Journal of Dermatological Science 74 (2014) 18–22

Contents lists available at ScienceDirect

Journal of Dermatological Science

journal homepage: www.jdsjournal.com

Women with alopecia exhibit a higher risk for thyroid cancer: A nationwide cohort study

Li-Min Sun [a,1], Ming-Chia Lin [b,1], Chih-Hsin Muo [c], Ji-An Liang [d,e], Fung-Chang Sung [d], Chia-Hung Kao [d,f,*]

[a] Department of Radiation Oncology, Zuoying Branch of Kaohsiung Armed Forces General Hospital, Kaohsiung, Taiwan
[b] Department of Nuclear Medicine, E-DA Hospital, Kaohsiung, Taiwan
[c] Management Office for Health Data, China Medical University Hospital, Taichung, Taiwan
[d] Graduate Institute of Clinical Medical Science, School of Medicine, College of Medicine, China Medical University, Taichung, Taiwan
[e] Department of Radiation Oncology, China Medical University Hospital, Taichung, Taiwan
[f] Department of Nuclear Medicine and PET Center, China Medical University Hospital, Taichung, Taiwan

ARTICLE INFO

Article history:
Received 7 November 2013
Received in revised form 9 December 2013
Accepted 16 December 2013

Keywords:
Androgenic alopecia (AA)
Thyroid cancer
Population-based study
National Health Insurance system

ABSTRACT

Background: Several studies have investigated the relationship between alopecia and prostate cancer. However, little information is available regarding the relationship between alopecia and the risk of cancers in women.
Objective: The purpose of this study was to evaluate the possible association between alopecia and thyroid cancer among Taiwanese women.
Methods: We used data from the National Health Insurance system of Taiwan. The alopecia cohort comprised 4534 women, and each woman was randomly frequency matched by age, index month, and index year with 4 women from the general population without alopecia. A Cox proportional hazard regression analysis with Bonferroni correction was conducted to estimate the effects of alopecia on the risk of thyroid cancer.
Results: In women with alopecia, the overall risk for developing cancer was 22% higher than for subjects without alopecia, but the difference was not significant [hazard ratio (HR) = 1.22, 97.5% confidence interval (97.5% CI) = 0.87–1.70]. However, the risk for developing thyroid cancer among women with alopecia was significantly higher (HR = 2.39, 97.5% CI = 1.05–5.42). Further analyses determined that the alopecia group had a higher incidence of Graves' disease, but not Hashimoto thyroiditis.
Conclusion: Although alopecia did not significantly increase cancer risks in women, we found that Taiwanese women with alopecia had a higher risk of developing thyroid cancer that is unlikely to be related to underlying thyroid diseases.

1. Introduction

Androgenic alopecia (AA) is the most common cause of hair loss, followed by alopecia areata and telogen effluvium. AA affects nearly 50% of men [1,2]. In females, AA occurs much more frequently than is generally believed [3]. By contrast, approximately 2% of the general population develops alopecia areata [4]. AA is usually described as a genetically determined condition leading to the permanent loss of hair in men and women [5]. Japanese researchers have suggested that the Sox21 gene is a master regulator of hair shaft cuticle differentiation, which provides evidence on the possible causes of human hair disorders [6]. It has been suggested that androgens play a central role in the pathophysiology of both prostate cancer and AA. A considerable amount of evidence supports the role of androgens in prostate cancer: Eunuchs rarely develop prostate cancer, castration has a palliative effect on prostate cancer, and testosterone alone can produce prostatic adenocarcinoma in rats [7,8]. Therefore, prostate cancer is typically considered a hormonally linked cancer. Likewise, eunuchs do not develop baldness if castrated before the age of 25 [9]. Several studies have investigated the relationship between AA and prostate cancer and have yielded inconsistent results [1,10–14]. Little information is available regarding the relationship between alopecia and the risk of hormone-related cancers in women. Thyroid cancer is thought to be a kind of hormone-related cancers [15]. Because hormones play an essential role in AA and alopecia was suggested to be related to certain

* Corresponding author at: Graduate Institute of Clinical Medicine Science, College of Medicine, China Medical University, No. 2, Yuh-Der Road, Taichung 40447, Taiwan. Tel.: +886 4 22052121x7412; fax: +886 4 22336174.
E-mail addresses: dr.kaochiahung@gmail.com, d10040@mail.cmuh.org.tw (C.-H. Kao).
[1] These authors contributed equally to this work.

0923-1811/$36.00
http://dx.doi.org/10.1016/j.jdermsci.2013.12.005

Table 1
Demographics between study subjects with and without alopecia.

	Alopecia				*p*-Value
	No (*N* = 18,128)		Yes (*N* = 4534)		
	n	%	*n*	%	
Age, years					>0.99
<20	3228	17.8	807	17.8	
20–34	7548	41.6	1887	41.6	
35–49	5011	27.6	1253	27.6	
50–65	1857	10.2	465	10.3	
≥65	484	2.67	122	2.69	
Mean (SD)	32.9	(14.8)	32.8	(14.6)	0.94
Comorbidity					
Hypertension	1435	7.92	380	8.38	0.30
Diabetes	590	3.25	176	3.88	0.04

Chi-square test and *t*-test.

thyroid diseases [16], we hypothesize that AA has an association with thyroid cancer in women.

Based on a thorough review of relevant literature, there are no studies that outline the possible relationship between alopecia and the risk of cancer in women. This study investigates the risk of overall and thyroid cancers among women with alopecia in Taiwan. The results were generated from a retrospective cohort study of women with alopecia. The data was derived from the database of the National Health Insurance (NHI) system in Taiwan.

2. Methods

This retrospective cohort study used the Longitudinal Health Insurance Database (LHID) and the Registry for Catastrophic Illness Patients. Those databases were formed by the Taiwan Bureau of National Health Insurance (TBNHI) and maintained by the National Health Research Institutes (NHRI). The TBNHI established a single-payer NHI program on March 1, 1995 and this program covers over 99.5% of population in Taiwan [17]. The LHID comprised one million insurants randomly selected from the original beneficiaries in 2000 and included all medical records for insurants from 1996 to 2010. The NHRI scrambled the identification of the insurants in accordance with the Personal Information Protection Act before releasing the information to researchers. This study was provided the Institutional Review Board of the China Medical University and Hospital. Our research group has referenced the LHID in previous studies [18,19].

We collected information on women with diagnosed alopecia [The International Classification of Diseases, 9th Revision, clinical modification (ICD-9-CM) 704.0] from 2000 to 2010. We excluded those with any history of cancer (ICD-9-CM 140–208) and the duration of follow-up was <0.5 year. Controls were selected from women without a history of alopecia before the entry date. We randomly assigned the year and month to controls and the entry date was the middle of month. Four controls were randomly frequency matched with age (5 years stratified: for example 0–4, 5–9, 10–14 and so on.), entry month, and entry year. The excluded criteria were the same in the control and case groups.

The demographic differences between the groups were analyzed using a chi-square test for the categorical variables of age group and comorbidity [including hypertension (ICD-9-CM 401-405) and diabetes (ICD-9-CM 250)], and a *t*-test for the continuous variable of age. We counted the person-years from the entry date to the date of cancer occurrence, or until the end of 2010, and calculated the incidence per 10,000 person-years. The hazard ratio (HR) and 95% confidence intervals (CIs) for cancer were assessed using Cox proportional hazard regression and the multivariable model was adjusted for age and comorbidity. The risks for cancer type assessed and the types were thyroid and others. According to Bonferroni correction, the significant level was set at 0.025 for multiple hypothesis testing. A Kaplan–Meier analysis was used to plot the cumulative incidence for cancer and a log-rank test was used to test the difference between the groups. In the further analysis, we estimated the risk levels for the subtypes of alopecia: unspecified, areata, and telogen effluvium. We also evaluated the effect of 2 thyroid autoimmune diseases (Graves' disease and Hashimoto thyroiditis) on the relationship between alopecia and thyroid cancer.

The NHRID encrypts the patients' personal information for privacy protection and provides researchers with anonymous identification numbers associated with the relevant claim information, which includes the patient's sex, date of birth, registry of medical services, and medication prescriptions. Patient consent is not required for accessing the NHIRD. This study was approved by the Institutional Review Board of China Medical University (CMU-REC-101-012). Our IRB specifically waived the requirement for consent.

3. Results

The case cohort comprised 4534 women with alopecia and the control cohort comprised 18,128 women. The majority of women were 20–34 years old (41.6%), and the mean age was 32.8 (standard deviation = 14.6). The case cohort was more likely to have a history of diabetes and hypertension than the control cohort, but only diabetes showed a significant difference (Table 1). After a nine-year follow-up, 59 and 192 events occurred in the case and control cohorts, respectively (Fig. 1A and Table 2). The incidences of overall cancer were 27.50 and 22.56 per 10,000 person-years for the alopecia and non-alopecia groups, respectively, and the HR was 1.22 (97.5% CI 0.87–1.70) compared with the control group. After analyzing the risk of subtypes of cancer, only thyroid cancer showed a significantly higher risk in the case cohort, with an HR of 2.39 (97.5% CI 1.05–5.42). Compared to controls, the women with unspecific alopecia had a significant 1.87-fold higher risk for thyroid cancer, but not for other cancers (Table 3). The cumulative incidence of thyroid cancer in the case cohort was significantly 0.3% higher than in the control cohort (log-rank $P = .024$, Fig. 1B).

Women with alopecia had a significantly higher risk for Graves' disease compared with women without alopecia (1.94% vs. 1.09%, $P < .05$), but the risk for Hashimoto thyroiditis was less and non-significant (0.26% vs. 0.33%). Because of the relatively small number of thyroid cancer cases in both groups of autoimmune diseases, the incidence rate does not reflect the statistical significance (Table 4). Table 5 illustrates that the positive