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Case Report Open Access

A Relationship between Hypoglycemia, Hypothyroidism and Zinc Deficiency

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Abstract

Background: The interaction of zinc deficiency and hypothyroidism has several reported presentations. The link between hypoglycemia and hypothyroidism is also known, but uncommon. For the last 40 years, the relationship between these two phenomena was illustrated in a handful of articles. To the best of our knowledge, the sequence of hypoglycemia, hypothyroidism and zinc deficiency has not yet been reported.

Case presentation: We present a six-month-old boy with the unusual combination of these three conditions, his diagnostic evaluation and management.

Conclusion: We suggest that the relationship between zinc and thyroid function should be considered in any case of severe intractable hypoglycemia and extensive skin eruption.

Keywords: Zinc; Hypothyroidism; Hypoglycemia

Case Report

A six-month-old boy of Palestinian descent was referred from Gaza with severe sepsis and respiratory failure unresponsive to treatment. He was a product of normal pregnancy and uncomplicated delivery.

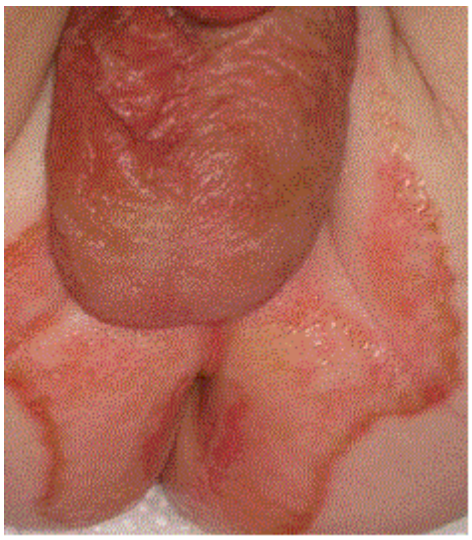

Figure 1: Eczematous lesions in perianal area and scrotum.

Both parents were healthy without any significant family history or consanguinity. The patient was born at term and his birth weight and length were within the 50th percentile. There are no records of neonatal screening in Gaza. During the first two months of his life, nutrition consisted solely of breastfeeding. A switch to a cow-milk-based formula was followed with intermittent diarrhoea, inadequate weight gain and a few episodes of apnea. During one episode of apnea, profound hypoglycemia (25 mg/dL) was documented. During that episode, the patient was intubated and ventilated. Extubation attempts failed due to recurrent apnea and severe hypoglycemic episodes. At age of four months, the patient was transferred to our Pediatric Intensive Care Unit.

Upon admission, the patient was mechanically ventilated with hemodynamic instability. Prominent multiple eczematous skin lesions, involving the face, chest and perianal area, as well as alopecia, were noted. The presence of the watery diarrhoea, skin lesions and low activity of alkaline phosphatase (22 U/L, normal range is 149-369 U/L) were compatible with acrodermatitis enteropathica (Figure 1). Zinc serum levels were low (38 mcg/dL, normal range is 50-150 mcg/dL).

A complete blood count revealed leukopenia with moderate neutropenia, anemia and thrombocytopenia. CRP (C reactive protein) was slightly elevated.

Candida albicans was found on peripheral and central line blood cultures, and urine culture.

Severe hypoglycemic events (serum glucose < 10 mg/dl) required a relatively high glucose delivery rate (up to 16 mg/kg/min). A critical sample, which was taken before the treatment, revealed normal results (Table 1). Adrenocorticotropic hormone (ACTH) stimulation test revealed normal response of the axis.

Recurrent events of sinus bradycardia and severe muscle hypotonia raised the suspicion for thyroid dysfunction. Thyroid stimulating hormone (TSH) level was extremely high (TSH>75 uIU/ml) with low free T4 levels (<0.30 ng/dl, normal range is 0.8-2.0 ng/dl). Antithyroid antibodies were negative.

Glucose	<10 mg/dL (74-106 mg/dl)
Insulin	<1 mIU/mL (5-25 mIU/mL)
C-peptide	<0.10 micg/l (0.9-7.1 micg/l)
Growth hormone	27.8 micg/l (0.0-5.0 micg/l)
Cortisol	9 mcg/ml (5-25 mcg/dl)
Free Fatty Acids	140 micromol/L
3-OH-butirate	280 micromol/L (< 400 micromol/L)
AcetoAcetate	78 micromol/L (< 100 micromol/L)
Lactate	1.70 mmol/L (0.5-2.2 mmol/L)
Ammonia	95 mcg/dl (27-90 mcg/dl)
Pyruvate	0.070 mmol/L (0.08-0.16 mmol/L)
Serum Amino acids	Normal profile
Urine Organic acids	Normal profile
Urine reducing substances	Negative
TSH	>75 mIU/ml (0.4- 4.0 mIU/mL)
Free T4	<0.30 ng/dl (0.8-2.0 ng/dl)
Anti Tg Ab	<20IU/ml (0-40IU/ml)
AniTPO Ab	<10IU/ml (0-35IU/ml)
Thyroglobulin	95.8 ng/ml (1.6-60 ng/ml)

Table 1: Critical Sample Results.

Severe concurrent hypomagnesaemia (Mg level as low as 0.99 mEq/L, normal range is 1.5-2 mEq/L) required multiple loading doses of Mg Sulfate intravenously.

Serum amino acids and urine organic acids were normal. Screening for urine reducing substances as well as phenylketonuria screening was within normal limits.

Initial treatment combined broad spectrum of antibiotics, antifungals and a high rate of parenteral glucose delivery.

Hemodynamic stabilization required aggressive fluid resuscitation and continuous infusion of vasopressors. The patient's respiratory failure required mechanical ventilation for two and a half weeks. Due to upper airway obstruction, a tracheostomy was performed after the diagnosis of subglottic stenosis.

Levothyroxine treatment was initiated (14 mcg/kg/day), resulting in the normalization of TSH and free T4 in ten days.

Zinc sulfate enteral supplementation was started on the second week of the treatment at 0.7 mg/kg/day.

Over the course of the next two weeks, the appearance of the patient's skin as well as his alkaline phosphatase activity had gradually improved. Hypoglycemic events had ceased after two weeks of treatment, coinciding with return of serum TSH to normal levels.

Blood count indexes had improved, gradually normalizing.

Zinc supplements and maintenance dose of levothyroxine were prescribed as a continuous treatment.

Discussion

Zinc is an essential factor in the metabolic homeostasis. Zinc deficiency may be congenital or acquired.

Acrodermatitis Enteropathica is rare congenital defect, which is the result of a mutation in the transporter gene SLC39A4. The syndrome is autosomal recessive and leads to the impaired absorption of zinc despite appropriate intake.

There are many causes for the secondary zinc deficiency, including low zinc intake, malnutrition, gastrointestinal diseases, associated with diarrhoea, chronic liver or renal illness, infection, extensive burns and etc. The differential diagnosis also includes an inborn error of metabolism, biotinidase deficiency and cystic fibrosis.

The diagnosis of zinc deficiency is based on presence of typical clinical phenotype, accompanied by the low serum zinc level. The exclusion of congenital defect is not essential in the absence of affected relatives [1].

Zinc deficiency usually presents after the weaning from breast to cow's milk, during first few months of life.

The clinical presentation and medical management of zinc deficiency are similar, regardless the cause of the deficiency. The cutaneous manifestation is remarkable for symmetric vesiculobullous, eczematous or psoriasiform lesions in the perioral, acral and perianal areas. Associated symptoms include alopecia, diarrhoea, growth retardation, impaired function of thymus and increased susceptibility to infections, particularly to candida albicans.

The complete resolution of symptoms with zinc supplementation confirms the diagnosis of zinc deficiency [2].

In relation to the case in question, the impact of zinc on endocrine homeostasis is interesting from two aspects - its effect on glucose metabolism and on thyroid function.

The endocrine importance of zinc, particularly its effect on growth, thyroid function and sexual development was extensively discussed in literature [3].

The direct association between serum level of zinc and hypoglycemia was previously evaluated. Serum levels of zinc directly correlated with levels of glucose and lactate. The effect is believed to be secondary to zinc-mediated alpha-cell dysfunction and impaired response of glucagon to hypoglycemia [1].

The exact nature of the antagonistic effect of zinc on glucagon remains obscure. A recent review, which was based on animal-model studies, has not reached univocal conclusions. Further studies are needed for investigation of the mechanism [4].

Improvement in thyroid functions with zinc sulfate supplementation was noted in children with Down's syndrome. The results can be explained by recovery of thymic function and its positive action on the pituitary-thyroid axis [5].

Some animal studies showed an interdependent relationship between zinc and thyroid functions [6].

Thyroid hormones seemed to be essential for zinc absorption and its normal biological activity. Zinc status and thyroid function are linked in clinical practice [7].

The role of thyroid function in glycemic balance is complex and poorly defined. Many studies showed the interaction of the thyroid and serum glucose levels in diabetic patients. However, despite the evidence of improved glycemic control after the improvement of thyroid status, the direct effect of thyroid hormones on insulin metabolism remains unclear [8].

Hypoglycemia due to impaired gluconeogenesis, associated with thyroid dysfunction was presented in several reports. Abnormal glucagon response to hypoglycemia during hypothyroid state was reported as well [9].

There is one pediatric case report noting the combination of hypoglycemia and hypothyroidism. The report describes a newborn with profound hypoglycemia and congenital hypothyroidism [10].

Conclusion

According to the literature, zinc deficiency adversely affects thyroid function. Moreover, thyroid function correlates with the glucose homeostasis.

Nevertheless, the association of zinc deficiency, hypothyroidism and hypoglycemia has not yet been described in the current available literature in English.

Therefore, we suggest that the relationship between zinc and thyroid function should be considered in any case of severe intractable hypoglycemia and extensive skin eruption.

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