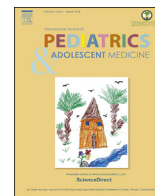


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Use of bone densitometry to assess bone disease in aluminum toxicity complicating parenteral nutrition: A case report

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ABSTRACT

Aluminum toxicity affecting bone mineral density is a known complication of long-term parenteral nutrition. In this report, we describe a similar patient who suffered from bone disease and had a favorable response to chelation therapy using deferoxamine. We believe this may be a possible agent improving the life quality for the above mentioned group of patients.

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1. Introduction

Patients on long-term Parenteral Nutrition (PN) are at risk of Aluminum (Al) toxicity, a condition that was first demonstrated in patients on hemodialysis (due to high Al concentration in dialysis fluids) [1]. Patients at risk of Al toxicity include preterm neonates, patients with compromised renal function, and any patient receiving long-term PN therapy.

One of the multiple complications of Al toxicity is bone disease. It can manifest in multiple forms including delayed longitudinal growth, osteopenia and rickets [2–4]. Bone immunohistochemical studies of these patients showed Al accumulation at the mineralization front [2–4].

As a protective measure, United States (US) Food and Drug Administration (FDA) set 5 mcg/kg/day as the upper limit of acceptable Al exposure. Furthermore, it mandates that products used in compounding PN should note the Al content on the label. Despite this, Poole et al. found that meeting those recommendations were not possible as patients exceeded the safe upper limits by 6–12 times [2,4,5].

In this report, we describe a patient who was on long term PN

and developed Al toxicity. She had a favorable response to deferoxamine, i.e. reducing Al effects on bone. We assessed its efficacy, objectively, using bone mineral density.

2. Case

A 10 year-old- girl was diagnosed to have syndromic diarrhea in early childhood due to typical clinical features and hair electron microscopy. She was on cyclic PN since early infancy (10 years period).

Her PN was prepared at the hospital's pharmacy as a customized PN solution which contained many PN components. She had a history of intermittent hospital admissions with central line infection requiring antibiotics treatment. At 9 years of age, the patient was admitted with gastroenteritis and dehydration and noted to have a high level of aluminum reaching 4.39 $\mu\text{mol/l}$ (Table 1). The patient had no other Al related complications.

Thus our patient received 5 doses of deferoxamine, 300 mg IV (10 mg/kg), as a chelating agent. First 4 doses received on a weekly basis and the fifth dose was received 4 months later. Her bone densitometry one year prior to starting deferoxamine dose showed a lumber spine Z-score of -4.2 . The test was repeated 6 weeks post final dose of deferoxamine and showed a Z score of -3.2 . At that time Al level decreased to 1.6 $\mu\text{mol/l}$. It further dropped to the upper limit of normal (0.4 $\mu\text{mol/l}$) seven months later. In addition to receiving the deferoxamine, PN contents were adjusted to minimize Al toxicity. Unfortunately we could not retrieve the exact

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Table 1
Aluminum level and different trace-elements at different points of time, where 1: at time of highest Aluminum level encountered, 2: time of initial drop in Aluminum post treatment with deferoxamine, 3: time of Aluminum normalization, 4: last readings before patient travelling abroad. Normal ranges: Aluminum (0.00–0.40), Copper (12.6–25.1), Zinc (10.6–19.0), Pre-albumin (0.2–0.4), Albumin (32–48), Selenium (0.89–1.52), Iron (6.0–27.0), Iron saturation (0.08–0.43).

Reading Number	Aluminum (umol/L)	Copper (umol/L)	Zinc (umol/L)	Pre-albumin (gm/L)	Albumin (gm/L)	Selenium (umol/L)	Iron (umol/L)	Iron Saturation
1	4.39	15.1	17.2	0.061	35	1.29	11.2	0.13
2	1.6	18.3	12.2	–	26	1.12	–	–
3	0.4	10.0	11.0	–	29	0.58	–	–
4	0.41	11.5	5.5	–	30	0.46	–	–

TPN Prescription of our patient:	
Cyclic TPN over 12 hours as follows:	
Amino Acid	55 gm
Dextrose	144 gm (~11%)
Na Cl	60 mMol
Na Acetate	30 mMol
K Cl	30 mMol
Calcium Gluconate	11 mMol
Magnesium Sulfate	6 mMol
Multivitamin	3 ml
Pediatric Trace Element	2 ml
Zinc	2 mg
Selenium	40 mcg
Sterile water Q.S. to	1320 ml
Cyclic TPN Rate:	
2100:2200	60 ml/hr for one hour
2200:0800	120 ml/hr for 10 hours
0800:0900	60 ml/hr for one hour
then hold and discard the remainder.	
IV Fat 20% (MCT/LCT): 180 ml over 12 hrs @ 15ml/hr (from 2100-09:00)	
Current TPN provides:	
Amino Acid	~ 2..8 gm/kg/day
IV fat emulsion	~ 1.8 gm/kg/day
Dextrose (TPN + IVF)	~ 10 mg/kg/min
Total Calories	~ 54 Kcal/kg/day (Used Patient weight 20 Kg)

Box 1: latest PN prescription of the patient prior to travelling. Note: RDA was kept as tolerated, in order to minimize hepato-toxicity associated with the long TPN course. It was not possible to maintain the goal due to the following limitations:

- 1) Aluminum toxicity related prolonged TPN course.
- 2) ON/off increase in LFTs

Fig. 1. Latest PN prescription of the patient prior to travelling. Note: RDA was kept as tolerated, in order to minimize hepato-toxicity associated with the long TPN course. It was not possible to maintain the goal due to the following limitations:

- 1) Aluminum toxicity related prolonged TPN course.
- 2) ON/off increase in LFTs.

changes done as the records have been discarded. Subsequently, the patient traveled abroad for social reasons and lost follow up in our hospital (Fig. 1).

3. Discussion

Infants and children are at greatest risk for Al toxicity from long term PN as they have high calcium requirements. In PN, Calcium gluconate has the highest Al contamination [1,6]. Another risk factor is that PN bypasses the gastrointestinal barrier and only 5% of the total Al in PN is ultra-filtrable by the kidneys. The rest is bound to plasma proteins [4,5]. On the other hand, studies have defined variable duration of PN that may increase risk of Al overload, varying from more than 10 days to more than 3 weeks [1,6]. Our patient was far beyond these cut limits.

Although bone biopsy is the only absolute proof of bone overload with Al, high plasma level of Al may indicate high risk of toxicity [1]. However, dual-energy x-ray absorptiometry (DXA) is one of the tests used to assess bone mineralization [3]. It assesses bone mineral density (BMD) using a 2 dimensional image (gm/cm^2) [7]. A Z-score < -2 is considered low. Each -1 drop in the Z score is associated with almost 80% increase in risk of fracture [8]. Thus we used BMD to assess bone disease, objectively and directly, pre and post deferoxamine administration.

Deferoxamine has been used to treat Al toxicity in uremic patients and has resulted in increased bone formation [9]. Doses as low as 2.5 and 5 mg/kg/week, in patients on dialysis, were suggested [10,11]. However doses ranging from 10 to 100 mg/kg have been used as well. It increases Al removal during dialysis by forming a dialyzable low molecular weight aluminum-deferoxamine complex [10].

The American Academy of Pediatrics Committee on Nutrition and FDA recommended keeping a strict control of Al content in PN [4]. On the other hand, it is important to recognize that currently there is no method to ensure that PN contents are manufactured at the recommended lower Al concentrations [3,4]. To our knowledge, this is the first time response to deferoxamine was assessed, using bone densitometry, following chelation in patients on long term PN with Al toxicity. The improvement in the Z-score of this patient might support the routine use of bone densitometry for at risk

patients. However, appropriately conducted interventional study may give stronger evidence.

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Conflict of interest

There is no conflict of interest to declare.

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