

Psoriasis and skin cancer.

Li Yin¹, Ying Ying Hu¹, Afzaal Ahmed Bin Jameel¹, Jia Li Xu^{2*}, Zhi Qiang Yin^{1*}

¹Department of Dermatology, the First Affiliated Hospital of Nanjing Medical University, Nanjing, PR China

²Department of Oncology, the First Affiliated Hospital of Nanjing Medical University, Nanjing, PR China

Abstract

Psoriasis is an immune-mediated inflammatory disease that involves skin and joints. Many studies have reported psoriasis was frequently associated with a growing list of comorbidities, such as cardiovascular disease, metabolic syndrome and diabetes mellitus. Psoriasis also may bring out a risk of skin cancer, which was possibly due to immune-suppressive drugs, ultraviolet phototherapy, habits of smoking and drinking, or the chronic inflammatory nature of the disease. Psoriatic patients are prone to suffer from non-melanoma skin cancer; however, they have a clearly lower possibility to suffer from melanoma.

Keywords: Psoriasis, Melanoma, Skin cancer

Accepted on October 10, 2016

Introduction

Psoriasis is an immune-mediated inflammatory disease of the skin. It also happens to be associated with several comorbidities, such as arterial hypertension, metabolic syndrome, cardiovascular diseases, diabetes mellitus, kidney damage, and may also pose as a potential risk for the development of skin cancer [1,2]. Herein, we have conducted a review focusing mainly on the detailed relationship between psoriasis and skin cancer.

Psoriasis and Non-Melanoma Skin Cancer (NMSC)

NMSC includes Squamous Cell Carcinoma (SCC), Basal Cell Carcinoma (BCC) and some rare tumors. NMSC is the commonest group of malignant tumors among the Caucasians and the incidence of NMSC has sustainably grown annually. Risk factors include ultraviolet radiation and immunosuppression [3-5]. Psoriasis is often treated with ultraviolet therapy and systemic immunosuppressants that may bring about the risk of skin tumorigenesis [6]. Chen et al. reported that psoriasis increased the risk of acquiring malignant tumor, which was independent of systemic treatment for psoriasis [7].

In recent years, more and more studies proposed that psoriasis is related with the risk of development of malignant tumor (NMSC was most common) [8] and this association was primarily driven by NMSC [9]. The incidence of malignancy was significantly higher in psoriatic patients than general population [6], and patients with psoriasis had an increased risk for the development of SCC and BCC [10-12]. The cancer risk is influenced by gender, geographic location, age, and severity of psoriasis. Among psoriatic patients, females had a relatively

higher risk for developing NMSC than their male counterparts. Psoriatic patients in the southern geographical regions or in the age group of 50-59 were prone to suffer from NMSC. The standardized incidence ratio of NMSC among severe psoriatic patients was clearly higher than that of patients with mild psoriasis [8,13].

Psoriasis is an inflammatory T cell-mediated autoimmune skin disease [14], and IL-23/Th17 signalling pathway plays a pivotal role in the pathogenesis of psoriasis [15,16]. Relevant reports showed that Th17 cytokines including IL-17 and IL-22 could signal to the cells of non-melanoma skin cancer, then induce cellular proliferation and reinforced migration of BCC and SCC cells *in vitro* [17]. Moreover, IL-17 could induce secretion of IL-6 and IL-8 for tumor progression, alone or combined with TNF- α [18].

Risk of skin cancer in psoriatic patients was also due to treatment modalities such as ultraviolet phototherapy, cyclosporine and possibly methotrexate [19]. Over the years, PUVA and narrow-band UVB were widely used to treat chronic plaque psoriasis [20]. Due to concerns for possible long-term adverse effects, especially cancer, studies were conducted focusing on their long-term risk and benefits and found that PUVA therapy could bring about increased risk of skin cancer, exposure to more than 350 PUVA treatments significantly increased SCC risk, exposure to fewer than 150 PUVA treatments had modest effects on SCC risk, and high-dose exposure to PUVA did not obviously increase BCC risk [20-22]. However, there were no significant relation between NB-UVB treatment and BCC, SCC or melanoma, and even several studies reported phototherapy with UVB reduced the risk of cancer in psoriasis [22,23].

Psoriasis and Melanoma

It is well known that melanoma is responsible for most skin cancer deaths globally [24]. The existence of T-cell infiltrates within melanoma lesions may be related to longer patient survival [25]. The role of T-cells in psoriasis is well established [14]. There was a statistically significant association between psoriasis and melanoma, and the association remained after adjusting the odds ratio for age and phototherapy [26]. Further studies have found that patients with melanoma showed a lower probability of psoriasis and psoriatic patients presented fewer melanomas [25]. In comparison with non-dermatological patients, psoriatic patients had a significantly lower frequency of suffering melanoma [10]. It is reported that psoriatic patients had fewer melanocytic naevi [27]. In particular, some of the cytokines including IL-1 α , IL-6 and TNF- α , could inhibit melanogenesis and melanocyte growth and were also found to be involved in the up-regulation of keratinocyte proliferation in the pathogenesis of psoriasis [28,29]. In psoriasis skin, proinflammatory cytokine network might inhibit melanogenesis, melanocyte growth and/or progression to naevi [27]. According to the above discussion, we suppose psoriasis could be a protective factor for melanoma. Further studies should be conducted to investigate the possible link between psoriasis and melanogenesis.

Psoriasis and Other Cancer

Smoking has been proven to be related with the prevalence and severity of psoriasis, and relevant meta-analysis were in favour to a positive association between the prevalence of smoking and psoriasis, and between smoking and severity of psoriasis [30]. On the other hand, psoriatic patients had a higher probability of cigarette abuse, which was associated with the incidence of cancer [31,32]. So the relationship between psoriasis and NMSC might be due to some unmeasured risk factors, such as smoking, drinking, etc. In addition, smoking was contrarily related to melanoma risk, especially on the head and neck [33].

Many epidemiological studies have reported that psoriasis was associated with metabolic syndrome, and psoriatic patients with diabetes tend to develop cancers of the digestive organs [34]. Obesity is one comorbidity of psoriasis, which is also related to poor wound healing, melanoma, and an incremental risk of other inflammatory skin diseases [23].

Psoriasis patients had high risk of suffering from lymphoma because of its pathophysiology, treatments, or both. The most common types were Hodgkin's lymphoma and cutaneous T-cell lymphoma [35,36]. Due to the immunological nature of psoriasis, an increase in lymphoma incidence in psoriatic patients could be observed. Moderate to severe psoriatic patients were often given systemic treatments such as azathioprine, methotrexate and PUVA [37], which were thought to increase lymphoma risk [8].

In conclusion, psoriasis has been proved to increase the risk of skin cancer, which is possibly due to its pathophysiology, treatments, or co-morbidities. Psoriatic patients have an

increased NMSC risk, to the contrary, a lower possibility of suffering melanoma. Patients with psoriasis and dermatologists should be vigilant for possible skin cancer development.

Acknowledgments

This work was supported by the National Natural Science Foundation of China (81301387), and the Priority Academic Program Development of Jiangsu Higher Education Institutions (JX10231801).

Conflict of Interest

The authors have no conflict of interest to disclose.

References

1. Svedbom A, Dalen J, Mamolo C. Increased cause-specific mortality in patients with mild and severe psoriasis: a population-based Swedish register study. *J Acta Derm Venereol* 2015; 95: 809-815.
2. Ogdie A, Yu Y, Haynes K, Love TJ, Maliha S. Risk of major cardiovascular events in patients with psoriatic arthritis, psoriasis and rheumatoid arthritis: a population-based cohort study. *Ann Rheum Dis* 2015; 74: 326-332.
3. Griffin LL, Ali FR, Lear JT. Non-melanoma skin cancer. *Clin Med (Lond)* 2016; 16: 62-65.
4. Saida T. Melanoma and non-melanoma skin cancers. *Gan To Kagaku Ryoho* 2016; 43: 419.
5. John SM, Trakatelli M, Ulrich C. Non-melanoma skin cancer by solar UV: the neglected occupational threat. *J Eur Acad Dermatol Venereol* 2016; 30 Suppl 3: 3-4.
6. Egeberg A, Thyssen JP, Gislason GH. Skin cancer in patients with psoriasis. *J Eur Acad Dermatol Venereol* 2016; 30: 1349-1353.
7. Chen YJ, Wu CY, Chen TJ, Shen JL, Chu SY. The risk of cancer in patients with psoriasis: a population-based cohort study in Taiwan. *J Am Acad Dermatol* 2011; 65: 84-91.
8. Lee MS, Lin RY, Chang YT, Lai MS. The risk of developing non-melanoma skin cancer, lymphoma and melanoma in patients with psoriasis in Taiwan: a 10-year, population-based cohort study. *Int J Dermatol* 2012; 51: 1454-1460.
9. Chiesa Fuxench ZC, Shin DB, Ogdie Beatty A, Gelfand JM. The risk of cancer in patients with psoriasis: a population-based cohort study in the health improvement network. *JAMA Dermatol* 2016; 152: 282-290.
10. Paradisi A, Tabolli S, Didona B, Sobrino L, Russo N. Reduced frequency of melanoma in 72,739 patients with psoriasis: A retrospective study. *Eur J Dermatol* 2015; 25: 133-137.
11. Kimball AB, Schenfeld J, Accortt NA. Cohort study of malignancies and hospitalized infectious events in treated and untreated patients with psoriasis and a general population in the United States. *Br J Dermatol* 2015; 173: 1183-1190.

12. Kimball AB, Schenfeld J, Accorrt NA. Incidence rates of malignancies and hospitalized infectious events in patients with psoriasis with or without treatment and a general population in the USA. 2005-2009. *Br J Dermatol* 2014; 170: 366-373.
13. Margolis D, Bilker W, Hennessy S, Vittorio C, Santanna J. The risk of malignancy associated with psoriasis. *Arch Dermatol* 2001; 137: 778-783.
14. Schakel K, Scon MP, Ghoreschi K. Pathogenesis of psoriasis. *Hautarzt* 2016; 67: 422-431.
15. AbuHilal M, Walsh S, Shear N. The role of IL-17 in the pathogenesis of psoriasis and update on il-17 inhibitors for the treatment of plaque psoriasis. *J Cutan Med Surg* 2016.
16. Malakouti M, Brown GE, Wang E, Koo J, Levin EC. The role of IL-17 in psoriasis. *J Dermatolog Treat* 2015; 26: 41-44.
17. McAllister F, Kolls JK. Th17 cytokines in non-melanoma skin cancer. *Eur J Immunol* 2015; 45: 692-694.
18. Nardinocchi L, Sonogo G, Passarelli F, Avitabile S, Scarponi C. Interleukin-17 and interleukin-22 promote tumor progression in human nonmelanoma skin cancer. *Eur J Immunol* 2015; 45: 922-931.
19. Pouplard C, Brenaut E, Horreau C, Barnetche T, Misery L. Risk of cancer in psoriasis: a systematic review and meta-analysis of epidemiological studies. *J Eur Acad Dermatol Venereol* 2013; 27 Suppl 3: 36-46.
20. Archier E, Devaux S, Castela E. Carcinogenic risks of psoralen UV-A therapy and narrowband UV-B therapy in chronic plaque psoriasis: a systematic literature review. *J Eur Acad Dermatol Venereol* 2012; 26: 22-31.
21. Stern RS. PUVA follow-up study. The risk of squamous cell and basal cell cancer associated with psoralen and ultraviolet-A therapy: a 30-year prospective study. *J Am Acad Dermatol* 2012; 66: 553-562.
22. Hearn RM, Kerr AC, Rahim KF, Ferguson J, Dawe RS. Incidence of skin cancers in 3867 patients treated with narrow-band ultraviolet B phototherapy. *Br J Dermatol* 2008; 159: 931-935.
23. Shipman AR, Millington GW. Obesity and the skin. *Br J Dermatol* 2011; 165: 743-750.
24. Bristow I, Bower C. Melanoma of the Foot. *Clin Podiatr Med Surg* 2016; 33: 409-422.
25. Megna M, Napolitano M, Balato N, Scalvenzi M, Ayala F. Psoriasis in melanoma patients: a prospective pilot study. *G Ital Dermatol Venereol* 2015.
26. Bhattacharya T, Nardone B, Rademaker A. Co-existence of psoriasis and melanoma in a large urban academic centre population: a cross-sectional retrospective study. *J Eur Acad Dermatol Venereol* 2016; 30: 83-85.
27. Balato N, Di Costanzo L, Balato A, Patruno C, Scalvenzi M. Psoriasis and melanocytic naevi: does the first confer a protective role against melanocyte progression to naevi? *Br J Dermatol* 2011; 164: 1262-1270.
28. Albanesi C, De Pita O, Girolomoni G. Resident skin cells in psoriasis: a special look at the pathogenetic functions of keratinocytes. *Clin Dermatol* 2007; 25: 581-588.
29. Alwan W, Nestle FO. Pathogenesis and treatment of psoriasis: exploiting pathophysiological pathways for precision medicine. *Clin Exp Rheumatol* 2015; 33: S2-S6.
30. Richer V, Roubille C, Fleming P, Starnino T, McCourt C. Psoriasis and smoking: a systematic literature review and meta-analysis with qualitative analysis of effect of smoking on psoriasis severity. *J Cutan Med Surg* 2016; 20: 221-227.
31. Hayes J, Koo J. Psoriasis: depression, anxiety, smoking, and drinking habits. *Dermatol Ther* 2010; 23: 174-180.
32. Gerdes S, Zahl VA, Weichenthal M, Mrowietz U. Smoking and alcohol intake in severely affected patients with psoriasis in Germany. *Dermatology* 2010; 220: 38-43.
33. Song F, Qureshi AA, Gao X, Li T, Han J. Smoking and risk of skin cancer: a prospective analysis and a meta-analysis. *Int J Epidemiol* 2012; 41: 1694-1705.
34. Lan CC, Ko YC, Yu HS. Psoriatic patients with diabetes are prone to develop digestive organ cancers: a population-based study in Taiwan. *J Dermatol Sci* 2012; 68: 82-88.
35. Gelfand JM, Shin DB, Neimann AL, Wang X, Margolis DJ. The risk of lymphoma in patients with psoriasis. *J Invest Dermatol* 2006; 126: 2194-2201.
36. Gelfand JM, Berlin J, Van Voorhees A, Margolis DJ. Lymphoma rates are low but increased in patients with psoriasis: results from a population-based cohort study in the United Kingdom. *Arch Dermatol* 2003; 139: 1425-1429.
37. Stern RS. Lymphoma risk in psoriasis: results of the PUVA follow-up study. *Arch Dermatol* 2006; 142: 1132-1135.

***Correspondence to**

Zhi Qiang Yin

Department of Dermatology

The First Affiliated Hospital of Nanjing Medical University

PR China

yzq2802@sina.com

Jia Li Xu

Department of Oncology

The First Affiliated Hospital of Nanjing Medical University

PR China

scarlett0830@sina.com