Clinical Characteristics of Alopecia Areata in Down Syndrome

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SUMMARY This study was undertaken to better understand clinical characteristics, environmental and physical events in Down syndrome (DS) and alopecia areata (AA). This cross-sectional study included 18 DS patients who were currently presenting or had presented AA. We evaluated gender, age, location and type of AA, presence of autoimmune disease or atopy, AA in first-degree relatives, and environmental, physical, and clinical intercurrences. The mean age of study subjects was 11.6 (SD ± 5.5) years and mean age at AA onset 7.2 (2.5 to 15.2) years. The duration of alopecia episodes varied, with a mean of 2.7 (0.1 to 18.7) years. Recurrence of AA was reported in 27.7% (5/18) of subjects, with a mean number of recurrences of 3.6. Localized type AA was seen in 83.4% of individuals, with the most frequent location on the scalp (100%). Seven of the individuals presented atopy. Fourteen individuals had undergone environmental and/or clinical intercurrences. In conclusion, the most frequent presentation of AA in DS is the non-recurrent, localized form on the scalp, with a varied period of duration. Changes in the individuals' routine occurred in more than half of the study group. We suggest further studies of the psychology and immunogenetics in the etiopathology of AA in DS.

KEY WORDS: alopecia areata, Down syndrome

INTRODUCTION

Down syndrome (DS), trisomy 21, is the most frequent chromosomal disease and a common cause of mental retardation, representing 10.0% to 30.0% of all cases with severe mental retardation (1). The prevalence of DS is approximately 1:770 births, with a slight preponderance in male gender (2). DS individu-

als present an abnormal immune system, which leads to susceptibility to infections, with abnormal lymphocyte function, such as a decrease in immune-dependent T-cell response (3,4) and IgG deficiency (5). Anatomic evidence suggests that the immune defect in DS individuals is primarily due to disarrangement of the thymus as a consequence of lymphocyte depletion, reduction of the cortex, loss of corticomedullary delimitation, and enlargement of Hassall's corpuscles in the thymic medulla. Consequently, there is an abnormal thymic maturation, resulting in phenotypic and functional abnormalities in the circulating T-lymphocytes (4).

DS individuals present an increased incidence of autoimmune disorders such as thyroiditis, (6,7), moyamoya disease (8), diabetes mellitus type I (9), vitiligo (10), pernicious anemia (11), systemic lupus erythematosus (12), chronic active autoimmune hepatitis (11) and alopecia areata (AA) (10,13). The most common autoimmune disease affects the thyroid gland and occurs more frequently after eight years of age (14). AA is described as asymptomatic, well-circumscribed, circular areas of hair loss ranging from 2 to 5 cm in diameter; in extensive cases, coalescence of the lesions and/or involvement of other hairy surfaces is observed. (15,16). This entity is known as an autoimmune disorder frequently associated with vitiligo (7,15,17), pernicious anemia, autoimmune adrenal insufficiency and/or Hashimoto thyroiditis (7). AA may also be associated with atopy, emotional stress, septic focal points, as well as DS (15). The frequency of AA in DS varies from 1.3% to 11.0% (7,17-20). Wunderlich and Braun-Falco (19) were the first to describe the association between AA and DS in 1965, although AA had already been described as a dermatologic finding among patients with DS in 1954 (21). Carter and Jegasothy studied 214 institutionalized DS patients and observed 19 (8.9%) cases with AA (17).

The purpose of this study was to describe clinical characteristics and events possibly related to AA in DS individuals.

SUBJECTS AND METHODS

Subjects

Eighteen children and adolescents with DS were evaluated at the Medical Genetics Service of Martagão Gesteira Pediatric Institute (IPPMG) – Federal University of Rio de Janeiro (UFRJ). Participants came from Martagão Gesteira Pediatric Institute, Fernandes Figueira Institute – FIOCRUZ and Gafreé-Guinle Hospital – UNIRIO (convenience sampling). All individuals were diagnosed by cytogenetic analysis (G-banded karyotype, 550 bands) and presented a documented medical history of AA or presented alopecia at the time of consultation at the Medical Genetics Services. AA was considered to be hair loss leading to a 'flaw' on any hairy body surface. The clinical research protocol was approved by the Ethical Research Committee (IRB) of the IPPMG. The patients that participated in this study were all included in the database and platform that we have been developing named DataGenno (22).

Methods

A cross-sectional study was performed on a convenience sample of children and adolescents with DS. The following variables were studied: gender; age; location of alopecia; type of hair loss; presence of vitiligo, autoimmune disease or a suggestive history of atopy; history of AA in first-degree relatives; and environmental, physical, and clinical intercurrences. Data were collected from the individuals' files and through interviews with parents and guardians then tabulated.

Statistical analysis

A descriptive analysis was performed and data were presented as percentage, mean, median and standard deviation.

RESULTS

Sample characteristics

Eighteen children and adolescents with DS (11 boys and 7 girls), mean age 11.6 years (SD ± 5.5; limits: 3.8 to 21.7 years; median = 10.1 years) and current or previous history of AA were included in this study. In the total of 18 individuals studied, the mean age at AA onset was 7.2 years (limits: 2.5 to 15.2 years), median 7.7 years. The mean interval between the ages of the first alopecia episode and the time of the study was 4.3 years (limits: 0.1 to 12.8 years). Seven (38.9%) patients presented a positive clinical history of atopy; three individuals presented asthma; while two individuals presented with rhinitis and two with asthma and rhinitis. We did not find any individual with vitiligo and/or autoimmune disease. There was no presence of AA observed among first-degree relatives.

Characteristics of alopecia episodes

The duration of alopecia episodes varied greatly. The mean duration was 2.7 years (limits: 0.1 to 18.7 years), median 1 year in individuals presenting only one episode (13/18). In the individuals who had more than one episode (5/18), the shorter-lasting episode was 0.4 years and the longer-lasting episode 2.4 years. In eight (41.1%) individuals, the clinical picture of AA persisted from the first episode, and in two of them, different body areas were affected, with periods of remission in one of the areas.

Recurrence of AA was reported in five (27.7%) individuals and the mean number of recurrences *per* individual was 3.6. Duration of the intervals between recurrences was obtained for only two of the subjects (2/5): 1.1 and 3.3 years. At the time of the study, 13 individuals presented alopecia (four recurrent cases and nine non-recurrent cases). In all five recurrent cases, alopecia was observed in the same area that was originally affected.

A localized type of hair loss was seen in 83.4% of patients, and the most frequent location was the scalp (18/18; 100%). Two individuals presented combined hair loss. In one case, the affected areas were the scalp, limbs, axilla, genitalia and face; in the second case, the scalp and genitalia. There were no cases of total hair loss of the scalp.

Environmental and clinical intercurrences

Fourteen (77.8%) individuals presented environmental and/or clinical intercurrences, as follows: environmental (8/14), environmental and clinical (4/14), and clinical only (2/14). The most frequent environmental intercurrences were change of school and teacher, followed by death of loved ones and parental separation.

Of the 18 participants, 36.6% (3/18) presented intercurrent illnesses (outpatient treatments of infections of the upper and lower respiratory tract and allergic manifestations) during the study period, which were taken in consideration (before, during, and after alopecia) (Table 1).

Change of school and/or teacher

Seventeen individuals attended school; 10 of them underwent changes related to their school and/or teacher (10/17; 58.9%). Six subjects moved to different schools (6/17; 35.3%); in four individuals, the alopecia episodes preceded the school change; in one individual, the change occurred during an episode and one individual changed school twice: the first took place before the episode of alopecia and the other took place during an episode (Table 1). There was a change of teachers at the school in 41.2% of cases (7/17); in two cases, the teacher change preceded the alopecia episode, in 2 other cases the teacher change occurred during the episode, in one case the change occurred after the episode of alopecia, and in two cases there were two teacher changes, one before an episode of alopecia and another change during the same episode of alopecia (Table 1). None of the individuals held jobs.

Change of residence

One of the individuals changed the place of residence during an episode of alopecia (Table 1).

Table 1. Distribution of environmental, physical and clinical intercurrences in Down syndrome individuals with alopecia areata

I	Age (yrs)	Gender	School change	Teacher change	Change of residence	Ill family member	Death	Separation	Puberty	Illness
01	3.7	M	NA	NA	N	N	N	N	N	N
02	3.7	F	S1	S2	N	N	S2 **	S1	N	N
03	6.0	F	N	N	N	N	N	N	N	N
04	6.4	F	N	N	N	N	N	S1	N	N
05	8.2	M	N	S1 + S2	N	N	N	N	N	N
06	8.6	M	N	S1	N	N	N	N	N	S6
07	10.0	M	N	S1	N	N	N	N	N	N
08	10.0	M	N	N	N	N	N	N	N	S6
09	10.0	F	N	N	N	N	N	N	N	N
10	10.2	M	S1	N	N	N	S3 *	N	N	S6
11	10.5	F	S2	N	S2	N	N	N	N	N
12	11.1	F	S1	S2	N	N	N	N	S2	N
13	15.6	M	N	N	N	N	N	N	N	N
14	15.9	M	N	N	N	S3	S3 *	N	N	N
15	17.5	F	N	N	N	N	N	N	S5	N
16	19.6	M	S1	N	N	N	N	N	N	N
17	20.3	M	S1 + S2	S1 + S2	N	S3	N	S2	S3	N
18	21.7	M	N	S3	N	N	S2	S2	N	N

I = individual; yrs = years of age; M = male; F = female; N = no; NA = does not attend school; S1 = before alopecia; S2 = during alopecia; S3 = after alopecia; S4 = before and during alopecia; S5 = during and after alopecia; S6 = before, during, and after alopecia; * = grandmother; ** = grandparents.

Family problems

Family problems occurred in six of the study individuals (6/18; 33.4%), the most frequent being death of a family member (2/6), parental separation (2/6), and parental separation along with death of a close family member (2/6). In cases of deceased family members, three cases were death of grandparents and one was death of an aunt. The deaths occurred equally during (2/4) and after (2/4) the episode of alopecia. In two cases, parental separation took place prior to the alopecia episode and in another two cases during the episode (Table 1). None of the individuals witnessed a conflict situation such as physical or verbal aggression. Two individuals had close family members who became ill during an episode of alopecia.

Puberty

Two individuals entered puberty during an episode of alopecia and one after AA (Table 1).

DISCUSSION

To our knowledge, this is the first study that describes the characteristics of AA, environmental and physical events in DS individuals. Due to its higher frequency in individuals with DS (7,17,19,20), AA is an entity that pediatricians, geneticists, and dermatologists should be aware of. This study presents limitations related to parents' memory (memory vice) and to convenience sampling. However, the results point to some important topics, which will be useful in the follow-up of these individuals.

The frequency of AA in DS has been reported by some authors, and it ranges from 1.3% to 11.0% (7,17-20). The variation observed probably occurred due to the different patient samples and the assessments performed by the authors. Wunderlich and Braun-Falco (19) predominantly studied children up to 8 years of age and this factor may have been a determinant for the lowest frequency observed (1.3%); Du Vivier and Munro (7) studied only the cephalic corporeal segment of alopecia and reported a frequency of 6.0%. Carter and Jegasothy (17) report on a frequency of 8.9%, although they studied a smaller number of patients (214 patients *versus* 1000 patients evaluated in each of the previous studies), suggesting that alopecia is more frequent in individuals that have DS with greater cognitive limitations, as the patients in this study were institutionalized. Finally, Daneshpazhooh *et al*. (20) report a frequency of 11.0% among 100 DS patients. At the Medical Genetics Service of the IPPMG – UFRJ, the frequency was 4.1%, within the range of variation described in the literature.

Although the literature reports AA to be more frequent in females (17,23), the sample in this study was predominantly male (61.2%). Schepis *et al*. (24) also report a higher proportion of male than female individuals with AA and DS (12 male and one female). In relation to the total cases registered at the IPPMG with and without AA (15/352), the more frequent occurrence of AA in male individuals was not significant (χ^2=3.39; *P*>0.05; DF=1).

There is no clear definition of age at AA onset, however, in a study of 736 patients carried out by Muller and Winkelmann (23), AA was more commonly observed in younger age groups (<16 years). The duration of the episodes varied, as did the intervals between the episodes. In the literature, we did not find a description of the duration of hair loss or the intervals between two episodes of AA. Muller and Winkelmann (23) demonstrated that after hair loss there was a tendency towards new hair growth, usually within a few months, and Rietschel (25) suggests that this type of alopecia tends to occur within a period of less than one year. Paradoxically, in the cases where only one episode was described, we found similar percentiles in relation to the duration of episodes when classified as less than one year and greater than or equal to one year. We acknowledge that long periods of hair loss may in fact signify the presence of subsequent episodes of alopecia that occurred after recovery from the initial episode, a frequent finding in many cases (23).

The recurrence of AA was observed in 5 (27.7%) cases. Muller and Winkelmann (23) found recurrence among adults and children without DS in 22.0% of cases. We suggest that individuals with DS tend to more frequently present recurrent episodes of AA, in addition to presenting a higher frequency than the general population. The most frequently observed alopecia was localized on the scalp, which is in accordance with some reports of alopecia in DS (6,26,27). In another study at the Medical Genetics Service of the IPPMG – UFRJ, we evaluated ten patients with AA, mean age 18.6 (SD 7.2) years and observed that all patients had one or more lesion in the scalp, two patients had lesions at other locations (eyelashes and eyebrows), and two patients evolved with total AA. Different reports in the literature demonstrate frequent association of alopecia with atopy (7,15,17,18,23). The percentile found in our casuistry was approximately 40.0%, which corroborates this association. It is important to note that we did not investigate the possible autoimmune diseases at the time of the study or when these individuals presented AA.

A positive family history of AA was observed in 10.0% to 25.0% of alopecia cases (18,23). However, we did not find an affected first-degree relative, suggesting that the occurrence of AA is more related to DS than to familial susceptibility in the cases studied.

Muller and Winkelmann (23) suggest that psychological factors may be important in the etiopathology of AA. The authors observed the precipitation and accentuation of episodes of AA in 12.0% of the population studied who had suffered acute emotional stress. We suggest that events such as change in school or family life might generate psychological stress in individuals with DS, who have a greater probability of presenting emotional and behavioral problems (28), a diminished adaptive capacity and difficulties in approaching new situations (29,30). As we did not compare the social background with age-matched DS individuals who did not present with AA, it was not possible to assume that environmental, physical, and clinical intercurrences may have played a role in the genesis of AA in our sample.

Despite the small sample size, at the Medical Genetics Service of the IPPMG – UFRJ we observed 352 individuals with DS and only 15 of them presented AA, yielding a frequency of approximately 4.2%. This finding is in agreement with the literature reporting on the frequency of AA in DS from 1.3% to 11.0%.

CONCLUSION

Based on the findings of this study, we suggest that the most frequent presentation of AA in DS is the localized, non-recurrent form on the scalp, with a varied period of duration. We also observed the presence of changes in school life in more than half of the study group. To contribute to the knowledge of this issue, we suggest further studies on emotional, immunogenetic, and other environmental aspects to better understand the etiopathologic mechanisms of AA in DS.

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