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MILD ANDROGEN INSENSITIVITY SYNDROME ASSOCIATED WITH LEFT HEMIHYPERTROPHY-A RARE CASE REPORT

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Abstract

Androgens are the main regulators of growth of hair follicles. After puberty they promote the transformation of vellus hair follicles into terminal hair follicles in the axillary, pubic and beard areas and cause regression of hair follicles over the scalp resulting in androgenetic alopecia known as 'androgen paradox'. Hemihyperplasia is the asymmetric overgrowth of a part or entire side of the body. It may occur in isolation or can be associated with certain genetic syndromes or embryonal tumors. Unilateral localized failure of beard growth may occur due to abnormal target tissue sensitivity to androgens, caused by a defect in the androgen receptor gene structure. We report a rare case of a 26-year-old male with right-sided beard growth failure, likely due to androgen receptor gene alterations despite normal androgen levels. Histopathology revealed primitive hair follicles and mild inflammatory infiltrates. This case suggests androgen insensitivity as a cause of unilateral beard growth failure, possibly associated with isolated left hemihypertrophy, a rare presentation not previously reported.

INTRODUCTION

Androgens play a complex role in hair follicle growth. They stimulate the transformation of vellus hairs to terminal hairs in areas like the beard, but conversely, contribute to androgenetic alopecia (scalp hair loss) [1]. This effect is mediated by androgen receptor (AR) signaling in the dermal papilla, regulating the production of growth factors like IGF-1, inducible nitric oxide synthase and stem cell factor [1]. Unilateral beard growth failure can be a sign of underlying androgen receptor dysfunction [2].To date, only one case of unilateral localized beard growth failure has been reported, in 1996 [2]. Androgen insensitivity syndrome (AIS), characterized by androgen receptor defects, manifests in varying degrees, including complete AIS with female external genitalia to mild AIS with normal male genitalia [3]. Hemihyperplasia, also known as hemihypertrophy, is an overgrowth of one body side that may be associated with internal organ asymmetry. It can occur in isolation or as part of syndromes, associated with an increased risk of embryonal tumours. Cutaneous features may include hyperpigmentation and hypertrichosis [4]. We present a unique case of a young male with unilateral beard growth failure, possibly due to androgen receptor gene alterations, and its unexpected association with isolated hemihypertrophy.

CASE REPORT

A 26-year-old male presented to the department of dermatology with complaints of right sided failure of beard growth. Patient is a known case of isolated left sided hemihypertrophy. On general examination, the patient was found to be moderately

built and nourished, height was 175.2 cms and weight 70 kgs. Facial asymmetry and hemihypertrophy was noted on the left side of the body. Vital signs and other system examination were normal. On cutaneous examination, multiple acrochordons were noted on the left side of the trunk (Figure 1) with diffuse hyperpigmentation over the left half of the face and neck (Figure 2). Inspection and palpation of the external genitalia revealed normal penis, urethral meatus, scrotum and scrotal contents. Among secondary sexual characteristics, axillary and pubic hair was found to be normal. Unilateral localized absence of beard hair growth was noted on the right side of the face (Figure 3). Examination of the oral cavity showed a scrotal tongue (Figure 4).

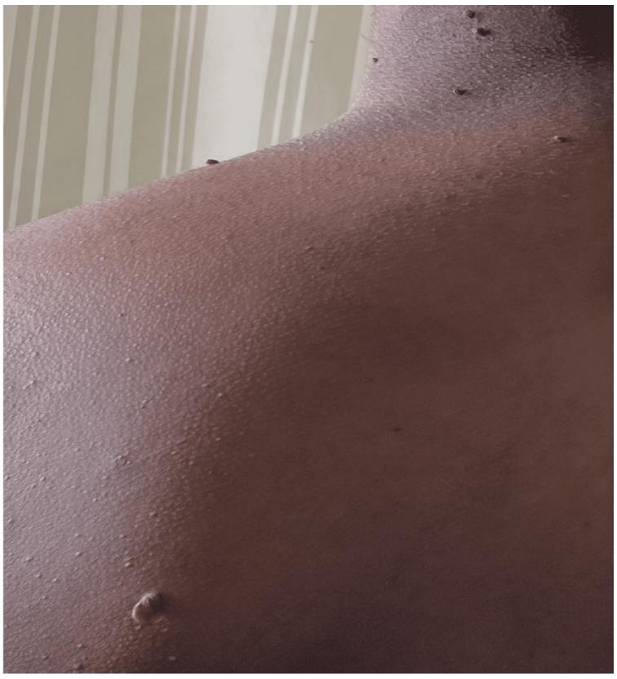

Figure 1: Multiple Acrochordons on the Left Side of the Trunk and Neck

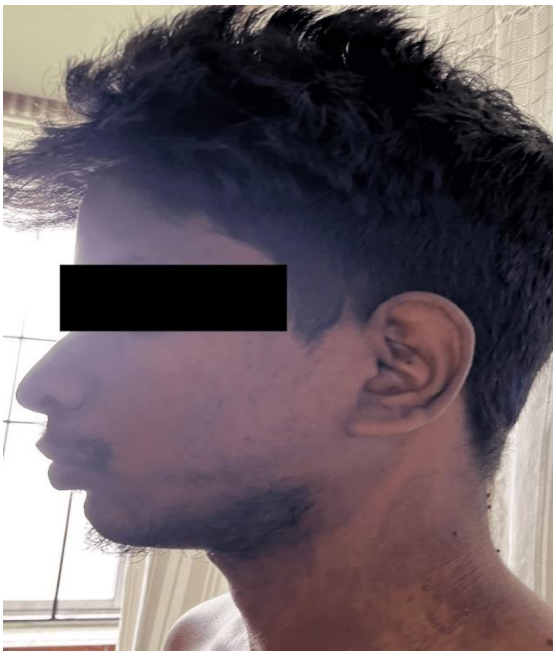

Figure 2: Diffuse Hyperpigmentation over the Left Half of the Face and Neck

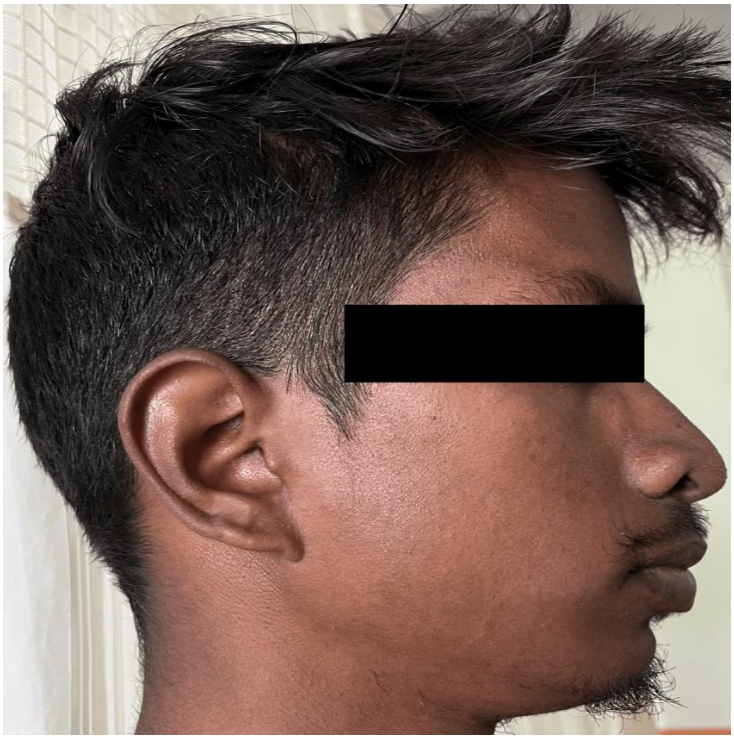

Figure 3: Unilateral Localized Absence of Beard Hair Growth on the Right Side of the Face

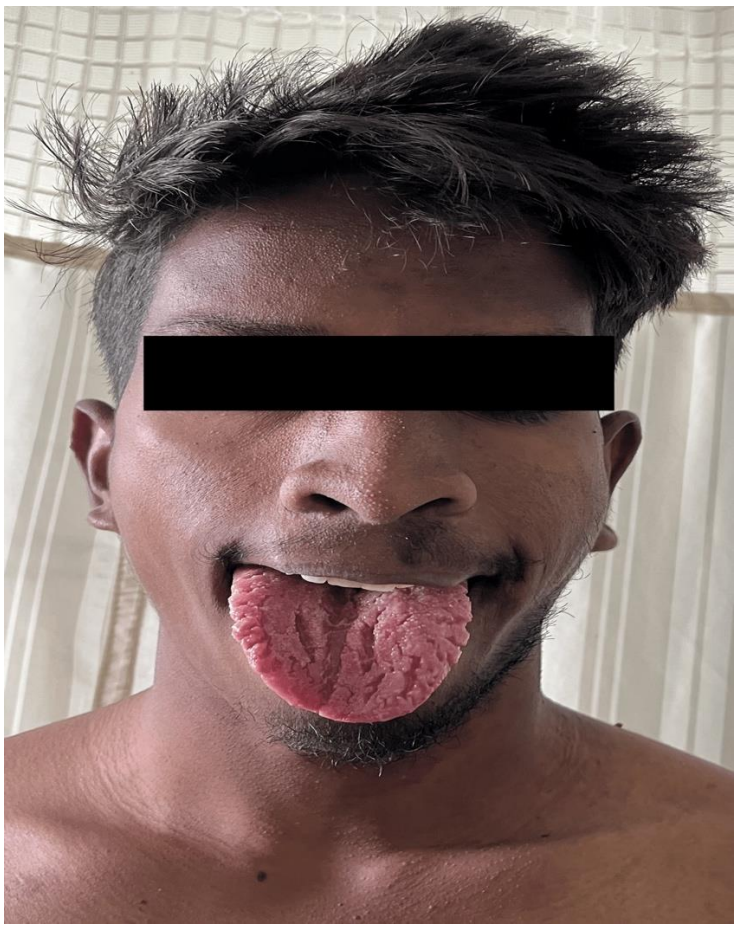

Figure 4: Oral Cavity Examination Showing a Scrotal Tongue

On dermoscopic examination, sparse, short, thin, lightly pigmented hairs was noted over the right side of the face in the beard area (Figure 5).

Figure 5: Dermoscopic Examination Showing Sparse, Short, Thin, Lightly Pigmented Hairs Over the Right Side of the Face in the Beard Area

On histopathological examination, epidermis showed focal thinning, hypogranulosis and mild increase in basal cell pigmentation. Superficial and deep dermis showed minimal perivascular lymphocytic and peri adnexal infiltration with mild increase in proliferating capillaries and focal extravasation of RBCs. Primitive hair follicles were noted with lack of mature pilosebaceous units (Figure 6).

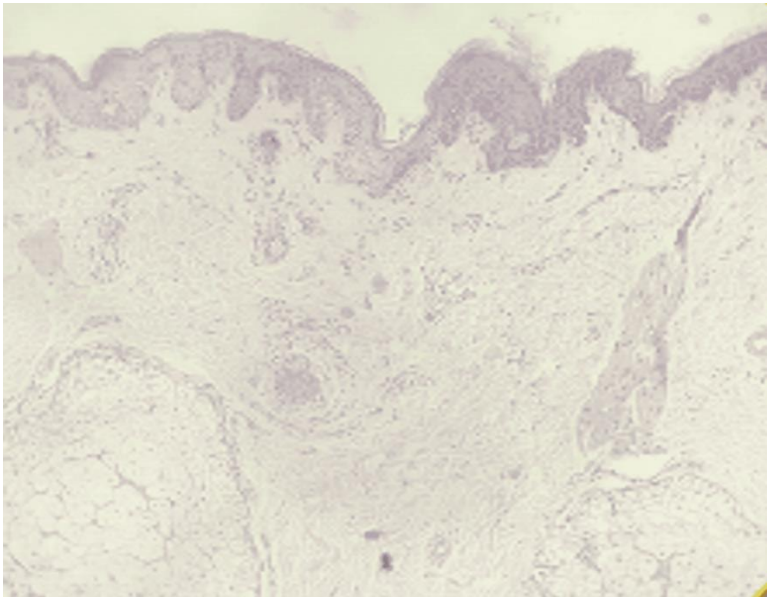

Figure 6:Histopathological Examination

All routine investigations done were found to be within normal limits. Karyotype analysis showed 46XY. Plasma androgen levels (dihydrotestosterone, dehydroepiandrosterone and dehydroepiandrosterone sulfate), follicle stimulating hormone (FSH), luteinizing hormone were found to be within normal limits. Ultrasound of neck, upper limbs, lower limbs and abdomen was normal. Patient was not willing for further androgen receptor studies.

DISCUSSION

The dermal papillae serve as the primary site for androgen action, mediated through low-capacity, high-affinity androgen receptors [5]. Testosterone is metabolized into 5 alpha-dihydrotestosterone (DHT), the major androgen produced by the beard dermal papilla [6]. Deficiency in 5-alpha reductase can lead to reduced beard growth [6]. Androgens modify the production of regulatory molecules, such as soluble paracrine factors and extracellular matrix proteins, which influence follicular growth [7]. Androgen resistance may arise from large-scale structural changes in the androgen receptor gene or single nucleotide substitutions causing premature termination or amino acid replacements, resulting in defective androgen receptor proteins [8]. These substitutions highlight residues essential for the normal function of the androgen receptor protein [8].

Androgen insensitivity syndrome can be subdivided into three phenotypes [9]:

1. Complete androgen insensitivity syndrome (CAIS) presents with typical female external genitalia and affects 2-5 per 100,000 individuals who are genetically male.
2. Partial androgen insensitivity syndrome (PAIS) manifests with predominantly female, predominantly male, or ambiguous external genitalia and is as common as CAIS.
3. Mild androgen insensitivity syndrome (MAIS) presents with typical male external genitalia and is less common.

The rare association of unilateral localized beard growth failure with hemihypertrophy is likely being reported for the first time in our case.

Isolated hemihypertrophy, also known as isolated hemihyperplasia, is characterized by asymmetric overgrowth of a body part due to abnormal cell proliferation and may be associated with internal organ asymmetry [7]. This condition is associated with an increased risk of embryonal tumors, including Wilms tumor, hepatoblastoma, neuroblastoma, adrenocortical tumors, and sarcomas [10]. Syndromic associations include Beckwith-Wiedemann syndrome, Proteus syndrome, neurofibromatosis Type 1, mosaic trisomy 8, and disorders associated with vascular malformations, such as Klippel-Trenaunay syndrome, CLOVES syndrome, and megalencephaly-cutis marmorata telangiectatica congenita [10].

Three common epigenotypes have been identified in Beckwith-Wiedemann syndrome and isolated hemihypertrophy, including uniparental paternal disomy of 11p15 (UPD), loss of maternal methylation of KCNQ1OT1, and hypermethylation of maternal H19 [10]. All patients with isolated hemihypertrophy should be referred to a clinical geneticist for evaluation [10]. Tumor surveillance is recommended for all hemihypertrophy patients during the first six years of life [11].

CONCLUSION

Patients with normal plasma androgen levels but localized hair growth absence under androgenic control may exhibit abnormal target tissue sensitivity. This patient, who presented with typical male external genitalia, normal plasma androgen levels, and normal beard growth on the left side but failed beard growth on the right side, likely has androgen resistance due to structural alterations in the androgen receptor gene. The patient declined further androgen receptor studies, leading to a clinical diagnosis of mild androgen insensitivity syndrome. To date, only one case of unilateral localized beard growth failure has been reported, in 1996. This unusual association with isolated hemihypertrophy appears to be reported for the first time in our case.

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