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Increased risk of psoriasis in patients with chronic rhinosinusitis without nasal polyps: a longitudinal follow-up study using Korean national sample cohort

Hyo Geun Choi[1] · **Ho Jun Lee**[2]

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Abstract

Purpose Focal chronic inflammation or infection is thought to be one of the causes of psoriasis. Few reports on the association between chronic rhinosinusitis (CRS) and psoriasis exist, thus it is poorly defined. This study seeks to investigate the incidence of psoriasis in patients with CRS with reference to a matched control group.

Methods This national cohort study relies on data from Korean Health Insurance Review and Assessment Service—National Sample Cohort (HIRA-NSC), which were entered from 2002 to 2013. A total of 34,219 patients with CRS without nasal polyps was matched with 136,976 controls. The Cox proportional hazard model was used to analyze the crude (simple) and adjusted hazard ratios (HRs) of psoriasis. For subgroup analysis, participants were grouped by age and sex.

Results The risk of psoriasis was higher in the CRS group than in the control group (adjusted HR 1.28, 95% CI 1.12–1.47, $P < 0.001$). Children, adolescents below 19 years regardless of sex, and old adult men above 60 years are at significantly higher risk for subsequent psoriasis after CRS diagnosis.

Conclusion CRS may increase the risk of psoriasis.

Keywords Chronic rhinosinusitis · CRS · Psoriasis · Risk factors · Cohort studies · Case–control studies · Epidemiology

Introduction

Psoriasis is an immune-mediated chronic inflammatory skin disease characterized by scaly thin erythematous papules and plaques. Psoriasis is relatively common throughout the world. About 1–3% of Caucasians and 0.5–1% of Asians including Koreans suffer this disease [1–6].

The epidemiology of psoriasis is not clear yet. Genetic factors, environmental factors, psychological stress and others factors have been suggested to cause psoriasis. In addition, focal infection or inflammation of the upper respiratory tract, for example, chronic tonsillitis, has been suggested as the important influential cause of psoriasis [7–9].

✉ Ho Jun Lee
leehj@hallym.or.kr

[1] Department of Otorhinolaryngology-Head and Neck Surgery, Hallym University College of Medicine, Anyang, Korea

[2] Department of Otorhinolaryngology-Head and Neck Surgery, Chuncheon Sacred Heart Hospital, College of Medicine, Hallym University, Chuncheon, Korea

The suggested hypothetical mechanism of association between upper respiratory tract infection and psoriasis is described below. Once the upper respiratory tract is infected, T cells become overactive, and immune products from T cells start to irritate keratinocytes. This results in hyperproliferation of keratinocytes and chronic inflammation.

Chronic rhinosinusitis (CRS) is a common upper respiratory tract disease characterized by chronic inflammation of the nasal and paranasal sinus mucosa. It was reported that about 5% of the population in Canada [10], 14% in US [11], and 6–10% in South Korea [12–14] are affected by CRS. If the previously suggested hypothesis is true, CRS may aggravate psoriasis.

Few reports on the association between CRS and psoriasis exist, thus it is poorly defined. Using population-based data in South Korea in this study, the authors investigated the subsequent risk of psoriasis after the diagnosis of CRS in Korean patients. Participants were matched to control for age, sex, income, region of residence, and previous medical history. Probably, this study may add to the already existing knowledge on the epidemiology of psoriasis.

Materials and methods

Study population and data collection

Before the study commenced, the ethics committee of Hallym University (2014-I148) approved the use of patient data. Written informed consents were exempted by the Institutional Review Board.

This national cohort study relies on data from the Korean Health Insurance Review and Assessment Service—National Sample Cohort (HIRA-NSC). The Korean National Health Insurance Service (NHIS) chose a sample directly from the population database to prevent non-sampling errors. Approximately 2% of (1 million) the people on the database were selected from the entire Korean population (50 million); they can be classified in 1476 levels [age (18 categories), sex (2 categories), and income level (41 categories)] using randomized stratified systematic sampling methods via proportional allocation to represent the entire population. After data selection, the appropriateness of the sample was verified by a statistician who compared the data from the entire Korean population with the sample data. Details of the methods used to perform these procedures were provided by the National Health Insurance Sharing Service [15]. The cohort database included (1) personal information (2) health insurance claim codes (procedures and prescriptions) (3) diagnostic codes using the International Classification of Disease-10 (ICD-10) (4) death records from the Korean National Statistical Office (using the Korean Standard Classification of disease) (5) socio-economic data (residence and income), and (6) medical examination data for each participant over the period from 2002 to 2013.

Since all Korean citizens are identified by 13-digit resident registration numbers from birth to death, exact population statistics can be determined using this database. It is mandatory for all Koreans to enroll in the NHIS. All Korean hospitals and clinics use this resident registration number to register individual patients in the medical insurance system. Therefore, the risk of overlapping medical records is minimal, even if a patient moves from one place to another. Moreover, all medical treatments in Korea can be tracked without exception using the HIRA system. In Korea, notice of death to an administrative entity is legally required before a funeral can be held. Causes of death and date are recorded by medical doctors on death certificates.

Participant selection

Out of 1,125,691 cases with 114,369,638 medical claim codes, we included participants who were diagnosed with CRS (ICD-10: J32). Among them, we selected participants who were treated for it at least twice, had undergone head and neck CT (Claim codes: HA401–HA416, HA441–HA443, HA451–HA453, HA461–HA463, or HA471–HA473), and were not diagnosed with nasal polyp (J33) ($n = 34,572$). The participants were followed for 12 years, from 2002 to 2013.

Psoriasis was defined using the ICD-10 codes L40. Among them, we selected the participants who treated it twice or more ($n = 12,921$) from 2002 to 2013.

The CRS patients were matched to participants (controls) that had not been diagnosed of the disease within the same period at the ratio, 1:4. The matches were processed in age groups, sex, income groups, region of residence, and the past medical histories (hypertension, diabetes, and dyslipidemia). To prevent selection bias during matching, the controls were sorted using a random number order, and then selected from top to bottom. It was assumed that the matched control participants were enrolled at the same time as their CRS partners (index date). Therefore, controls who died before the index date were excluded. In both groups, participants who had histories of psoriasis before the index date were also excluded; to that effect, 230 participants were excluded in the CRS group. Furthermore, CRS patients for whom enough matching participants were not identified were excluded ($n = 123$). Finally, a 1:4 matching ratio resulted in the inclusion of 34,219 CRS participants and 136,976 control participants (Fig. 1). However, they were not matched for the ischemic heart disease and stroke histories.

Variables

Eighteen age groups were formed from the classification in 5-year intervals: 0–4, 5–9, 10–14…, and 85 + years old. The income groups were initially divided into 41 classes

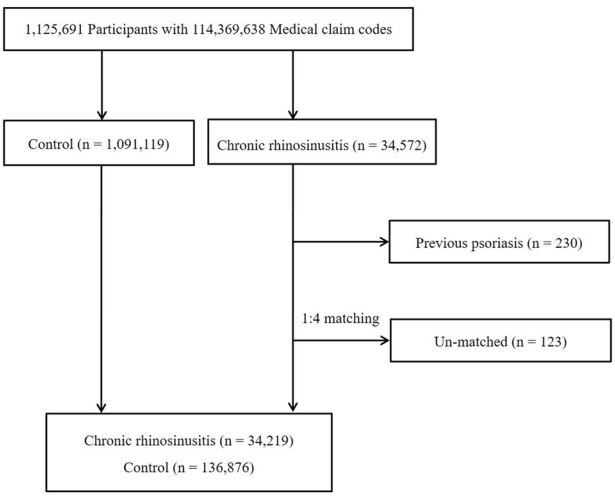

Fig. 1 A schematic illustration which was used in this study in the participant selection process. Out of a total of 1,125,691 participants, 34,219 participants with chronic rhinosinusitis were matched with 136,876 control participants by age, group, sex, income group, region of residence, and past medical histories

(one health aid class, 20 self-employment health insurance classes, and 20 employment health insurance classes). These groups were re-categorized into 11 classes [class 1 (lowest income) to 11 (highest income)]. Regions of residence were divided into 16 areas according to the administrative districts. These regions were regrouped into urban (Seoul, Busan, Daegu, Incheon, Gwangju, Daejeon, and Ulsan) and rural (Gyeonggi, Gangwon, Chungcheongbuk, Chungcheongnam, Jeollabuk, Jeollanam, Gyeongsangbuk, Gyeongsangnam, and Jeju) areas.

The medical histories of participants were evaluated using ICD-10 codes. For accuracy in diagnosis, hypertension (I10 and I15), diabetes (E10–E49), and dyslipidemia (E78) were checked if the participants were treated twice or more. Ischemic heart disease (I24 and I25) and stroke (I60–I66) were checked if the participants were treated once or more.

Statistical analyses

Chi-square test was used to compare the rate of general characteristics between both groups. To analyze the hazard ratios (HRs) of CRS on psoriasis, the Cox-proportional hazard model was used. In this analysis, crude (simple) and adjusted (age, sex, income, region of residence, hypertension, diabetes, dyslipidemia, ischemic heart disease, and stroke) models were used. For the subgroup analysis, the participants were divided according to age and sex (0–19 years old, 20–39 years old, 40–59 years old, 60 + years old; men, and women).

A two-tailed analysis was conducted, and a *P* value less than 0.05 indicated statistical significance. The results were analyzed using SPSS v. 21.0 (IBM, Armonk, NY, USA).

Results

The general characteristics of age groups, sex, income, region of residence, and medical histories of hypertension, diabetes and dyslipidemia were exactly matched between the CRS group and control group (Table 1). However, ischemic heart disease and stroke histories were not matched. The significant and potentially relevant association between stroke, ischemic heart disease and CRS may exist. It will be discussed in the discussion session.

The incidence of psoriasis in the CRS and control group during the study period was 0.8% and 0.6%, respectively; and this difference was statistically significant (Table 1). The HRs for subsequent psoriasis in the CRS group were statistically significantly higher than that of the control group. The adjusted HR was 1.28 (95% CI 1.12–1.47, $P < 0.001$) (Table 2).

Table 1 General characteristics of participants

Characteristics	Total participants		
	CRS (*n*, %)	Control (*n*, %)	*P* value
Age (years old)			1.000
0–4	4206 (12.3)	16,824 (12.3)	
5–9	3297 (9.6)	13,188 (9.6)	
10–14	1902 (5.6)	7608 (5.6)	
15–19	1540 (4.5)	6160 (4.5)	
20–24	1325 (3.9)	5300 (3.9)	
25–29	1763 (5.2)	7052 (5.2)	
30–34	2194 (6.4)	8766 (6.4)	
35–39	2324 (6.8)	9296 (6.8)	
40–44	2315 (6.8)	9260 (6.8)	
45–49	2477 (7.2)	9908 (7.2)	
50–54	2549 (7.4)	10,196 (7.4)	
55–59	2298 (6.7)	9192 (6.7)	
60–64	1944 (5.7)	7776 (5.7)	
65–69	1782 (5.2)	7128 (5.2)	
70–74	1243 (3.6)	4972 (3.6)	
75–79	706 (2.1)	2824 (2.1)	
80–84	258 (0.8)	1032 (0.8)	
85 +	96 (0.3)	384 (0.3)	
Sex			1.000
Male	17,124 (50.0)	68,496 (50.0)	
Female	17,095 (50.0)	68,380 (50.0)	
Income			1.000
1 (lowest)	504 (1.5)	2016 (1.5)	
2	1815 (5.3)	7260 (5.3)	
3	1867 (5.5)	7468 (5.5)	
4	2009 (5.9)	8036 (5.9)	
5	2261 (6.6)	9044 (6.6)	
6	2806 (8.2)	11,224 (8.2)	
7	3215 (9.4)	12,860 (9.4)	
8	3904 (11.4)	15,616 (11.4)	
9	4751 (13.9)	19,004 (13.9)	
10	5187 (15.2)	20,748 (15.2)	
11 (highest)	5900 (17.2)	23,600 (17.2)	
Region of residence			1.000
Urban	16,469 (48.1)	65,876 (48.1)	
Rural	17,750 (51.9)	71,000 (51.9)	
Hypertension			1.000
Yes	9022 (26.4)	36,088 (26.4)	
No	25,197 (73.6)	100,788 (73.6)	
Diabetes			1.000
Yes	4982 (14.6)	19,928 (14.6)	
No	29,237 (85.4)	116,948 (85.4)	
Dyslipidemia			1.000
Yes	7752 (22.7)	31,008 (22.7)	
No	26,467 (77.3)	105,868 (77.3)	
Ischemic heart disease			< 0.001*
Yes	1956 (5.7)	5701 (4.2)	

Table 1 (continued)

Characteristics	Total participants		
	CRS (*n*, %)	Control (*n*, %)	*P* value
No	32,263 (94.3)	131,175 (95.8)	
Stroke			< 0.001*
Yes	4409 (12.9)	8707 (6.4)	
No	29,810 (87.1)	128,169 (93.6)	
Psoriasis			< 0.001*
Yes	290 (0.8)	889 (0.6)	
No	33,929 (99.2)	135,987 (99.4)	

CRS chronic rhinosinusitis

*Chi-square test or Fisher's exact test. Significance at $P < 0.05$

Table 2 Crude and adjusted hazard ratios (95% confidence interval) of chronic rhinosinusitis for psoriasis

Characteristics	Hazard ratio (95% CI)			
	Crude	*P* value	Adjusted[a]	*P* value
CRS		< 0.001*		< 0.001*
Yes	1.31 (1.14–1.49)		1.28 (1.12–1.47)	
No	1.00		1.00	

CRS chronic rhinosinusitis

*Cox-proportional hazard regression model, Significance at $P < 0.05$

[a]Adjusted model for age, sex, income, region of residence, hypertension, diabetes, dyslipidemia, ischemic heart disease, and stroke histories

In the subgroup analysis, HR of psoriasis was higher in children and adolescents regardless of sex and in old adult male (Table 3). The adjusted HRs for under 19-year-old males and females were 1.47 (95% CI 1.02–2.14) and 2.10 (95% CI 1.29–3.43), respectively; for over 60-year-old males, adjusted HR was 1.71 (95% CI 1.21–2.43).

Discussion

Patients diagnosed of CRS without nasal polyps are at 1.28 times higher risk than the control group for subsequent psoriasis after adjusting for age, sex, region of residence, income level, and important medical history. In a previous study in Taiwan, the incidence rates of psoriasis in CRS without nasal polyps was 1.41 times higher than the controls [16].

The authors propose several possible mechanisms for this observed association between CRS and psoriasis. First, T cell-mediated cross-reaction to bacterial components and human dermal or epidermal components. This kind of mechanism was suggested in another upper respiratory tract infection, chronic tonsillitis. Chronic tonsillitis is a well-known aggravating factor for psoriasis, and tonsillectomy frequently releases symptoms of psoriasis [8, 9, 17–23]. They explain that Group A β-hemolytic *Streptococcus pyogenes* (GABHS) infection is important in the pathogenesis of tonsillitis related psoriasis. Human keratin and streptococcal M-protein share immunological determinants, and when tonsillar infection occurs, tonsillar and peripheral blood T cells recognize streptococcal antigens, cross-react to keratin determinants in the skin, and aggravate psoriasis. Since tonsils are one of the major organs for GABHS infection, tonsillectomy may be beneficial for the treatment of psoriasis [22, 24, 25]. Like tonsils, nasal cavity and paranasal sinuses are also located at the entrance of the upper respiratory tract, and frequently present focal infections and inflammations.

Several studies have reported the possibility of an association between CRS and dermatologic pathologies [21, 26–29]. Till now, unlike GABHS infection which aggravates tonsillitis and psoriasis, the evidences for the cross-reactivity between well-known rhinosinusitis-causing bacteria, *Staphylococcus aureus*, *Streptococcus pneumonia*, *Moraxella catarrhalis*, *Hemophilus Influenza and Pseudomonas aeruginosa*, and human dermal components are insufficient. Future studies are needed.

Second, the role of bacterial super-antigenic effect [30–32], which may affect immunological status in psoriatic patients can also be considered. *Staphylococcus aureus* is known as the most common pathogen in CRS, therefore, staphylococcal superantigen may exist in the patients with CRS. Several studies reported that staphylococcal superantigens are significantly increased in patients with psoriasis than in the non-psoriatic control group, and suggested that staphylococcal superantigen may be an exacerbating or triggering factor for psoriasis [33, 34].

The third is the association between two different Th1 pathologies. Prior understanding assumed that CRS is a Th2 pathology, whereas psoriasis presents Th1 pathology. Therefore, CRS and psoriasis were thought unlikely to coincide [35]. However, recent studies have revealed that CRS shows different T helper cell patterns according to different phenotypes. CRS without nasal polyps (CRSsNP) incites mainly neutrophilic Th1 polarized inflammation, whereas CRS with nasal polyps (CRScNP) incites predominantly eosinophilic Th2 polarized inflammation [36]. According to previous reports, the existence of one Th1 pathology is strongly associated with the presence of another comorbid Th1 pathologies [37, 38]. The authors thought that CRSsNP are more likely to be associated with psoriasis, because both of them are mainly Th1 pathologies. In this study, the authors excluded patients with CRScNP, and were successful in detecting the association between CRSsNP and psoriasis. To the best of our knowledge, there was no study that found the association between CRScNP, which presents

Table 3 Subgroup analysis of crude and adjusted hazard ratios (95% confidence interval) of chronic rhinosinusitis for psoriasis according to age and sex

Characteristics	Hazard ratio (95% CI)			
	Crude	*P* value	Adjusted[a]	*P* value
Children and adolescent male (0–19 years old, *n* = 36,830)				
CRS		0.027*		0.043*
Yes	1.52 (1.05–2.19)		1.47 (1.02–2.14)	
No	1.00		1.00	
Children and adolescent female (0–19 years old, *n* = 17,895)				
CRS		0.002*		0.003*
Yes	2.13 (1.31–3.46)		2.10 (1.29–3.43)	
No	1.00		1.00	
Young adults male (20–39 years old, *n* = 16,515)				
CRS		0.812		0.835
Yes	0.95 (0.59–1.50)		0.95 (0.60–1.52)	
No	1.00		1.00	
Young adults female (20–39 years old, *n* = 21,515)				
CRS		0.087		0.071
Yes	1.37 (0.96–1.96)		1.39 (0.97–2.00)	
No	1.00		1.00	
Middle aged adults male (40–59 years old, *n* = 19,840)				
CRS		0.691		0.409
Yes	0.93 (0.65–1.33)		0.86 (0.60–1.23)	
No	1.00		1.00	
Middle aged adults female (40–59 years old, *n* = 28,355)				
CRS		0.380		0.547
Yes	1.16 (0.83–1.61)		1.11 (0.79–1.55)	
No	1.00		1.00	
Old adult male (60 + years old, *n* = 12,435)				
CRS		0.001*		0.002*
Yes	1.82 (1.30–2.56)		1.71 (1.21–2.43)	
No	1.00		1.00	
Old adult female (60 + years old, *n* = 17,710)				
CRS		0.241		0.212
Yes	1.27 (0.85–1.89)		1.29 (0.86–1.93)	
No	1.00		1.00	

CRS chronic rhinosinusitis

*Cox-proportional hazard regression model, significance at $P < 0.05$

[a]Adjusted model for age, sex, income, region of residence, hypertension, diabetes, dyslipidemia, ischemic heart disease, and stroke histories

mainly as Th2 inflammation, and psoriasis, which presents mainly as Th1 inflammation.

The strength of this study is the use of a large, representative, nationwide population sample, which is consistent with our previous studies [39–41]. Since NHIS data include all citizens of the nation without exception, no participants were missing during the follow-up period. The control group was randomly selected by matching age, sex, income, region of residence, and medical history to avoid confounding effects. Furthermore, an adjusted regression model was used to minimize the confounders. The large number of participants helped maintain the statistical power even when participants were sub-grouped, thus allowing subgroup analyses. In addition, the cohort study design was helpful with the evaluation of the time sequence of the relation between CRS and psoriasis. Additionally, we used the claim codes for CRS and psoriasis, which were not distorted by patient memory.

The authors acknowledge that there may be some limitations to this study. First, it does not exclude that patients with recurrent acute rhinosinusitis are included in the study group. Second, some patients particularly those who have minor symptoms of CRS may not seek medical services, therefore may not have been included in this study. Third, inclusion of CT scans might potentially lead to an

underestimation of the number of patients with CRS, since not all of the CRS patients will receive CT scan for diagnosis. In addition, the severity of CRS and psoriasis among the participants were not analyzed. For the accuracy of diagnosis, only participants who had treated their CRS and psoriasis symptoms twice or more were included. Therefore, the participants who visited the clinic only once were excluded from this study. In addition, we could not analyze possible confounding factors between CRS and psoriasis, such as obesity, smoking, and dietary habits. Furthermore, participants were not matched to control for ischemic heart disease and stroke histories. Previous studies report that CRS increases the risk of ischemic heart disease and stroke significantly [42–49]. Proinflammatory cytokines, altered the activation of coagulation system, promoted intravascular thromboses, and aggravated sleep disordered breathing have been suggested as hypotheses to explain this relationship. This study showed similar results as previous studies. Finally, our study could not confirm a pathophysiological mechanism between CRS and psoriasis, as only odd ratios (ORs) were calculated.

Conclusion

The adjusted HR for psoriasis was 1.28 times higher in the CRS group than in the control group. In subgroup analysis, the adjusted HRs for psoriasis were 1.47 and 2.10 times higher in under 19-year-old males and females, respectively, and 1.71 times higher in the old adult male group than in control groups.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

Research involving human participants and/or animals All procedures performed in studies involving human participants were in accordance with the ethical standards of the Ethics Committee of Hallym University (2014-I148) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Written informed consent was exempted by the Institutional Review Board.

References

1. Rachakonda TD, Schupp CW, Armstrong AW (2014) Psoriasis prevalence among adults in the United States. J Am Acad Dermatol 70:512–516
2. Lee JY, Kang S, Park JS, Jo SJ (2017) Prevalence of psoriasis in Korea: a population-based epidemiological study using the Korean National Health Insurance Database. Ann Dermatol 29:761–767
3. Youn JI (2012) Psoriasis in Korean. Korean J Dermatol 50(5):387–402
4. Lin XR (1993) Psoriasis in China. J Dermatol 20:746–755
5. Yip SY (1984) The prevalence of psoriasis in the mongoloid race. J Am Acad Dermatol 10:965–968
6. Yasuda TIE, Mori S (1971) Psoriasis in Japanese. In: Farber EM (ed) Psoriasis, proceedings of an international symposium, 1st edn. Stanford University Press, Palo Alto, pp 225–234
7. Allen HB, Jadeja S, Allawh RM, Goyal K (2018) Psoriasis, chronic tonsillitis, and biofilms: tonsillar pathologic findings supporting a microbial hypothesis. Ear Nose Throat J 97:79–82
8. Simoes JF, Ribeiro J, Ferreira BR, Paiva S (2015) The role of tonsillectomy in psoriasis treatment. BMJ Case Rep. https://doi.org/10.1136/bcr-2014-206899
9. Wu W, Debbaneh M, Moslehi H, Koo J, Liao W (2014) Tonsillectomy as a treatment for psoriasis: a review. J Dermatol Treat 25:482–486
10. Chen Y, Dales R, Lin M (2003) The epidemiology of chronic rhinosinusitis in Canadians. Laryngoscope 113:1199–1205
11. Pleis JR, Lucas JW (2009) Summary health statistics for US adults: National Health Interview Survey, 2007. Vital Health Stat 10:1–159
12. Cho YS, Choi SH, Park KH, Park HJ, Kim JW et al (2010) Prevalence of otolaryngologic diseases in South Korea: data from the Korea national health and nutrition examination survey 2008. Clin Exp Otorhinolaryngol 3:183–193
13. Kim JH, Cho C, Lee EJ, Suh YS, Choi BI et al (2016) Prevalence and risk factors of chronic rhinosinusitis in South Korea according to diagnostic criteria. Rhinology 54:329–335
14. Kim YS, Kim NH, Seong SY, Kim KR, Lee GB et al (2011) Prevalence and risk factors of chronic rhinosinusitis in Korea. Am J Rhinol Allergy 25:117–121
15. National Health Insurance sharing service. http://nhiss.nhis.or.kr/. Accessed 4 May 2015
16. Keller JJ, Wu CS, Lin HC (2013) Increased risk of psoriasis following chronic rhinosinusitis without nasal polyps: a population-based matched-cohort study. Br J Dermatol 168:289–294
17. Fry L, Baker BS (2007) Triggering psoriasis: the role of infections and medications. Clin Dermatol 25:606–615
18. Fujihara K (1991) A study on the tonsil with focal infections–with special reference to the newly devised tonsillar cryptscope and the architecture of vessels in crypts. Nihon Jibiinkoka Gakkai Kaiho 94:1304–1314
19. Krstic A, Zivkovic M, Janjatovic T (1969) Significance of focal infection in psoriasis vulgaris and psoriasis arthropathica. Hautarzt 20:274–276
20. Ruszczak Z, Bednarowicz G, Proszynska-Kuczynska W (1969) The role of focal infection in the etiopathogenesis of psoriasis. Przegl Dermatol 56:15–20
21. Yamamoto T (2011) Triggering role of focal infection in the induction of extra-palmoplantar lesions and pustulotic arthro-osteitis associated with palmoplantar pustulosis. Adv Otorhinolaryngol 72:89–92
22. Thorleifsdottir RH, Sigurdardottir SL, Sigurgeirsson B, Olafsson JH, Sigurdsson MI et al (2012) Improvement of psoriasis after tonsillectomy is associated with a decrease in the

frequency of circulating T cells that recognize streptococcal determinants and homologous skin determinants. J Immunol 188:5160–5165
23. Thorleifsdottir RH, Sigurdardottir SL, Sigurgeirsson B, Olafsson JH, Sigurdsson MI et al (2017) Patient-reported outcomes and clinical response in patients with moderate-to-severe plaque psoriasis treated with tonsillectomy: a randomized controlled trial. Acta Derm Venereol 97:340–345
24. Valdimarsson H, Baker BS, Jonsdottir I, Powles A, Fry L (1995) Psoriasis: a T-cell-mediated autoimmune disease induced by streptococcal superantigens? Immunol Today 16:145–149
25. Valdimarsson H, Thorleifsdottir RH, Sigurdardottir SL, Gudjonsson JE, Johnston A (2009) Psoriasis—as an autoimmune disease caused by molecular mimicry. Trends Immunol 30:494–501
26. Chandra RK, Lin D, Tan B, Tudor RS, Conley DB et al (2011) Chronic rhinosinusitis in the setting of other chronic inflammatory diseases. Am J Otolaryngol 32:388–391
27. Wedi B, Raap U, Kapp A (2004) Chronic urticaria and infections. Curr Opin Allergy Clin Immunol 4:387–396
28. Goga D, Vaillant L, Pandraud L, Mateu J, Ballon G et al (1988) The elimination of dental and sinusal infectious foci in dermatologic pathology. A double-blind study in 27 cases confined to chronic urticaria. Rev Stomatol Chir Maxillofac 89:273–275
29. Buchter A, Kruse-Losler B, Joos U, Kleinheinz J (2003) Odontogenic foci-possible etiology of urticaria? Mund Kiefer Gesichtschir 7:335–338
30. Seiberling KA, Grammer L, Kern RC (2005) Chronic rhinosinusitis and superantigens. Otolaryngol Clin N Am 38(1215–1236):ix
31. Bachert C, Zhang N, Patou J, van Zele T, Gevaert P (2008) Role of staphylococcal superantigens in upper airway disease. Curr Opin Allergy Clin Immunol 8:34–38
32. Zhang N, Gevaert P, van Zele T, Perez-Novo C, Patou J et al (2005) An update on the impact of *Staphylococcus aureus* enterotoxins in chronic sinusitis with nasal polyposis. Rhinology 43:162–168
33. Atefi N, Noorbakhsh S, Ghavidel Darestani S, Tabatabaei A, Rezaee M (2014) The rise of staphylococcal super antigens in psoriatic patients: a case–control study. Jundishapur J Microbiol 7:e9912
34. Sayama K, Midorikawa K, Hanakawa Y, Sugai M, Hashimoto K (1998) Superantigen production by *Staphylococcus aureus* in psoriasis. Dermatology 196:194–198
35. Rashid RM, Miller A, Scianna JM, Stankiewicz JA (2007) Chronic rhinosinusitis and psoriasis: do mutually exclusive systemic Th1 and Th2 disease patterns exist? Acta Otolaryngol 127:780–783
36. Van Zele T, Claeys S, Gevaert P, Van Maele G, Holtappels G et al (2006) Differentiation of chronic sinus diseases by measurement of inflammatory mediators. Allergy 61:1280–1289
37. van Roon JA, Bijlsma JW (2002) Th2 mediated regulation in RA and the spondyloarthropathies. Ann Rheum Dis 61:951–954
38. Zachariae H (2003) Prevalence of joint disease in patients with psoriasis: implications for therapy. Am J Clin Dermatol 4:441–447. https://doi.org/10.2165/00128071-200304070-00001
39. Kim MS, Kim SY, Kim JH, Park B, Choi HG (2017) Depression in breast cancer patients who have undergone mastectomy: a national cohort study. PLoS One 12:e0175395
40. Kim SY, Kim HJ, Park EK, Joe J, Sim S et al (2017) Severe hearing impairment and risk of depression: a national cohort study. PLoS One 12:e0179973
41. Choi HG, Park B, Sim S, Ahn SH (2016) Tonsillectomy does not reduce upper respiratory infections: a national cohort study. PLoS One 11:e0169264
42. Arter JL, Chi DS, Girish M, Fitzgerald SM, Guha B, Krishnaswamy G (2004) Obstructive sleep apnea, inflammation, and cardiopulmonary disease. Front Biosci 9:2892–2900
43. Drager LF, Polotsky VY, Lorenzi-Filho G (2011) Obstructive sleep apnea: an emerging risk factor for atherosclerosis. Chest 140:534–542. https://doi.org/10.1378/chest.10-2223
44. Kang JH, Wu CS, Keller JJ, Lin HC (2013) Chronic rhinosinusitis increased the risk of stroke: a 5-year follow-up study. Laryngoscope 123:835–840. https://doi.org/10.1002/lary.23829
45. Mayberg MR (1998) Cerebral vasospasm. Neurosurg Clin N Am 9:615–627
46. Rochat P, von Buchwald C, Wagner A (2001) Sinusitis and ischemic stroke. Rhinology 39:173–175
47. Sejima T, Holtappels G, Bachert C (2011) The expression of fibrinolytic components in chronic paranasal sinus disease. Am J Rhinol Allergy 25:1–6. https://doi.org/10.2500/ajra.2011.25.3537
48. Shimizu S, Gabazza EC, Ogawa T, Tojima I, Hoshi E, Kouzaki H, Shimizu T (2011) Role of thrombin in chronic rhinosinusitis-associated tissue remodeling. Am J Rhinol Allergy 25:7–11. https://doi.org/10.2500/ajra.2011.25.3535
49. Wu CW, Chao PZ, Hao WR, Liou TH, Lin HW (2012) Risk of stroke among patients with rhinosinusitis: a population-based study in Taiwan. Am J Rhinol Allergy 26:278–282. https://doi.org/10.2500/ajra.2012.26.3783