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Alopecia areata and Down's syndrome

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Abstract

The Down syndrome (DS) present different skin manifestations as: alopecia areata (AA), vitiligo, atopic dermatitis, pityriasis rubra pilaris, among others. AA is a chronic autoimmune inflammatory condition T-cell mediated against pilosebaceous follicle with stop of the anagen phase. AA is presented in 6-10% of patients with DS (general population: 1.7%) and it is more frequent in women. Politerapy is more effective than monotherapy in the treatment of AA in that cases, and the prognosis is different depending of the clinical type of AA.

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PALABRAS CLAVE

Síndrome de Down;
Alopecia areata;
Folículo piloso

Alopecia areata y síndrome de Down

Resumen

El síndrome de Down (SD) presenta diversas manifestaciones dermatológicas; entre ellas, hay un aumento de incidencia de alopecia areata (AA), vitiligo, dermatitis atópica, folliculitis, acné, pitiriasis rubra pilar, entre otras. La AA se debe a un proceso inflamatorio crónico de origen autoinmune, mediado por células T que afectan al folículo piloso, lo que conlleva a la interrupción del ciclo folicular en la fase de anágeno. La incidencia de AA en pacientes con SD es del 6-10%, comparado con el 1,7% en la población general, y con predominio en el sexo femenino. El tratamiento comprende varias medidas, de las cuales la politerapia es más efectiva que la monoterapia, y el pronóstico es variable según la forma clínica de presentación.

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Down's syndrome (DS) is a genetic disorder caused by the presence of an extra copy of the 21st chromosome (Trisomy 21), and was first described in 1866 by John Langdon Down. A genetic relationship was proposed in the 1930s, but it was not until 1958 when Jérôme Lejeune and Pat Jacobs were able to verify the chromosomal origin of the syndrome on chromosome 21.¹ Confirmation by karyotype is necessary for its definitive diagnosis. It affects one in every 800 births, regardless of gender or racial group,²⁻⁴ and is the syndrome that most often leads to mental retardation. The risk increases with the age of the mother.

The phenotype is variable but there are common clinical signs among people with DS. The typical clinical presentation of DS is characterised mostly by hypotonia, folds on the inner corner of the eyes, a small head and mouth, short stature and a single palmar transverse crease (simian crease) and other conditions.³ The level of mental retardation is variable.^{1,3} There is an increased risk of deafness (75%), congenital heart disease (50%), hypothyroidism (15%), cataracts (12%-15%) and gastrointestinal atresias (12%),³ among others. There is also higher mortality caused by infection and increased incidence of malignancies such as leukaemia.⁴

DS also shows an increase in various dermatological manifestations when compared with control groups: for example, there is an increased incidence of alopecia areata, vitiligo, atopic dermatitis, folliculitis, acne,

pityriasis rubra pilaris, anetoderma, cheilitis, xerosis and tinea pedis.^{2,3,5,6}

Alopecia areata

Alopecia areata (AA) is a relatively common disorder in children and adults. Clinically, it is characterised by well-circumscribed patches of non-scarring hair loss on the scalp and beard, but may involve the entire epidermis.^{3,7} It is due to a chronic inflammatory process of autoimmune origin, mediated by T cells that affect the follicle, leading to an interruption of the follicular anagen cycle, and hair loss in the telogen phase.⁷

The classical clinical forms of AA are: AA monocularis (alopecia in a single location) (fig. 1), AA multilocularis (multiple areas of hair loss) (fig. 2), AA totalis (affecting the entire scalp) and AA universalis (complete hair loss throughout the epidermis).⁷

The incidence of AA in patients with DS is 6%-10% compared with 1.7% in the general population.^{6,8-11} The predominance of AA is equal for both sexes in the latter, but there is a predominance of females with AA in patients with DS (17.4% vs 3.1%).^{2,6} It appears between 5 and 20 years of age in 60% of cases, but can occur at any age. Patients with Down's syndrome may have any clinical type of alopecia areata.

In 1967, Muller and Winkelmann first reported the association between AA and DS.⁸ The study by Du Vivier and Munro^{12,13} showed that AA is more common in the Mongolian race. In their analysis of 1000 patients with DS, they found 60 patients with AA, of whom 14 (23%) had antibodies: there were 11 cases of anti-thyroid antibodies, 2 cases of parietal cell antibodies and 1 case of antinuclear antibodies. These antibodies were also more common in females.

Carter and Jegasothy⁶ reviewed 214 hospitalised patients with DS and reported 19 cases of AA and 4 of vitiligo. Also,



Figure 1 Alopecia areata monocularis in the occipital area in a patient with Down's syndrome.



Figure 2 Alopecia areata multilocularis in an infant with Down's syndrome.

3 cases of the vitiligo patients had AA. This association was explained by the deficit of T lymphocytes. In these cases, therefore, an immune factor played an important role in the incidence of AA, thyroid disease, vitiligo, premature ageing and high rate of malignancies, among others.⁷

Brown et al¹⁴ demonstrated a decrease in the number of T cells in people with AA, compared with the general population. The percentage of T cells in peripheral blood was 58% in people with AA vs 74.9% in the control group, which was statistically significant.

In 2000, Tazi-Ahnini R et al¹⁵ reported an increase in Mx1 protein in the perilesional skin of the AA patches. The MX1 gene is responsible for the synthesis of interferon induced by the protein P78 (MxA). This protein is present in the anagen phase of hair follicles in patients with AA, but does not exist in normal follicles.

In a retrospective analysis of 100 patients with Down's syndrome, Daneshpazhooh et al¹⁶ reported 11% with AA. Articles published in the literature addressing the association between AA and DS report an increased incidence of AA in this syndrome.^{6,8,9,12-18}

Alopecia areata treatment

The treatment of AA in patients with DS is the same as in the general population: topical treatments, systemic treatments or both can be used. Although there have been no controlled studies, it appears that a combination therapy is more effective than monotherapy.¹⁹ The type of AA treatment selected depends on several factors, including the extent of the alopecia, patient age and associated conditions.

For topical treatment, corticosteroids, minoxidil, immunomodulators (diphenylpyrone and squaric acid dibutylester), among others, are used. Phototherapy and photochemotherapy are not used, as retrospective studies have noted low response rates for them.²⁰

Before starting any systemic treatment, it is important to assess the risk/benefit ratio, as well as to consider the side effects and impact in the short and long term.

Examples of systemic treatment options include oral corticosteroids (continuous or pulsed), cyclosporine, methotrexate and sulfasalazine. Biological therapy has not shown any clear benefits.^{19,20}

Galán-Gutiérrez et al¹⁹ performed a review of the literature on the update of the treatment for alopecia areata and proposed an algorithm for therapeutic guidance. Patients with the poorest response to AA treatment include those with the following features: early onset of the disease, extensive affectation, a history of AA and DS itself.¹⁵

Summary and conclusions

AA is more common in patients with DS than in the general population. Treatment should be individualised for each patient, with the risk/benefit ratio evaluated. AA in patients with DS follows a more chronic course and has a worse prognosis.

Although it is not as serious as other manifestations of this syndrome, AA may have a major psychological impact on patients and their families.

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