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CASE REPORT

An atypical case of a 14-year-old Filipino female with non-classical congenital adrenal hyperplasia presenting with alopecia universalis

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ABSTRACT

INTRODUCTION Non-classical congenital adrenal hyperplasia (CAH) represents a group of inherited, autosomal recessive disorders that typically presents with androgenetic alopecia, but may present with alopecia universalis on rare occasions.

CASE REPORT We report a case of a 14-year-old Filipino female with non-classical congenital adrenal hyperplasia presenting with alopecia universalis, treated with a combination of Tretinoin and Minoxidil solution, low dose prednisone and an oral supplement containing zinc gluconate, nicotinamide, superoxide dismutase, vitamin E and selenium, with noted gradual hair regrowth and improvement in Dermatology Life Quality Index (DLQI).

CONCLUSION Alopecia universalis in a patient diagnosed with non-classical congenital adrenal hyperplasia is a rare and atypical manifestation, with no case reports available to describe its occurrence. Due to its rarity, there is no standard treatment for patients with this condition. However, the combination of tretinoin and minoxidil solution, low dose prednisone and an oral supplement containing zinc gluconate, nicotinamide, superoxide dismutase, vitamin E and selenium shows promising results.

KEYWORDS alopecia universalis, minoxidil, tretinoin,

INTRODUCTION

Congenital adrenal hyperplasia (CAH) represents a group of inherited autosomal recessive disorders affecting 1 in 15,000 live births.[1] Majority of cases are caused by 21-hydroxylase deficiency (21-OHD) with mutations found on the CYP21A2 gene, leading to dysfunctional steroidogenesis. CAH comes in two major forms: 1) classical CAH, with manifestations such as severe adrenal crisis and androgen excess leading to ambiguous genitalia in female infants and 2) non-classical CAH, which is a milder form of the condition that also presents during late childhood with symptoms of androgen excess such as precocious puberty, menstrual irregularities, and hirsutism. Patients with non-classical CAH may also present with hair loss but limited studies have been reported to describe its prevalence and characterize its occurrence. In this case report, we present an atypical case of a 14-year-old Filipino female with non-classical CAH presenting with alopecia universalis.

CASE SUMMARY

We are presented with a 14-year-old female with a two-year history of generalized gradual hair loss. Her hair loss started as few, hairless patches on the scalp that eventually became multiple, even involving the eyebrows, eyelashes, and axillary and pubic hair. There was no associated fever, weight loss, or other systemic symptoms. Moreover, the patient has no other known co-morbidities at the time of consult and has no allergies to food or medications. She further claims to have family members with hair loss from the paternal side. Upon consult with our institution, patient was diagnosed as alopecia universalis.

Physical examination revealed complete loss of hair on the scalp, eyebrows, and eye lashes (Figure 1), as well as axillary and pubic hair. Dermatology Life Quality Index (DLQI) was also obtained with a score of 8 signifying a moderate effect on the patient's life. Biopsy was not done. Patient was initially treated with minoxidil 5% + tretinoin 0.05% combination spray solution, to be applied on the scalp twice daily for two (2) weeks, prednisone 25 mg/day (0.5mkd), to be taken per orem for two (2) weeks and a supplement containing zinc gluconate, nicotinamide, superoxide dismutase, vitamin E, and selenium - to

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be taken orally twice daily for two (2) weeks. The patient was also referred to Endocrinology service for further workup and co-management. Biochemical tests showed normal cortisol level, normal thyroid hormone levels, low dehydroepiandrosterone sulfate (DHEAS) and elevated 17-OH progesterone, which were diagnostic of non-classical CAH. The patient was advised by Endocrinology service to take prednisone 5 mg (0.5mkd) once daily for four (4) months. The patient also continued to follow-up with Dermatology service where she was asked to continue applying topical medications and to continue taking the oral supplement for a total of three (3) months with noted gradual hair regrowth on the frontal and occipital scalp, with vellus hair growth on the parietal scalp and vertex. Hair regrowth was also noted on the eyebrows (Figure 2) and DLQI improved with a score of 5, signifying a small effect on the patient's life.

DISCUSSION

Congenital adrenal hyperplasia (CAH) refers to a group of inherited autosomal recessive disorders, majority of which is characterized by 21-hydroxylase deficiency from mutations in the CYP21A2 gene. The resulting dysfunctional process of steroidogenesis is characterized by glucocorticoid and mineralocorticoid underproduction and androgen excess.[2]

About 1/15,000 births in the general population develop classic CAH. Meanwhile, the frequency of non-classical CAH appears to be ethnicity-based with an increased incidence of 1/1000 among Caucasians and other minority and ethnic groups.[3]

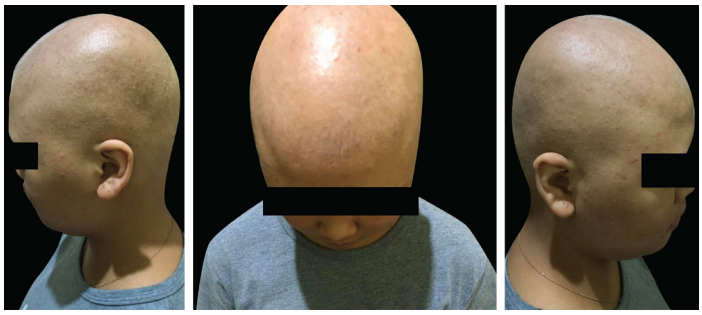

Figure 1. Physical examination showed generalized hair loss affecting the entire scalp and eyebrows.

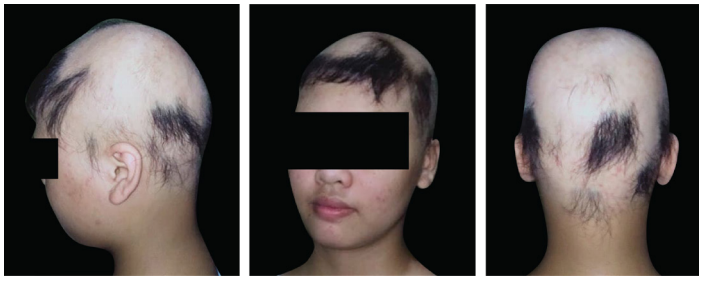

Figure 2. Physical examination after three (3) months of treatment show areas of hair regrowth on the frontal, and occipital scalp with vellus hair growth on the parietal scalp and vertex.

CAH can be of the classical type, with 75% of patients presenting upon birth or in infancy with severe-salt wasting phenomena as a result of aldosterone deficiency leading to dehydration, hypovolemia, and shock. Moreover, female infants with CAH may also present with ambiguous genitalia, premature puberty, and growth abnormalities. On the other hand, female patients with non-classical CAH present with milder symptoms consisting of menstrual irregularities, premature development of pubic hair, abnormal growth, and signs of androgen excess such as hirsutism and virilization.[4] These manifestations are usually present at birth and only become apparent in late childhood or early adolescence. A small number of patients may also manifest with hair loss secondary to increased androgen sensitivity. In a multicenter cohort study by Moran et al. involving 220 female patients with non-classical CAH, the researchers aimed to determine the most common clinical features of 21-hydroxylase-deficient non-classical CAH in various age groups. Results of the study showed that in patients aged 10-19 years of age (n=64), the most common manifestations were: hirsutism (59%), oligomenorrhea (54%), acne (33%), infertility (13%), clitoromegaly (10%), androgenetic alopecia (8%), primary amenorrhea (4%), and premature pubarche (4%).[5] The hair loss associated with non-classical CAH is that of a male pattern type of androgenetic alopecia and variations in presentation correspond to the degree of enzyme deficiency.[6,7] In the hair follicle, excess androgen exerts its effects leading to follicular miniaturization because of a prolonged anagen phase; thus resulting in the characteristic hair loss. Only a handful of studies exist describing the pattern of hair loss in patients with non-classical CAH and interestingly, none of these describe a pattern that could be seen in our patient.

A diagnosis of non-classical CAH in children is made based on 17-hydroxyprogesterone (17-OHP) values. A 17-OHP level great than 2 ng/mL is highly suggestive of non-classical CAH. Our patient's 17-OHP level is 3.81 ng/mL. For hair loss, the diagnosis of alopecia in patients with non-classical CAH is the same as alopecia universalis, with clinical history and physical examination as essential tools for a proper assessment of the patient's condition.

Treatment of non-classical CAH is usually not indicated unless the patient presents with symptomatic disease in the form of symptomatic hyperandrogenism. Treatment generally consists of low dose oral glucocorticoids until symptoms abate. Standards have not been established regarding the duration of treatment for these patients but it is prudent that concentrations of 17-hydroxyprogesterone, androstenedione, and testosterone be monitored regularly. Our patient was initially given prednisone 25 mg/day (0.5mkd) for two (2) weeks before she was referred to Endocrinology service. With this, she was advised to

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watch out for side effects of oral corticosteroids such as weight gain, bone changes, and increased susceptibility to infections among many others. Eventually, the patient was maintained on a lower dose of prednisone at 5 mg/day (0.5mkd) for a duration of four (4) months with eventual hair growth, specifically in the frontal and occipital area of the scalp and improvement in DLQI.

At present, there are no established guidelines for the treatment of alopecia among patients with CAH, particularly among the pediatric population other than oral glucocorticoids. Information regarding the safety and use of conventional hair regrowth treatment products in children are still insufficient.[8] However, therapeutic agents that are being used to treat adults have been tested in the pediatric population with promising results. In one retrospective study, topical 5% minoxidil was reportedly used for a duration of six (6) months in patients aged 11-18 with noted cessation of hair loss and thicker hair reported at six (6) months upon initiation of therapy and stabilization of hair loss after one (1) year of use.[9] In another study by Sharma et al., topical 0.1% tretinoin was shown to augment minoxidil 2% topical solution response, resulting in regimens combining the two medications which produced better outcomes in the management of androgenetic alopecia.[10] However, clinicians should prescribe with caution because of the risk of systemic absorption. Finally, there are only a few studies to support the role of vitamins and supplements for the treatment of alopecia. However, these supplements may still be used off-label as adjunctive treatment.

CONCLUSION

Alopecia universalis in a patient diagnosed with non-classical congenital adrenal hyperplasia is a rare and atypical manifestation, with no case reports available to describe its occurrence. Due to its rarity, there is no standard treatment guideline for patients with this condition. However, the combination of tretinoin and minoxidil spray solution, low dose prednisone, and an oral supplement containing zinc gluconate, nicotinamide, superoxide dismutase, vitamin E, and selenium shows promising results.

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