Case Report ISSN 2768-6647

Medical and Clinical Case Reports

Association between Alopecia Areata and Thyroid Dysfunction

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Received: 14 Jun 2023; **Accepted:** 21 Jul 2023; **Published:** 26 Jul 2023

Citation: Mabingui A, Bassir G, Mrida M, et al. Association between Alopecia Areata and Thyroid Dysfunction. Med Clin Case Rep. 2023; 3(3): 1-4.

ABSTRACT

Alopecia areata is an inflammation and T-cell mediated autoimmune disease against hair follicles. It is characterized by patchy hair loss. The exact etiology is unknown. It is thought that autoimmunity and stress may be causative. The incidence rate is 0.1-0.2% of the general population. The lesions may be single or multiple and can be self-limited or permanent. Multiple autoimmune thyroiditis, celiac disease and lupus erythematosus seem to be associated co-morbidity disorders. However, patient with Hashimoto thyroiditis and hypothyroidism seem to have strong association with autoimmune Alopecia. This article will explore in details the association between Alopecia Areata and thyroid dysfunction in patients with Alopecia.

Keywords

Autoimmune thyroid disorder, Alopecia areata, Thioperoxides, Thyroglobulin antibodies, Thyroid hormones, TSH, AA, TG, TPO.

Methods

Literature review using PubMed, EMbase and Web of Science and clinical experience from our clinical practice in the National Center of Allergy, Asthma & Immunology. In one retrospective study, non-scarring alopecia was associated with 36 of 41 patients with abnormal thyroid findings. The most common cause of hair loss was in patient with thyroid dysfunction [1].

In a descriptive study alopecia pattern and their relation to thyroid function, Vincent, et al found 57-60% had significant association with alopecia. Thyroid dysfunction was found in Urticaria (62.5%), Vitiligo (50%), hirsutism (27%), psoriasis (27%), seborrheic dermatitis (25%) and ichthyosis (18%), in total of 1232 patients in 25 months. The main types of alopecia seen was diffuse Alopecia (71.35%), Alopecia Areata (11.8%) and androgenetic (14.29%) [2].

In another study by Pearce, EN it was found the older the patient, the higher the association between alopecia and thyroid abnormalities [3] (autoimmune thyroid dysfunction).

In another study, a cross-sectional population survey by Usha Menon V, et al., showed a thyroid dysfunction (19.6%) among adults in Indian population [4]. A significant difference between females and males was observed in diffuse alopecia and androgenetic alopecia, but there were no significant differences between sexes in alopecia areata.

More patients with alopecia were seen in the 21-40 years age group, with diffuse alopecia (44.64%). In the age group of 0-20 years and 21-40 years, thyroid dysfunction was seen more in alopecia areata and diffuse alopecia. It was observed as age advanced the thyroid dysfunction associated with alopecia also increased in all types of alopecia, Kinoshita-Ise M, et al [5]. Thyroid antibodies, thyroid peroxidase and thyroglobulin antibodies are markers of thyroid autoimmunity.

Thioperoxides antibodies increase is a good indicator of hypothyroidism and other autoimmune diseases. High levels of antibodies and TSH suggest progression to hypothyroidism. The author concluded that all patients with alopecia of any kind should be screened for thyroid TSH and thyroid peroxidase [6].

In meta-analysis study for the association between Alopecia Areata (AA) and thyroid dysfunction were evaluated. Four hundred and

eighty-nine research papers were identified and 17 studies with 262,581 patients and 1,302,655 control subjects were included for quantitative analysis. It was concluded that alopecia areata is significantly associated with the existence of thyroid antibodies rather than with clinical or laboratory thyroid abnormality [7]. A recent cohort study from Taiwan included 5929 matched patients with Alopecia areata and 59,290 matched controls. They found that AA patients had an increased risk of all thyroid diseases, in contrary a significant increased risk of developing AA was observed among patients with thyroid disease, concluded that there is bidirectional association between all type of thyroid diseases and AA, suggesting shared biological mechanisms underlying these two diseases [8].

In another meta-analysis of 50 studies reviewed by Lee and colleagues concluded that current evidence suggests that thyroid dysfunction and autoimmune thyroid diseases are more in patients with Alopecia Areata [9]. Patel and colleagues made a retrospective study and made guidelines for evaluating thyroid function in children with AA. In 8 years, 289 patients with AA had thyroid function screening. The patterns of AA included patchy (68%), opliasis (13%), totalis (9%) and universalis (10%). A total of 59 (20%) patients had abnormalities on thyroid testing result [10].

Hypothyroidism was the most frequent 29 (49%) with Hashimoto thyroiditis being the most common 24 (20%). Other abnormalities included Hyperthyroidism 12 (20%) and subclinical thyroid dysfunction 7 (12%). They found that history of Down's Syndrome and family history of thyroid diseases had association with Alopecia and autoimmune disease. They recommended that routine thyroid function screening be limited to AA patients with medical history of Down's syndrome, personal history of atopy, family history of thyroids disease or clinical diagnosis of goiter suggestive of potential thyroid dysfunction.

In conclusion, several studies showed the close association between alopecia and autoimmune thyroid disease. Therefore, patient with alopecia should be investigated for autoimmune thyroid diseases.

In a recent study from Brazil concluded that severe alopecia and fibrosis and atrophy with thyroid deficiency is associated with zinc and selenium deficiency in sheep. The researchers also noticed that deficiency of these two elements is associated with hypothyroidism and that addition of zinc and selenium improve thyroid function both in animals and humans [11].

In a study from Nepal which included 75 patients with Alopecia and 75 healthy controls were evaluated for thyroid dysfunction. Prevalence of thyroid disorder was significantly higher in AA group (17.3%) as compared to controls (1.3%) (P=0.001) [12].

Fricke and Mitera reviewed the literature within the last 51 years that measured AA's incidence, prevalence, distribution, disability-adjusted life years (DALYs), quality of life and associated psychiatric and medical comorbidities were included. They found the lifetime incidence of AA is approximately 2% worldwide. There was no sex predominance. First onset is most common in the third and fourth decades of life but may occur at any age. Early onset indicates increased lifetime risk of extensive disease. AA patients are at risk for depression and anxiety, atopy, vitiligo, thyroid disease and other autoimmune diseases. AA is the most prevalent autoimmune disorder and the second most prevalent hair loss disorder after androgenetic alopecia [13].

Arousse, et al from Tunisia evaluated 204 patients prospectively between 2012 and 2016. The mean age at presentation was 23 years old. Positive family history of Alopecia was present in 22% of patient. Personal history of atopy associated with AA was 18.1%, autoimmune thyroid disease was 12.7%, Vitiligo (15%), Psoriasis (three cases), polyendocrinopathy, pemphigus vulgaris and other autoimmune disorders. Patchy AA was the most common (49.5%) followed by Alopecia Universalis (27.5%), Alopecia Ophiasis (12.7%) and Alopecia Totalis (10.3%). Nail changes was common association with Alopecia. AA was more severe in females. Severe forms showed more persistent disease duration (P=0.005), earlier onset (P=0.001) and more recurring episodes (P=0.002) and were significantly associated with nail involvement (P=<0.001) [14].

In a retrospective study Kortipek, et al evaluated 200 patients 92 AA and 108 Vitiligo diagnosed, were surveyed retrospectively. Thyroid function tests and serum thyroid autoantibody levels were evaluated in all patients. In Vitiligo patients 9 (8.3%) had elevated anti TG levels and 16 (14.8%) anti-TPO and 17 patients (15.7%) TSH levels were elevated. Within AA patients, 2 (2/25) had anti-TG elevation and 13 (14.1%) and anti-TPO elevation in 7 patients (7.6%) TSH were elevated. They concluded that impaired thyroid function and thyroid autoantibodies in Vitiligo and AA patients were identified at lower levels than previous studies [15].

In a study from Egypt, Bakry, et al. evaluated 50 patients with AA, 37 males and 13 females without clinical evidence of thyroid disorders, fifty age and sex matched healthy volunteers. All patients had detailed history and examination and thyroid hormones and auto antibodies were measured. Subclinical hypothyroidism was detected in 16% of case. There were statistically significant differences between patients and controls both in thyroid function and autoantibodies [16].

Kurtev and Iliev evaluated 46 children (23 males and 23 females) with a mean age of 17.5 years, to assess thyroid function and thyroid autoantibody in AA. They evaluated the size and function of the thyroid including thyroid hormones and autoantibodies. Thyroid was enlarged in 29 children (63%), increased basal TSH in 6 of 24 (13.35) and hypo TSH in 2 out of 12. Antithyroglobulin was high 17 (39.5%) with AA. The author recommends that size and function and autoantibody be evaluated [17].

Noso, et al evaluated 126 patients with AA and tested them for anti-islet and Thyroid autoantibodies and their genotypes of HLA genes. They found AA associated with thyroid autoimmunity but not islet autoimmunity, which correlated with class 11 HLA haplotypes susceptible or resistant to each autoimmune disease [18].

Ghaffari and colleagues, made a case-control study by questionnaire to evaluate the prevalence of thyroid disease, Atopic Dermatitis and atopic diseases in children with AA and compared it with the result in healthy individuals. The patients were 50 children with AA and 150 healthy controls. Prevalence of Asthma was 22% in the case group and 12.5 % in the control group. Allergic Rhinitis and Eczema were 20% and 22%of the subject of the case group, but was 18% and 10% in the control group. The researchers concluded that their study showed a significant association exists between the prevalence of AA and atopic conditions, such as Allergic Rhinitis and Atopic Dermatitis and thyroid dysfunction [19].

A recent study by Kridin and associates based on a large population investigated the atopic comorbidity among patients with AA. The study population included 51,561 patients with AA and 51,410 matched control subjects. The prevalence of Asthma, Atopic Dermatitis, Allergic Rhinitis and Allergic Conjunctivitis was statistically significantly higher in AA patients as compared with the matched controls, suggesting T_{H2} pathogenicity in AA [20].

Case Reports

Case 1

RA a nine-year-old girl, presented to our Center complaining of total hair loss of the scalp, eyebrows and eyelashes and the rest of the body since she was two years old. The family history was negative for any autoimmune diseases. CBC, ANA and anti-DNA were all normal. Anti-thyroglobulin antibody was very high (283.10) with normal less than 18. Anti-microsomal antibody was 101.5 (N: <8), TSH 2.49 uiU/ml (up to 4) and T4, 16.46 (14-22).

Case 2

FO, a 57-year-old male presented with total hair loss for four years. He has thyroid deficiency and complains of fatiguability and intolerance to cold temperature. His family history is positive for thyroid dysfunction. Anti-thyroglobulin Ab 519.5 (<18), anti-microsomal antibodies 107.2 (<8), TSH 3.91 (0.4-4.0), T4, 15mg/dL (10-28.2).

Case 3

AAH; a 24-year-old male, seen with history of total hair loss for the last two years. He started with recurrent attacks of AA which progressed to Alopecia Totalism in the last year. There is family history of hypothyroidism and gout. CBC, ANA, and anti-DNA were normal. Anti-thyroglobulin Ab 413.8 (<18), Anti-microsomal Ab 15.3 (<8), TSH 18.1 (<4), T4,12 (12-22).

Conclusion

Review of studies and meta-analysis showed strong association between Alopecia and thyroid autoimmunity and thyroid dysfunction. Recent study in animals showed Zinc and Selenium deficiency in sheep with severe alopecia was associated with autoimmunity of thyroid. There were thyroid auto antibodies against thyroglobulin and thyroid peroxidase antibody in all cases of Alopecia and thyroid dysfunction. Therefore, the minimal work up for all cases of Alopecia should include anti-thyroglobulin and anti-thioperoxides antibodies and TSH, and may be Zinc and Selenium serum levels. Also there should be outlook for other autoimmune disease associated with thyroid dysfunction such as Vitiligo, Diabetes Mellitus, Celiac disease and Lupus erythematosus and other autoimmune diseases. Some studies showed presence of atopic diseases as comorbidity association with alopecia. Also, there seems to be bidirectional association between alopecia and thyroid autoimmune diseases.

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