

CASE REPORT

The triad of Iron deficiency anemia, hepatosplenomegaly and growth retardation with normal serum zinc levels in a 14-year-old boy

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Abstract

A triad of iron deficiency anemia, hepatosplenomegaly and growth retardation occurring in tandem with zinc deficiency has been reported in the past as components of either Prasad's syndrome or hypopituitarism. There are no documented cases of such triad occurring in the presence of normal serum zinc levels. We report a case of a 14-year-old boy who presented with iron deficiency anemia, hepatosplenomegaly, geophagia and growth retardation with pubertal delay. Investigations ruled out hypopituitarism and coeliac disease. The patient improved dramatically and attained puberty within 15 months of intense nutritional intervention. In conclusion, iron deficiency anemia occurring in the triad without zinc deficiency as seen in this case report has not been reported before; this calls for more research to be able to explain the findings.

Key words: Growth retardation, hepatosplenomegaly, iron deficiency anemia, serum zinc

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Introduction

Iron deficiency is one of the most common nutritional deficiencies in children throughout the world and particularly in developing countries.^[1] A diet rich in cereals but poor in animal proteins may easily lead to the development of iron and zinc deficiencies.^[2,3]

The triad of iron deficiency anemia, hepatosplenomegaly and growth retardation has been described before where it was associated with zinc deficiency in Prasad's syndrome, hypopituitarism^[4-6] or coeliac disease.^[7]

Deficiencies of zinc and iron almost always occur together. There are no reported cases of puberty delay in iron deficiency anemia without zinc deficiency, neither has lack of testicular development secondary to iron deficiency alone been reported.^[4]

We report a case of a 14-year-old boy who presented with symptomatic iron deficiency anemia, hepatosplenomegaly

and growth retardation. Hypogonadotropic hypogonadism, Prasad's syndrome and coeliac disease were ruled out. The patient had hypogonadism with low testosterone levels most likely due to nutritional deficiency; the clinical picture improved gradually within 15 months of intense nutritional intervention.

Case Report

A 14-year-old standard six primary school boy was referred to our hospital with a history of severe anemia presenting with headache, palpitations and dizziness. He was also to be evaluated for growth retardation compared to his siblings and peers at school. The boy came from a family with poor socioeconomic status with poor dietary habits; his meals consisted mainly of carbohydrates in the form of maize, flour and wheat products taken with cow milk, with virtually absent meat, fish and vegetables. He also

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gave a history of drinking around 4–5 cups of black tea on daily basis and soil eating for the past 2 years. There was no history suggestive of chronic illnesses like tuberculosis, diabetes mellitus and epilepsy. He is the fourth of six children from the same mother and has five siblings who were reported to be of good height and had moved out of the village 3 years prior to his illness. There was no history of sickle cell disease or any other hematological conditions in the family.

Physical examination on admission revealed a chronically ill looking boy who was short in stature, severely pale, afebrile, pulse rate of 88 beats/min (60–100) and blood pressure of 101/67 mmHg (100–120/60–80), his respiratory rate was 17 breaths/min (14–18). He weighed 26 kg (below 3rd percentile), height of 123 cm (below 3rd percentile) and body mass index of 17.1 kg/m² (10th–25th percentile). He had scarce scalp hair and absent axillary and pubic hair with testes measuring 4 cm bilaterally (50th–90th percentile) and stretched penile length of 5 cm (below 10th percentile). Systemic examination of the patient was significant for grade two systolic murmurs on the mitral area, hepatomegaly of 7.6 cm and splenomegaly of 6.7 cm below the costal margins. The rest of systemic examinations were normal.

Laboratory investigations results of the patient are shown in Tables 1 and 2. The other investigations included liver and renal function tests, urinalysis and echocardiogram which were all within normal range.

The bone age X-ray of the patient matched that of age 11.5 years [Figure 1]. Sagittal magnetic resonance imaging of the brain was planned to rule out pituitary hypoplasia but deferred because of normal pituitary hormonal assays. Bone marrow aspirate was to be done in subsequent follow-up but deferred as the patient was showing clinical improvement.

On the background of above history, physical examination and laboratory investigations, a possibility of short stature, anemia and hepatosplenomegaly secondary to chronic nutritional deficiency was entertained as investigations had already ruled out multiple hormone deficiency, Prasad's syndrome and coeliac disease.

The patient stayed in the hospital for 1-month during which he received 3 units of blood, and tablets of iron sulfate 200 mg 3 times daily and was referred to dietician for intense nutritional therapy, where he was also counseled to stop pica habits.

Patient continued with nutritional therapy at a nearby local hospital and was reviewed at the endocrinology and medical clinics after 6, 12 and 15 months of nutritional intervention respectively. He also had stopped pica habits completely by 6 months of intervention. He showed

Table 1: Laboratory investigations of the patient at admission showing hemogram, stool examination and zinc levels

Laboratory investigation	Patient results	Reference value
Full blood picture		
WBC	5.33/mm ³	4-11
Hb	2.9 g/dl	12-16
MCV	60.3fl	80-100
MCH	24.5 pg	28-32
MCHC	30.5 g/dl	32-36
RDW (%)	22.5	11.5-14.5
Platelet	670×10 ³ /μl	150-400
Peripheral blood smear showed	Tear drops, fragmented microcytic forms, normal white blood cells and increased platelets	
Iron studies		
Total iron	13.30umol/l	11.6-31.3
Transferrin	42.86umol/l	25.2-34.0
Saturation	15.52%	16-50
Ferritin	38.87 ng/ml	>50
Serum Vitamin B12	826 pmol/l	148-590
Serum folic acid	23.60 nmol/l	5.7-45.3
Serum gliadin and endomysium antibodies	Negative	
Stool analysis for parasites and occult blood	Negative	
Reticulocyte count (%)	<1	0.5-1.5
Serum zinc level	24.80	10.7-18.4
Hemoglobin electrophoresis genotype	Genotype AA	
HIV test	Negative	

HIV=Human immunodeficiency virus; WBC=White blood cell; Hb=Hemoglobin; MCV=Mean corpuscular volume; MCH=Mean corpuscular hemoglobin; MCHC=Mean corpuscular hemoglobin concentration; RDW=Red cell distribution width

Table 2: Laboratory investigations of the patient at admission showing Hormone profiles

Laboratory investigation	Patient results	Reference value
Serum testosterone	1.56 nmol/l	3.47-18.74
FSH	2.96 Miu/mL	0-5.0
LH	3.32 Miu/ml	0.3-6.0
Thyroid function tests		
TSH	1.53 Miu/l	0.5-5.0
T4	11.5 μg/dl	4.6-12.0
Growth hormone at rest	0.06 μg/l	<5.4
IGF-1 (somatomedin)	237.20 nmg/ml	54-204.4
Serum ACTH	20.4 pg/ml	0-46
Serum cortisol	107 nmol/l	101-535

FSH=Follicular stimulating hormone; LH=Luteinizing hormone; IGF-1=Insulin-like growth factor-1; TSH=Thyroid stimulating hormone; ACTH=Adrenocorticotrophic hormone

a gradual but steady improvement noted more from 12 months follow-up, whereby at 15 months of follow-up, his hemoglobin was 12.5 g/dl, other indices such as



Figure 1: Left hand X-ray of the patient corresponding to bone age of 11.5 years

mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC) and mean corpuscular hemoglobin (MCH) had normalized testosterone level had normalized at 4.25 nmol/l; he had attained puberty, his parameters were as follows; weight = 29 kg (gained 3 kg), height = 135.3 cm (gained 12.1 cm), penile length = 10 cm, testicular volume = 15 cm bilaterally. The hepatosplenomegaly found in the patient also gradually decreased in size in subsequent visits; it was not picked at 15 months of follow-up.

Discussion

Evidence from previous case reports in patients presenting with a triad of iron deficiency anemia, hepatosplenomegaly and growth retardation occurring together with low serum zinc levels have been secondary to either Prasad's syndrome or hypopituitarism.^[4-6] In Prasad's syndrome; pica and hypogonadism were accompanying features, and the disorder improved with intense nutritional intervention and iron supplementation.^[5,8]

Our patient presented with anemia of iron deficiency type which was consistent with laboratory results of low MCV, low MCH, low MCHC, low serum ferritin and high transferrin, also peripheral smear picture; he also had isolated low testosterone levels. Previous evidence shows that the testosterone plays a part in stimulating erythropoiesis via production of hematopoietic growth factors and improvement of iron bioavailability,^[6,9] which could partly have contributed to the severity of anemia in our patient.

Iron deficiency anemia usually occurs together with zinc deficiency, and presentation of patients with the triad has been thought to be mainly due to zinc deficiency, we found this

case to be unique because we did not find published reports of isolated iron deficiency occurring in the triad without zinc deficiency. Previous documented case reports postulated zinc deficiency to be the cause of growth retardation. In this report, our patient had no evidence of hemolysis as this would cause a negative zinc balance and mask existing zinc deficiency.^[10]

Conclusion

Despite the fact that in most African settings, iron deficiency anemia is very common, there is a lack of reported cases of patients presenting with the triad of iron deficiency anemia, hepatosplenomegaly and growth retardation. On the other hand, iron deficiency anemia occurring in the triad without zinc deficiency has not been reported before, this calls for more research to be able to explain the findings. The triad of iron deficiency anemia, hepatosplenomegaly and growth retardation requires aggressive investigations to rule out multiple etiologies such as Prasad's syndrome, coeliac disease and hypopituitarism, once the diagnosis has been established and treatment initiated, efforts can be rewarding as shown in this case report.

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