Hypopituitarism masquerading as Prasad’s syndrome: a case report

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Prasad’s syndrome is characterized by geophagia, growth retardation, hypogonadism, and zinc deficiency. We report a 15-year-old boy whose medical history and clinical and laboratory findings were fully compatible with Prasad’s syndrome. In addition to severe growth retardation and pubertal delay, iron deficiency anemia and zinc deficiency were determined. His gliadin and endomysium antibodies were negative. The thyroid hormone levels were in normal range but basal gonadotropins and testosterone levels were low for his age. Detailed endocrinological evaluation revealed growth hormone deficiency and hypogonadotropic hypogonadism. Pituitary gland magnetic resonance imaging revealed pituitary hypoplasia. In our opinion, before the diagnosis of Prasad’s syndrome, endocrine evaluation should be done in these patients and hypopituitarism should be ruled out. Hypogonadotropic hypogonadism and growth hormone deficiency may be masked by Prasad’s syndrome.

Key words: Prasad’s syndrome, zinc, hypopituitarism, hypogonadism.

Prasad’s syndrome, which was first described by Prasad¹,² in 1961, is a rare disorder characterized by geophagia or pica, growth retardation, hypogonadism, iron deficiency anemia, and zinc deficiency. Iron and zinc deficiencies are considered as an explanation for the pica, hypogonadism and short stature, and the entire range of clinical features improve following adequate supplementation of the diet with zinc and iron. In our country, although the prevalence of zinc and iron deficiency is steadily decreasing, severe iron and zinc deficiency with growth retardation and delayed puberty is still observed³-⁵.

Here, we report a case that presented initially with growth retardation and severe anemia who had all the characteristic features of Prasad’s syndrome. However, he was diagnosed with growth hormone (GH) deficiency and hypogonadotropic hypogonadism associated with hypopituitarism. Thus, we wanted to point out that Prasad’s syndrome might mask hypopituitarism in certain cases.

Case Report

A 15-year-old boy was admitted to our hospital because of growth retardation, weakness and paleness. His weight and height were always delayed compared to his age- and sex-matches, but weakness and paleness had developed within the last 2-3 years. The socioeconomic status of his family was very low, and their diet was rich in carbohydrates and poor in animal proteins. He also reported that he consumed about 15-20 cups of black tea daily. He was born from unrelated parents after an uneventful pregnancy, and his family history was unremarkable.

On physical examination, he appeared pale and droopy. His blood pressure was 105/60 mmHg and heart rate 96 beats per minute. His height was 133.3 cm (Z score: -5.6) and weight 26.8 kg (Z score: -4.9). His body mass index was 15.1 kg/m² (<3rd percentile), and bone age was 10 years. On abdominal palpation, the liver and spleen were palpable 2 cm below the costal margins. There was a 2/6 systolic murmur on the left lower sternal border. He
had no axillary or pubic hair, testes measured 2 ml bilaterally, and stretch penile length was 6.5 cm (<3rd percentile).

On laboratory evaluation, hemoglobin level was 5.1 g/dl, main corpuscular volume was 52.3 fl, and red blood cell distribution width (RDW) was 20.7%. Peripheral smear revealed microcytic and hypochromic erythrocytes with anisopoikilocytosis. Serum iron level was 9 μmol/L [normal range (N): 50.00-160 μmol/L], totally iron binding capacity was 413 μmol/L (N: 250-400 μmol/L), serum ferritin level was 1.5 ng/ml (N: 70-150 μg/dl), and serum zinc level was 54 μg/dl (N: 70-150 μg/dl). Vitamin B12 and folic acid levels were normal and serum gliadin and endomysium antibodies were negative. Stool analysis for parasites and blood reaction were also negative. Thyroid hormone levels were in normal range, but basal gonadotropin and testosterone levels were low for his age [luteinizing hormone (LH), follicle-stimulating hormone (FSH) and testosterone levels were 0.42 IU/L, 1.54 IU/L and 20 ng/dl, respectively]. Luteinizing hormone-releasing hormone (LH-RH) test (100 μg/intravenous) was performed, and peak LH and FSH levels were found as 2.7 IU/L and 3.99 IU/L, respectively. Test results were low according to the patient’s age and appropriate for prepubertal stage. Insulin-like growth factor-1 level was 45.7 ng/ml (<-3 SD) and insulin-like growth factor binding protein-3 level was 2240 ng/ml (<-3 SD). Four days after priming with testosterone enanthate (Sustanon® 100 mg intramuscular), GH provocation tests were done with L-dopa and clonidine. Peak GH levels were 7.47 ng/ml and 6.85 ng/ml, respectively. Endocrinological evaluation revealed partial GH deficiency and hypogonadotropic hypogonadism. The magnetic resonance imaging (MRI) of the pituitary gland showed pituitary hypoplasia (anterior pituitary height 4 mm). GH therapy and zinc and iron supplements were started, and tea consumption was limited. The anemia resolved following three months of therapy. It was decided to initiate testosterone therapy for management of his delayed puberty after his bone age reaches 12 years.

Discussion
Iron deficiency is one of the most common nutritional deficiencies in children throughout the world, and particularly in developing countries. A diet rich in cereals but poor in animal proteins may easily lead to development of iron and zinc deficiencies. Since iron and zinc are essential for cell growth and differentiation, their deficiencies together may cause severe growth retardation in childhood. Prasad et al. reported an anemic patient with a prolonged history of geophagia, who had growth retardation and hypogonadism. They suggested that not only iron but also zinc deficiency was responsible for this condition, and the clinical features of the patient were corrected with a well-balanced animal protein diet and iron administration.

Geophagia is the most commonly reported unusual dietary habit seen in patients with iron and zinc deficiencies. Occasionally, some patients consuming extraordinary things such as flour, raw potato, ice, or paper have been reported, and in general, this abnormal pattern of eating is defined as pica. Our patient had a history of consuming 15–20 cups of tea per day. Tea contains polyphenols and tannins that can negatively influence the bioavailability of iron by forming complexes with nonheme iron in the digestive tract. Therefore, similar to pica, both iron and zinc deficiency may occur due to excessive tea consumption. Further, certain components of cereals and legumes, such as phytic acid, fiber and calcium, negatively affect zinc and iron absorptions. Moreover, loss of appetite is seen in children with malnutrition because of the deficiency of these minerals.

Hypogonadism is a common component of Prasad’s syndrome. Generally, it improves after zinc and iron supplementation with a protein-rich diet. However, the mechanism of hypogonadism caused by zinc deficiency is not a well-known entity. Some animal studies have shown that the effect of zinc deficiency was exerted directly on testicular steroidogenesis and that the gonadotropins were not affected. In patients with Prasad’s syndrome, gonadotropins show normal pubertal response to LH-RH stimulation test. However, in patients with hypogonadotropic hypogonadism, a satisfactory rise in LH and FSH levels following stimulation is not seen. In two case reports from our country, patients who had the characteristic clinical and laboratory findings...
findings of Prasad's syndrome were diagnosed with Prasad's syndrome after excluding GH deficiency or hypogonadotropic hypogonadism. GH provocation and LH-RH stimulation test results were found to be normal in these patients. Improvement in the clinical conditions of both patients was reported following zinc and iron replacement1-4.

All children with short stature, delayed puberty and iron deficiency should be screened for celiac disease and certain endocrinological problems, particularly for GH deficiency and hypogonadism, even if all clinical features support the diagnosis of Prasad's syndrome. In our case, endocrinological evaluation revealed hypopituitarism, and GH treatment was started. We plan to initiate testosterone treatment in addition to GH after his bone age reaches 12 years. If such patients are misdiagnosed as Prasad's syndrome and given only zinc and iron supplements, these treatments will not be sufficient. Moreover, a very valuable period for initiation of appropriate treatment for patients may be delayed.

In conclusion, zinc and iron deficiencies are still important health problems in developing countries. Before making the diagnosis of Prasad's syndrome, endocrinological evaluation should be done, and the possibility of hypopituitarism should be ruled out.

REFERENCES