Autoimmune polyglandular syndrome type 1 in a 12-year-old Ugandan girl

Kibirige D, MBChB, MMed-Intern Med, Specialist Physician
Makerere University College of Health Sciences and Dermatology Unit, Mulago National Referral and Teaching Hospital, Kampala, Uganda
Kambugu F, MBChB, MMed-Intern Med, Senior Consultant Physician and Dermatologist
Makerere University College of Health Sciences and Endocrine Unit, Mulago National Referral and Teaching Hospital, Kampala, Uganda
Correspondence to: Davis Kibirige, e-mail: davouirek@yahoo.co.uk
Keywords: autoimmune polyglandular syndrome type, autoimmune diseases, APS-1, chronic mucocutaneous candidiasis, chronic hypoparathyroidism

Abstract

Autoimmune polyglandular syndrome type 1 (APS-1), also known as autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy syndrome, is a very rare disorder of childhood. It is mainly characterised by the presence of at least two of the following: chronic mucocutaneous candidiasis, chronic hypoparathyroidism and autoimmune Addison's disease. We report on the case of a 12-year-old Ugandan female patient who presented with features that were most consistent with APS-1 (chronic mucocutaneous candidiasis and hypoparathyroidism). Significant clinical improvement was noted following oral antifungal therapy.

Ⓟ **Peer reviewed. (Submitted: 2011-12-20. Accepted: 2012-11-14.)** **JEMDSA 2013;18(1):65-67**

Introduction

Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy syndrome (APS-1), is an extremely rare and frequently debilitating disorder of childhood. A clinical diagnosis of APS-1 classically requires the presence of two of the three cardinal components: chronic mucocutaneous candidiasis, autoimmune hypoparathyroidism and autoimmune adrenal failure.[1]

Typically, the first manifestation is mucocutaneous candidiasis, which develops in infancy or early childhood. This is followed by the development of hypoparathyroidism, which may be asymptomatic or which typically presents with tetany and seizures. Adrenal insufficiency often develops later. Other conditions which are associated with APS-1 include autoimmune thyroid disease, type 1 diabetes, hypogonadism, alopecia, vitiligo, autoimmune hepatitis, pernicious anaemia and chronic gastritis.[2]

There are no documented case reports of APS-1 among African patients. Most of the described case reports are from Europe[3-7] and the Middle East.[8]

Case study

A 12-year-old female patient was referred to the dermatology unit of Mulago National Referral and Teaching Hospital, Uganda. She had a six-year history of a generalised, intensely itchy skin rash on the limbs, trunk and face. The rash was initially responsive to topical steroid therapy, but was later refractory. The patient had a three-year history of progressive wart-like growths on the face and scalp. She also presented with a three-month history of nail deformities and oral sores. Her history was not suggestive of any autoimmune condition. There was no familial history of autoimmune conditions or of a similar condition among her siblings.

Figure 1: Extensive facial and scalp growths with alopecia

A physical examination revealed extensive facial and scalp growths with alopecia (Figure 1) and widespread oral thrush and angular cheilitis. There were generalised scaly skin lesions on the hands and legs (Figure 2), and markedly thickened, pitted nails with a distorted

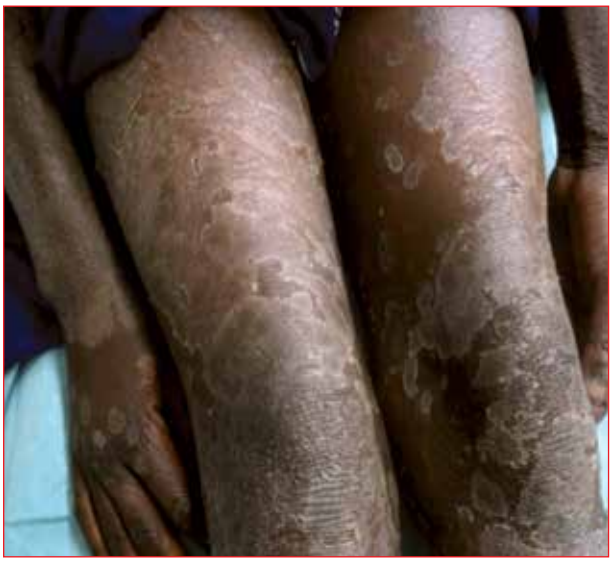

Figure 2: Generalised scaly skin lesions on the hands and legs

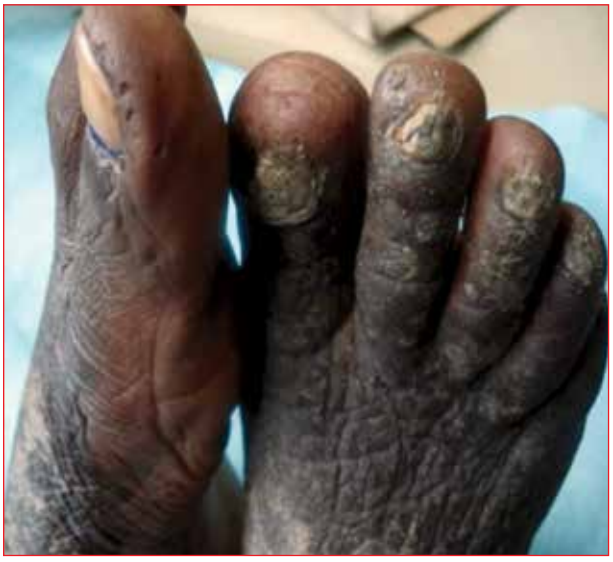

Figure 3: Markedly thickened, pitted nails with a distorted appearance

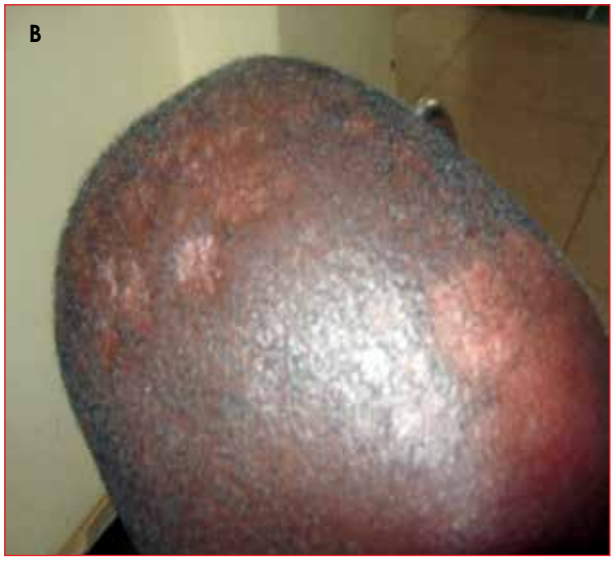

Figure 4 a and b: Total resolution of the facial and scalp growths

appearance (Figure 3). Chovstek's and Trousseau's signs were negative. Her height and body mass index were normal for her age (height of 1.3 m, weight of 31 kg and body mass index of 18.3 kg/m^2). She had normal secondary sexual characteristics for her age (Tanner stage II).

The haematological evaluation that was carried out showed a mild hypoalbuminaemia of 32.7 g/dl (normal range 35-50). The complete blood count and renal and liver function tests were normal. Human immunodeficiency virus serology was negative. She had a mild corrected hypocalcaemia of 8.4 mg/dl (normal range 9-10.6 mg/dl), and the parathyroid hormone levels were reduced (6 pg/ml, normal range 15-65 pg/ml). Serum phosphorus, magnesium and vitamin D levels were not ascertained.

An endocrine screen was performed to rule out any co-existing autoimmune conditions. Thyroid function tests, fasting blood glucose, follicle-stimulating hormone, oestradiol, luteinising hormone and cortisol levels at 08h00 were all normal. Skin scrapings for fungal culture were not taken. Genetic testing for the different mutations of the autoimmune regulator (AIRE) gene was also not carried out because it cannot be performed in Uganda.

A diagnosis of APS-1 was made on the basis of the presence of chronic mucocutaneous candidiasis and hypoparathyroidism. The patient was started on oral vitamin D and calcium supplementation to treat the hypoparathyroidism, as well as on daily oral fluconazole. Significant clinical improvement was noticed within three weeks, with total resolution of the facial and scalp growths (Figures 4 a and b). To date, her clinical

follow-up and endocrine screening for associated autoimmune conditions has been uneventful.

Discussion

In this case report, we report on the case of a young African patient with typical features of APS-1 (mucocutaneous candidiasis, hypoparathyroidism and alopecia areata). These cardinal clinical features are similar to those that have been reported elsewhere in patients with APS-1.

To our knowledge, this is the first documented case report of APS-1 from Africa. APS-1 has been noted to occur more frequently among homogeneous populations, such as those in Finland,[3] northern Italy,[4] Norway[5] and Sardinia,[6] as well as among Iranian Jews.[8]

APS-1 is an extremely rare condition that is characterised by multiple, organ-specific autoimmune and mucocutaneous manifestations. It is an autosomal-recessive condition and a monogenic disorder linked to a defect of the AIRE gene located on chromosome 21q22.3.[9]

The AIRE protein is thought to play a role in the thymic process of induction of self-tolerance, its maintenance and the regulation of transcription.[10]

Early immunogenetic testing for the different mutations of the AIRE gene and human leukocyte antigen (HLA) typing are essential for identification of patients at risk. This is because APS-1 occurs sporadically or in siblings.[11] HLA-A28 has been demonstrated to occur more frequently in patients with APS-1 than in normal controls. Generally, HLA-A3 is mostly observed in patients with APS-1 and ovarian failure.[12] However, these tests are not readily available in most resource-limited settings.

Chronic mucocutaneous candidiasis is a frequent cutaneous manifestation in APS-1. Usually, it develops because of a selective immunological deficiency which involves the T-cell lineage that predisposes the patient to *Candida albicans*. Patients with APS-1 still possess a normal B-cell response which prevents the development of systemic candidiasis.[13]

Endocrine evaluation is of paramount importance in patients with APS-1. This is because a wide spectrum of endocrine and non-endocrine conditions occur at varying frequencies.[11] These include hypergonadotropic hypogonadism, autoimmune thyroid diseases, type 1 diabetes mellitus, pernicious anaemia, celiac disease, autoimmune hepatitis, vitiligo and alopecia areata.[7] In our case, on evaluation, the patient did not have any additional endocrine condition.

Patients with APS-1 should be followed-up on a regular basis because the majority of the above conditions develop later in the course of the disease.[11] Functional screening, by measuring organ-specific autoantibodies, aids in confirming the diagnosis of autoimmune conditions, and also in identifying patients who are at risk of developing other endocrinopathies.[1]

Conclusion

The common occurrence of chronic mucocutaneous candidiasis among patients with APS-1 signifies its relevance in the diagnosis. Since the majority of other autoimmune disease components develop later in life, long-term follow-up and endocrine evaluation are integral aspects in the management of patients with APS-1.

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