: 90/60 mm Hg, heart rate: 80 beats/min, respiratory rate: 13/min. Electrocardiogram (ECG) was sinus rhythm. He had applied to hospitals several times before came to our admission, thorax CT and abdomen CT had been performed and no pathological finding had been seen. According to his relatives, he had been drinking well water which he described as 'healthy water'. We sent blood specimen and water specimen to Istanbul University-Cerrahpasa, Institute of Forensic Sciences And Legal Medicine, Forensic Toxicology Laboratory

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for toxicological analysis.

His test results were negative for Hepatitis-B, Hepatitis-C and HIV infection meanwhile Quantiferon Tuberculosis was positive. Laboratory results revealed a normocytic anemia [Hgb: 9.3 gr/dL (13.6-17.2), MCV: 91 fl (80-99)] with normal nutritional and iron status, normal parathormon level [63 pg/mL (15-65)] despite low 25-OH vitamin D [6.8 ng/mL (>30)], primary hypothyroidism [T4:0.9 ng/dL(0.93-1.7), T3:2.9 pg/mL(2-4.4), TSH:7 µIU/mL (2.5-5)]

On blood smear test; predominantly lymphocytes, codocytes, normocytic erythrocytes and large platelets were observed. No basophilic stippling of red blood cell was seen.

Due to complain of fatigue, emesis and hypotension, serum basal cortisol level and ACTH checked up and cortisol: 0.067 µg/dL, ACTH >600 pg/mL (sodium and potassium level were normal). He was diagnosed as primary adrenal insufficiency. Hydrocortisone 100 mg (po) q24h was administered.

According to systematic toxicological analysis, Al level in water was: 20.6 mg/L (acceptable value <0.23) and no other organic or inorganic toxic material was found. Serum-Al level: 56.2 ng/mL (Reference value <5 ng/ml). Patient consulted to psychiatrists to evaluate expression reliability and cognitive functions. Referring to difficulty in remembering and forgetfulness, mini mental test was applied and score was 27/30. Elektroencephalogram (EEG) revealed low amplituded activities bilaterally both hemispheres. Contrast-enhanced cranial MR and diffusion MR showed no pathology. Electromyelogram (EMG) exhibited sensory response amplitudes at lower limit and globally slow motor fibers transmission rate with normal amplitudes. Echocardiography (ECO) was performed, no pathological finding was observed. Bone densitometry showed T score was in normal range. We checked anterior hypophysis hormone level and executed a hypophysis sella MR due to the possibility of involving hypophysis gland by Aluminum. Hormone levels were normal and sella MR elicited pituitary midline height loss consistent with partially empty sella. Abdomen MR was performed and revealed a calcification on right surrenal, which could be associated with a previous granulomatous disease. Tuberculosis blood culture resulted in negative; sputum specimen Ehrlich-Ziehl-Neelsen (EZN) staining was also negative.

We checked up serum Al level two weeks later and level was 94 ng/mL. We immediately started desferrioxamine 5 mg/kg intravenosus (iv) once a week. Three days after the chelation, serum Al level was 46 ng/mL. We continued to treatment, as a result anemia was ameliorated and complaints of patient regressed. Serum Al level was followed up periodically and consistent decline was observed as shown in Figure 1. At the sixth month of treatment, we checked up serum and urine Al levels and these were found in order 7.6 and 4.3 ng/mL, also hemoglobin level was 13 g/dL. We stopped chelation treatment and decided to follow up once in three months.

Aluminum analysis by ICP-MS

Quantitative Al analysis was used to determine Al levels both in water and blood samples. Analytical performance parameters was followed according to the previously published study [7]. Water sample firstly analyzed by ICP-MS by diluting 10 times by 2% HNO3 solution and 20 ng/mL internal standards (Indium and Gallium) were added to all samples which collected before and after chelation treatment periodically. Blood samples (500 uL) were digested with 65% HNO3 (500 µL) by heating up to 90oC. Digested samples were diluted by ultrapure water for 10 times and analyzed by ICP-MS. Certified blood samples were also analyzed at the same batch of each analysis and acceptable accuracy was found (>85% Recovery).

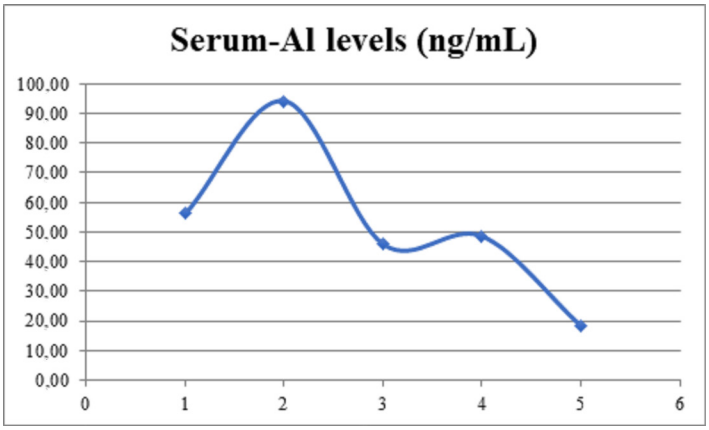

Figure 1. Serum-Aluminum levels of the patient during chelation treatment

Discussion

Al toxicity predominantly affects nervous system, musculoskeletal system, hematopoietic system and endocrine system. Its impact on nervous system to modify hippocampal calcium signal pathways that is crucial to neuronal plasticity. As a result, temporary memory loss, disorientation and in advanced stage dementia can be seen [8]. Additionally convulsion, tremor and motor movement coordination disorders could be findings of Al neurotoxicity. The early signs of neurotoxicity can be observed, as serum Al level is approximately 13 ng/mL and above [9].

Al reduces the erythrocyte lifespan and interferes with hemoglobin synthesis, which result in hypochromic microcytic anemia. Anemia unresponsive to iron replacement can be observed among these patients due to the inhibition of d-aminolevulinic dehydratase, decreased expression of transferrin and impaired intracellular delivery of Fe from transferrin [10].

Al toxicity causes osteomalasia, pathological bone fractures and proximal myopathy. Endocrine system involvement usually presents as impaired function of parathyroid, hypophysis and adrenal gland. Some studies have demonstrated that Al accumulation on adrenal glands resulted in primary adrenal insufficiency [11]. Some studies have shown Al toxicity reduced amount of PTH [12]. Al effects on thyroid gland activity is one of the controversial issues and recent studies have been suggested that although Al inhibited sodium-iodin transport system and impaired secretion of thyroid hormones, it was found statistically insignificant [13].

In our case, some Al toxicity findings as hypo proliferative anemia unresponsive to iron replacement, temporary memory loss and personality changes were observed. Given the association between Al toxicity and developing dementia, mini mental test

was applied but score was normal. Also psychiatric examination revealed no demential sign and cranial MR yielded any aluminum accumulation in brain parenchyma. Nevertheless, EEG showed low amplituded activities bilaterally both hemispheres.

Primary adrenal insufficiency was attributed to accumulation of Al on surrenal gland which was observed as calcification on right surrenal, yet biopsy could not be obtained because patient did not allow us to perform this procedure. Given that TB infection is very common in Turkey, we investigated Quantiferon-TB test and despite a positive Quantiferon-TB test, TB blood culture and and three consecutive morning sputum specimen EZN staining were both negative and thorax CT which had been performed before came to our admission did not reveal any cavity or sequential density could be associated with TB.

Conclusion

In conclusion, adrenal insufficiency is an uncommon cause of unexplained weight loss. Serum cortisol level should be checked up in the coexistence of hypotension and cognitive dysfunction. Al has toxic effects on endocrine system as well as neurotoxicity and toxicity should not be only confined to dialyzed individuals.

Conflict of interests
The authors declare that they have no conflict of interest.

Financial Disclosure
We declare that we do not make any application for financial support.

Patient informed consent
The patient consents to permit all related images and information about his illness and himself as a patient to be published by Medicine Science.

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