CASE REPORT

HAIR-AN syndrome. Case report and literature review.

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RESUMEN

HAIR-AN syndrome, hyperandrogenism (HA), insulin resistance (IR) and acanthosis nigricans (AN), is a common multisystem disorder in adolescent women, associated with the presence of acne, hirsutism, obesity and/or amenorrhea, which can lead to the development of infertility, diabetes, cardiovascular problems and metabolic disorders.

Early detection, diagnosis, and treatment can help reduce morbidity, improve self-esteem, and have a positive impact on quality of life.

The case of a 31-year-old woman with acanthosis nigricans in almost all body folds, obesity, diabetes, dyslipidemia, menstrual cycle disorders, and hirsutism not diagnosed since adolescence is reported.

INTRODUCTION

HAIR-AN syndrome was reported in 1983 in a group of women with hyperandrogenism, insulin resistance, and acanthosis nigricans.[1,2]

This syndrome is found in approximately 5% of women with hyperandrogenism worldwide, with an average age from 15 to 16 years to reproductive age.[3,4]

The clinical manifestations can be serious and potentially irreversible, the diagnosis in this pathology is mainly clinical.[1,5]

The therapy is carried out based on the clinical manifestations, laboratory and findings in the ultrasound. Reduce (HA) and restore fertility with combined oral contraception, such as cyproterone acetate + ethinyl estradiol, improve peripheral insulin sensitivity with pharmacological and non-pharmacological measures to prevent, among others, cardiovascular risks.[1,3]

CLINICAL CASE

This is a case of a 31-year-old female patient, with a history of grade III obesity for 13 years, infertility due to partial hysterectomy with right oophorectomy, amenorrhea for 3 years, sedentary lifestyle, and family history of dyslipidemia.

He came to the clinic for presenting a progressive dermatosis since adolescence, located in folds (cervical, axillary and submammary), sternal region, interscapular region, extensor face of elbows and knees, characterized by thick extensive velvety, hyperchromic grayish-brown plaques (Figure 1).

The physical examination also revealed mild acne, female pattern alopecia (grade I on the Ludwig Scale), positive hirsutism (13 points on the Ferriman-Gallwey score), BMI 35 and an abdominal circumference of 115cm.

Extension studies show insulin resistance (HOMA Resistance Index 75.4mmol/mL), mixed dyslipidemia (HDL: 23mg/dL; LDL: 64.8mg/dL), hyperglycemia (fasting blood glucose: 235mg/dL), LH/FSH ratio of 1.53 and total testosterone 0.34.

Ultrasound reports the presence of a polycystic left ovary.

A 5mm punch biopsy of the cervical region was performed, with histological findings corresponding to acanthosis nigricans (Figures 2a and 2b).

With all these findings: insulin resistance, signs of hyperandrogenism and acanthosis nigricans, it is concluded as HAIR-AN Syndrome associated with Diabetes Mellitus II and metabolic syndrome. Treatment is started with oral antiglycemic agents, fibrates, combined oral contraceptives, topical retinoid, along with non-pharmacological measures (lifestyle changes, diet, and exercise).

DISCUSSION

Most adolescents tend to be concerned about their body image and are very sensitive to any change that may interfere with their appearance, such as the symptoms of HAIR-AN syndrome, where there is an increase in the severity of acne, hirsutism, acanthosis nigricans, obesity and cardiovascular complications.[4]

The exact pathophysiology is unknown, it is inferred that HAIR-AN syndrome may belong to a specific and rare sub phenotype of polycystic ovarian syndrome (PCOS), where severe insulin resistance is found, or; if it is a variant of SAHA syndrome (seborrhea, acne, hirsutism and alopecia); but it also refers to the fact that they can be completely different entities, which present common characteristics in clinical manifestations. Scientific reports are fundamentally case series and case reports.[1,3,6]

The evidence found about the pathophysiology of the disease reports that due to the existence of insulin resistance and hyperinsulinism, gonadal functional activity is exacerbated, clinically observed as hirsutism and AN.

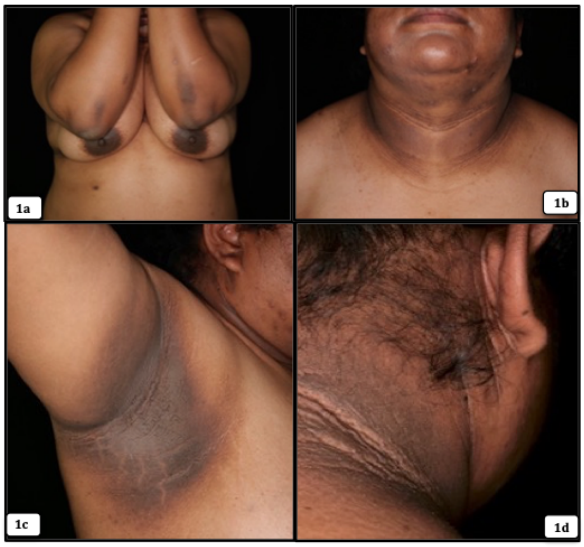

Figure 1. Clinical image of acanthosis nigricans. **1a y 1b.** Brown gray hyperchromic plaques on the elbows and anterior neck region. **1c y 1d.** Extensive, thick, velvety hyperchromic plaques in the armpits and posterior cervical region.

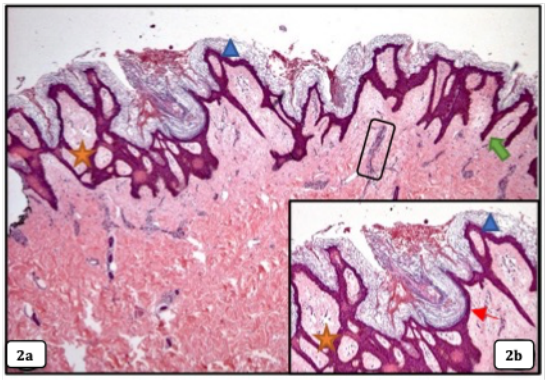

Figure 2a. Histopathological image of acanthosis nigricans. 40x. Hematoxylin and eosin staining. **Figure 2b.** Histopathological image. 40x. Hematoxylin and eosin staining.
Findings in the figure 2: ★ Pseudopapillomatosis with valleys, ⬅ Irregular elongation of the ridge rete, ▲ Hyperorthokeratosis, ▢ Superficial perivascular lymphohistiocytic inflammatory infiltrate, ➘ Basement membrane pigment.

On the other hand, AN is related to various conditions of hyperinsulinemia, non-insulin dependent diabetes mellitus, obesity and PCOS; Due to the fact that insulin cannot be recognized by cells at the peripheral level and in response, the pancreas increases the synthesis and production of insulin to later join IGF-1, stimulating the stromal theca of the cells. In addition, when there is hyperinsulinemia for a long time, they act synergistically with LH, which increases androgen production by stimulating ovarian steroidogenesis, so that HA produces virilization and chronic anovulation. The clinical findings that are developed in the pathophysiology of this disease are similar to those found in this clinical case.[1,2,7,8]

The clinical manifestations of the HAIR - AN syndrome can have a significant impact on the quality of life of the affected people, as in the case described, it is aesthetically affected by acanthosis nigricans at the level of folds, metabolic syndrome and infertility.[1,5]

It is considered that this entity is underdiagnosed, both for HAIR-AN syndrome and for PCOS, which can delay diagnosis, as in the case presented. The patient was diagnosed with HAIR-AN due to clinical and biochemical hyperandrogenism (normal levels of LH and FSH, while in PCOS the LH/FSH ratio is elevated), insulin resistance, and acanthosis nigricans. It should be noted that this syndrome is rare and causes controversy in its diagnosis.[1,5,9,10]

The treatment will depend on the patient's symptoms and their desire to conceive. Hyperandrogenism, since it is the cause of the development of the entire syndrome, insulin resistance must be decreased and lifestyle changed to avoid future complications and improve quality of life.[1,3]

CONCLUSIONS

The study of the case in the referred patient allows us to infer that the HAIR-AN syndrome is a rare disease, whose clinical presentation makes its diagnosis difficult. The treatment of choice is to reduce the levels of hyperandrogenism through combined oral contraception, to decrease gradually the rest of the symptoms, in addition to changing the lifestyle, eating habits and the diabetes treatment in this patient, are a key to improving her quality of life.

In the future, it is recommended to investigate, carry out more research on this entity, because the findings do not allow for quality information or high scientific evidence. Currently its pathophysiology is not clear and therefore it is necessary to define if it is an isolated entity, or if it is a variant of another disease.

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