

Section

Medicine

Case

Report

HAIR-AN Syndrome: Inside Story

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ABSTRACT

15-year-old adolescent girl presented with weight gain, irregular menstrual cycle, skin lesions suggestive of acanthosis nigricans and hirsutism. On evaluation, she was found to have elevated testosterone levels with normal FSH, LH and fasting blood sugar, decreased glucose insulin index suggestive of Insulin resistance. In view of above features, diagnosis of hyperandrogenism-insulin resistance-acanthosis nigricans syndrome (HAIR-AN syndrome) was made. This syndrome is considered as a sub-type of polycystic ovary syndrome (PCOS). HAIR-AN syndrome has varied presentation and is usually seen by primary care physician, gynaecologist or dermatologist. Life style modification with weight reduction and drugs such as metformin helps in alleviating the symptoms. With limited resources in our country, diagnosis is frequently delayed leading to systemic complications. Early diagnosis and appropriate treatment would help in preventing complications of obesity, insulin resistance leading to

coronary artery disease, Type 2 diabetes mellitus, hyperlipidemia. Depression and suicidal behavior may be associated with it and should be aggressively addressed in young adults suffering from HAIR-AN syndrome.

Keywords: HAIR-AN syndrome, acanthosis nigricans, hirsutism, hyperandrogenism, insulin resistance.

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INTRODUCTION

HAIR-AN syndrome is combination of hyperandrogenism, insulin resistance and acanthosis nigricans, an unusual condition usually affecting females of prepubertal age. This syndrome may affect 1 to 3 percent of females presenting with hyperandrogenism, many of such cases remain undiagnosed. The importance of this constellation of symptoms lies in undiagnosed multisystem disorder with multiple ramifications to unsuspected malignant disorder in rare cases. We want to emphasize on early diagnosis which may help astute clinician in better management of

underlying condition.⁽¹⁾ Various endocrine disorders which may present with HAIR-AN syndrome such as Hashimoto's thyroiditis and Graves' disease (autoimmune disorders). Cushing's syndrome, polycystic ovary syndrome, acromegaly and congenital adrenal hyperplasia are few other nonmalignant endocrine disorders which may present with features of hyperandrogenism.⁽²⁾

CASE HISTORY

15-year-old adolescent girl presented with complaints of excessive weight gain and menstrual disturbances in form of oligo-hypomenorrhoea since 2 years. The family history of diabetes in father and mother was present. On clinical examination, she was an obese girl with body mass index of 33 (Fig 1). Signs of hyperandrogenism were present in the

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form of excess hair on face and body (Fig 2). There were blackish velvety patches of hyperpigmented skin (acanthosis nigricans) (Fig 3) over base of neck and axilla. In view of the above features, she was investigated and found to have elevated serum testosterone levels {117.81ng/dl (normal 14-76)}, with normal FSH {5.34 microIU/ml, (normal 4-13)}, normal LH {5.46 microIU/ml(normal 1.9-12)} and normal fasting glucose levels {91 mg/dl (normal 70-100)}. Her fasting insulin level was 63.55 microU/ml (normal 2-15) and fasting glucose insulin index 1.43 (normal more than 4.5) suggestive of insulin resistance. TSH, prolactin, DHEAS 17(OH) progesterone, cortisol was in the normal range. Ultrasound of abdomen showed no abnormality. In view of hyperandrogenism, insulin resistance and acanthosis nigricans diagnosis of HAIR-AN syndrome was made. She was advised for dietary changes and exercise for reducing weight and put on estrogen-progesterone pills, metformin and spironolactone (antiandrogen). On 6 month follow up she lost around 8 kg body weight and had regular menstrual cycles. Hyperpigmentation and hirsutism also improved.



Figure 1: Adolescent girl with features of weight gain and hyperpigmented skin.

DISCUSSION

HAIR-AN is a relatively rare subset of the polycystic ovary syndrome. Insulin resistance, which is considered the primary pathology, may be due to blocking antibodies against the insulin receptor or genetically absent/reduced insulin receptor function or number. Both these subtypes have similar presentation with excess of androgens. Clinical suspicion usually leads the clinician to diagnosis and helps in planning further management. Laboratory evaluation is helpful in supporting the diagnosis and excluding rare life threatening conditions as well as better management of systemic complications.⁽³⁾

Stromal ovarian cell synthesizes androgens on stimulation by LH or HCG, which can be further increased in the

presence of insulin. This stimulation is the key pathophysiology and degree of resistance to insulin and resulting level of insulin determine the severity of hirsutism.⁽⁴⁾ Degree of hirsutism correlates more with the level of insulin resistance than the level of observed hyperandrogenism.⁽⁵⁾ Insulin like growth factor 1 (IGF1) which has high degree of structural homology with insulin can also stimulate androgen synthesis in a similar way and is equally potent to insulin in this property.



Fig 2: Excessive hair growth on face.



Fig 3: Blackish velvety patches of hyperpigmented skin around neck (Acanthosis nigricans).

HAIR-AN syndrome has varied presentation and is usually seen by primary care physician, gynaecologist or dermatologist. As initial concerns are usually cosmetic, many patients delay their primary visit to a doctor. Diagnosis is frequently delayed leading to agony and suffering for the patient. A high level of clinical suspicion and early diagnosis can prevent further complications.

Goal of treatment is to decrease insulin resistance. Life style modification with focus on planned weight reduction (10 % weight reduction over baseline as initial goal) over period of six months with weekly goal of 500gm to 1 kg is advised. Avoiding crash diets with gradually increasing level of physical activity helps in achieving above goals. Reduction of weight helps by improving insulin resistance, decreasing serum insulin levels, ovarian androgen production as well as conversion of androstenedione to testosterone. With time there is increase in production of sex hormone-binding globulin (SHBG) causing further reduction in free androgen level.⁽⁶⁾

Insulin-sensitizing agents such as metformin play an important role in correcting ovarian hyperandrogenism. Metformin use should be avoided in adolescents without established glucose intolerance due to limited evidence. Further metformin is inferior to life style modification in improving hyperandrogenism, obesity and signs of insulin resistance.⁽⁷⁾ Other drugs which can be used are estrogenic pills, Antiandrogens such as spironolactone and flutamide, and inhibitors of 5 α -reductase. Basic role of all these drugs is to decrease the level of testosterone.⁽⁸⁾

CONCLUSION

HAIR-AN Syndrome is an underdiagnosed endocrinopathy characterized by triad of hyperandrogenism, insulin resistance and acanthosis nigricans. Incidence is 5% of adolescent girls and 40% of adolescent patients with menstrual disorder may have it. Symptoms occur from

adolescence but diagnosis is often delayed until adulthood. Early diagnosis and treatment may improve the quality of life of patient. Undiagnosed and untreated insulin resistance is linked to long term sequelae such as coronary artery disease, type 2 diabetes mellitus, hyperlipidemia. In adolescents depression and suicidal behavior may associated with it and should be aggressively addressed. Patients with the syndrome should also be screened for an underlying malignancy or autoimmune disorder.

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