

Autoimmune polyendocrine syndrome type 1 – a case report from Bangladesh

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Abstract

We describe a case of a 26 years old man who presented with adrenocortical insufficiency followed by hypoparathyroidism and subsequently mucocutaneous candidiasis. He also had nail dystrophy, cataract and alopecia, but no other endocrinopathies. He was diagnosed as a case of autoimmune polyendocrine syndrome type 1 (APS 1). APS1 is a rare endocrine disorder and only a few cases have been reported from Bangladesh.

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Introduction

Autoimmune polyendocrine syndrome (APS) type 1 is a rare disorder characterized by multiple endocrine organ dysfunctions due to autoimmune activity [1]. This rare condition typically presents with mucocutaneous candidiasis followed or accompanied by endocrinopathies. We report a case of autoimmune polyendocrine syndrome type 1, which has rarely been reported in Bangladesh. However, our patient did not manifest candidiasis until several years after his initial presentation.

Case report

A 26 years old man born of non-consanguineous parents came to BIRDEM hospital in July 2012 with the complaints of whitish skin lesions for 4 months. The lesions were itchy, painless with no photosensitivity. He also complained of loss of hair all over his body for the last two years.

On query, he mentioned that when he was 10 years old, he suffered from anorexia, weakness, weight loss and failure to gain height followed by an acute

attack of vomiting and diarrhea with unconsciousness. He regained consciousness after being treated with intravenous fluids and hydrocortisone. At the age of ten, his height was 117 cm (below 3rd percentile), weight 21 kg (below 3rd percentile), BMI 15.3 kg/m² (between 10 and 25th percentile), arm span 112 cm, upper segment 58 cm and lower segment 59 cm. Growth velocity was reduced (1cm/year). His blood pressure at the time was 110/90 mmHg lying and 100/75 mmHg standing. There was pigmentation over the lips, palate, buccal mucosa and widespread darkening of the skin. The thyroid gland was not palpable. Systemic examinations including the genitalia were unremarkable. At that time fasting blood glucose level was 5.1 mmol/L (3.5-5.5 mmol/L), serum sodium was 118 mmol/L (135-145 mmol/L), potassium was 5.2 mmol/L (3.6-5.5 mmol/L), and bicarbonate was 17 mmol/L (21-29 mmol/L). Bone age was not delayed. Primary adrenal insufficiency was suspected and confirmed by rapid adrenocorticotrophic hormone (ACTH) stimulation test. Morning cortisol level was 80 nmol/L (95-571 nmol/L). Serum cortisol at 30 min and 60 min was 143.26 nmol/L and 39.99 nmol/L

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respectively. He was prescribed lifelong replacement steroids (prednisolone 7.5 mg and fludrocortisone 0.1 mg daily). Subsequently, he noticed dimness of vision and was diagnosed with bilateral cataract a year later. The cataract was surgically removed and intraocular lens implanted. At the age of 12 years, he noticed tingling, numbness and cramps in his hand and had signs of latent tetany i.e. trousseau's sign. Calcium profile was done at that time and serum calcium was found to be 5.6 mg/dl (9-11 mg/dl), phosphate was 10.5 mg/dl (1.7-4.5) and serum alkaline phosphatase was 173 IU/L (<370). Despite a low serum calcium level, intact parathyroid hormone level was 3.5 pmol/L (1.6-7.5 pmol/L), i.e. not elevated. This confirmed a diagnosis of hypoparathyroidism. Accordingly, calcium 3 gm with vitamin D 800 IU were prescribed daily.

When he presented at BIRDEM in July 2012 at the age of 26 years, his height was 140 cm and weight 37 kg. He entered puberty at the expected age and was father of two healthy children. His younger brother was also diagnosed with polyendocrine endocrinopathy. Physical examination revealed normal dentition, depapillated tongue, pitted and dystrophic nails (Figure 1), patchy alopecia, no eye brows or eye lashes and white patches in the oral cavity and skin. Scrapings were taken from the skin lesions and budding oval fungal cell with hyphae were identified by microscopy and a diagnosis of mucocutaneous candidiasis was made. Thyroid dysfunction was excluded as free thyroid hormone was 149.55 nmol/L (67-163 nmol/L) and TSH was 4.58 μ IU/ml (0.6-4.5 μ IU/ml). Hematological parameters were normal and vitamin B₁₂ level was more than 2000 pg/ml (>

200 pg/ml) excluding pernicious anemia. Bone mineral density by DEXA scan showed osteoporosis (T score -2.5 and Z score -1.1). Renal and liver functions and abdominal imaging were all unremarkable. Finally, a diagnosis of APS type 1 was made based on the previous diagnosis of primary adrenal insufficiency and hypoparathyroidism, together with the current features of mucocutaneous candidiasis. He was put on replacement steroids and calcium supplementation therapy. He was given systemic and local antifungal therapy for candidiasis and triamcinolone injections for alopecia areata.

Discussion

Autoimmune polyendocrine syndrome (APS) is a heterogenous group of rare diseases characterized by autoimmune activity against more than one endocrine organ. However, non-endocrine organs can also be affected [1]. The two major autoimmune polyendocrine syndromes are type 1 and 2, with type 2 being more common. APS 1 is inherited as an autosomal recessive manner and linked to mutation of the AIRE gene (autoimmune regulator gene) on chromosome 21 [2-4]. Strong genetic components have been reported in APS. Though the type 2 syndrome occurs in multiple generations, type 1 is most commonly reported among siblings [2]. Patients with APS type 1 express autoantibody which react with specific antigens. For example, the presence of anti-adrenal antibody (antibody against 21-hydroxylase) is linked to the development of Addison's disease [5]. The clinical manifestation of type 1 APS is widely variable. Although the classic triad is composed of mucocutaneous candidiasis, hypoparathyroidism and primary adrenal insufficiency (Whitaker's triad), many other components like autoimmune thyroid disease, diabetes mellitus type 1, hypergonadotropic hypogonadism, pernicious anemia, autoimmune hepatitis, tubulointerstitial nephritis, vitiligo and alopecia areata may also develop [6-8]. The disease presents with dental enamel dystrophy, nail dystrophy and ectodermal dysplasia. The onset of APS is usually in infancy and mucocutaneous candidiasis followed by primary adrenal insufficiency is typically the first manifestations to be observed. It is well recognized that several years may elapse between the onset of



one endocrinopathy and the development of the next endocrine disorder. For example, 40 to 50% patients with Addison's disease will subsequently develop other autoimmune diseases [9]. Therefore, continued monitoring for the development of other autoimmune diseases is mandatory. Diagnosis is made by the presence of two out of three components of the classic triad, or the presence of one criterion and a sibling previously diagnosed with APS 1. Patients presenting without overt features of the syndrome can be diagnosed by molecular genetics.

Our patient was diagnosed with APS 1 as he presented with the classic triad of primary adrenal insufficiency, hypoparathyroidism and mucocutaneous candidiasis. He also had alopecia arcata and dystrophic nails. The adrenal glands were typically the first endocrine organs to be affected, followed by the parathyroid glands. However, contrary to other cases, our patient presented mucocutaneous candidiasis very late in the course of the disease (16 years after the initial presentation). In other cases of APS 1 that have been so far reported, mucocutaneous candidiasis was always one of the presenting features [8]. In Bangladesh, Ali *et al* reported a case of APS 1 in a 15 year old boy who presented with features of chronic mucocutaneous candidiasis, hypoparathyroidism, primary hypothyroidism, nail dystrophy and dental enamel hypoplasia [10].

APS 1, though rare, is found in the community. It should be differentiated from other autoimmune polyendocrine syndromes such as APS 2. The patient with APS should be followed up and monitored for several years for the development of other endocrinopathies. Since the disorder runs in families, siblings should be screened for the disorder as well.

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