Kocatepe Tıp Dergisi
Kocatepe Medical Journal
17:121-127/Temmuz/2016

DERLEME / REVIEW

Psoriazis ve Eşlik Eden Hastalıklar

Psoriasis and Concomitant Diseases

Derya UÇMAK[1], Zeynep MELTEM AKKURT[1], Mustafa ARICA[1]

[1]Dicle University Faculty of Medicine, Department of Dermatology, Diyarbakir

ÖZ

Psoriazis kronik inflamatuar bir hastalıktır. Psoriazis ile ilgili yapılan çalışmalarda bu inflamatuar durumun klinik yansımasının artık deriye sınırlı olmadığı, eşlik eden bazı inflamatuar hastalıkların psoriaziste normalde beklenenden farklı sayıda olduğu fark edilmiştir. Psoriazisle ilişkili eskiden beri bilinen depresyon ve yaşam kalitesi, psoriatik artrit, malignensi gibi bazı komorbiditelere ek olarak kardiovasküler hastalık, metabolik sendrom, inflamatuar barsak hastalıkları, uyku apne sendromu gibi yeni araştırılan komorbiditeler tanımlanmıştır. Bu derlemede sık görülen komorbiditelerin ve konu ile alakalı yapılmış çalışmalardan bahsedilecektir.

Anahtar Kelimeler: İnflamasyon; kardiyovasküler hastalık; komorbidite; metabolik sendrom; psoriazis.

ABSTRACT

Psoriasis is a chronic inflammatory disease. It has been noticed in the studies on psoriasis that the clinical reflection of this inflammatory condition is not limited to the skin any more and the number of some concomitant inflammatory diseases in psoriasis is higher than expected. Newly studied comorbidities such as cardiovascular disease, metabolic syndrome, ınflammatory bowel diseases, sleep apnea syndrome have been defined in addition to depression and quality of life, psoriatic arthritis, malignancy that have long been known to be associated with psoriasis. In this review, common comorbidities and the relevant studies in the literature are presented.

Keywords: Cardiovascular disease; comorbidity; inflammation; metabolic syndrome; psoriasis.

Geliş Tarihi / Received: 10.02.2014
Kabul Tarihi / Accepted: 27.03.2014
Yazışma Adresi / Correspondence: Yrd. Doç. Dr. Derya UÇMAK
Dicle University, 21280, Diyarbakir - TURKEY
ucmakderya@gmail.com

INTRODUCTION

Psoriasis vulgaris is a common skin disease. The incidence of psoriasis in Western industrialized countries ranges from 2% to 3%. It is chronic in more than 90% of cases (1). Morbidity in psoriasis patients is significant due to chronic and excessive inflammation in skin and joints. Psoriasis a prevalent T lymphocyte-mediated disorder; therefore, both the disease itself and the side effects associated with its treatment affect patients globally (2).

Chronic T-cell stimulation in psoriasis seems to be caused by the constant stimulation of the T cells in the skin by the mature Langerhans cells in the skin lesions. The psoriatic process is suspected to be a constant immune response to the lesional skin (acting like peripheral lymphoid tissue). Although T cell activation is in the lymph node or chronic skin lesion, there are also various specific molecular interactions in order to stimulate the proliferation of the antigen reactive T cell clones (3).

Clinical effects of psoriasis are not limited only to the skin. Other diseases appear to be concomitant in psoriasis patients with varying rates more than expected. Such concomitance of diseases is referred to as comorbidity (4). Such diseases are influenced by certain shared risk factors such as genetic background, environmental exposure and smoking. This interaction varies depending on the duration of psoriasis and the treatment modalities (5).

There may be comorbidities that accompany psoriasis. Some of these are referred to as established comorbidities, while some are known to be emergent comorbidities. According to a recent systematic classification, established comorbidities are classified as depression and health-related quality of life, psoriatic arthritis and malignancy. Emerging comorbidities of psoriasis are classified under cardiovascular disease and metabolic syndrome (6).

Prevalence of the core components of metabolic syndrome including obesity, dyslipidemia, and insulin resistance is high in psoriasis patients. The underlying chronic inflammatory nature of psoriasis most probably explains the relationship between psoriasis and comorbidities such as metabolic syndrome and cardiovascular disease (6). Various classification systems in the literature group the common comorbidities that are concomitant with psoriasis under cardiovascular (CV) diseases (including obesity, hypertension, hyperglycemia and dyslipidemia), psychological co-morbidities (including depression, alcohol abuse and smoking) and PsA (7). In this review, we aimed to present newly defined comorbidities in addition to the already known ones.

Depression and Quality of Life

Psoriasis is a chronic skin disease and may impair the patient's quality of life significantly. In a recent study aiming to find the prevalence of depression in psoriasis; the quality of life was found to be influenced negatively in 61% of the psoriasis patients, which is a high rate. Furthermore, this study also demonstrated that the quality of life was influenced negatively in patients with shorter histories compared to those with longer histories and in female patient compared to male patients (8). In the study of Gupta et al., the global severity of psoriasis was proportional to the degree of depression and psoriasis was construed as more severe in patients who made suicidal attempts than those who didn't make suicidal attempts (9). According to the General Health Questionnaire that was conducted to avoid confusing the general psychiatric morbidity with the other skin diseases, the prevalence of certain psychiatric disorders such as depression, anxiety, sleep disorder was 53% and 16,7% in psoriasis and vitiligo, respectively (10).

People with psoriasis suffer from stress, depression, anxiety and worry. They use alcohol to avoid these conditions and relieve their present symptoms. Alcohol use must be definitely explored in assessing the patients and planning the treatment (11).

In another study, 17-30% of the cases with psoriasis reported varying degrees of alcohol problems (12). There exists an association between smoking and the severity of psoriasis. Smoking

is also correlated with greater impairment of psoriasis-related quality of life (13- 15).

There is a limited number of studies that analyze the impact of psoriasis on working life. In a study performed in the USA, decreased productivity at work due to psoriasis was found to exceed 100 million dollars a year (6, 16).

Psoriatic Arthritis:

Psoriatic arthritis is a typical comorbidity in psoriasis. Additional diseases may be typically associated with inflammatory joint disorders. Psoriatic arthritis, ankylosing spondylitis, and HLA-B27-positive spondyloarthropathies may occur concomitantly. These concomitant diseases represent a cluster of comorbidities (17). Psoriatic arthritis is especially associated with HLA-B27 positivity and often accompanies type 2 psoriasis (late-onset psoriasis). Psoriatic arthritis occurs approximately in 5-30% of patients with psoriasis (18). Psoriatic arthritis is categorized into five types: 1) asymmetric distal interphalangeal joint involvement, 2) symmetrical polyarthritis, 3) oligoarthritis, 4) arthritis mutilans, 5) ankylosing spondylitis (19). Asymmetrical oligoarthritis is the most common form involving primarily the distal interphalangeal joints. As it usually has a progressive and destructive course that may leave sequelae, early diagnosis and treatment are very important (18).

Malignancy

In addition to non-melanoma skin cancer in psoriasis, increased risks of head and neck malignity have also been found. Although the mechanism of this increase could not be demonstrated fully, it has been associated with life style factors such as alcohol use and smoking (6,20). An average 9.3-year follow-up of 6905 patients with a hospital discharge diagnosis of psoriasis in Denmark showed that the risk increased 1.4 times compared to the national cancer rates (such as non melanoma skin cancer, oral cavity cancer, pharynx, larynx, colon cancers) (21).

Olsen et al. reported that the increased relative risk ranged from 1.4 to 2.5 in patients with psoriasis. The risk was found to increase in colon (1.4 fold), larynx (2.4 fold), lung (1.4 fold), kidney (1.7 fold) and non-melanoma skin (2.5 fold) cancers (22).

153,197 patients with mild and severe psoriasis as well as 765,950 matched control individuals were included in a large-scale population study performed to identify the risk of lymphoma and the lymphoma and its subtypes were determined. The respective adjusted relative risks for lymphoma and its subtypes were found to be as follows in mild and severe psoriasis patients: all lymphoma 1.34 (1.16, 1.54) and 1.59 (0.88, 2.89); non-Hodgkin's lymphoma 1.15 (0.97, 1.37) and 0.73 (0.28, 1.96); Hodgkin's lymphoma (HL) 1.42 (1.00, 2.02) and 3.18 (1.01, 9.97); cutaneous T-cell lymphoma (CTCL) 4.10 (2.70, 6.23) and 10.75 (3.89, 29.76). The risk of lymphoma increases in psoriasis. HL and CTCL have the strongest association with the increased risk of lymphoma (23).

In a field study performed in the UK, Gelfand et al. found an 2.95 times higher risk of developing lymphoma in psoriasis patents older than 65 compared to non-psoriasis individuals (24).

PUVA is mutagenic and patients exposed to PUVA therapy have an increased risk of squamous-cell skin cancer. This therapy can lead to irregular, pigmented skin lesions. Stern et al. assessed 1380 patients exposed to PUVA therapy and followed 30.000 patients with moderate psoriasis annually. SCC risk was found to increase 100 times after 337 sessions of PUVA therapy (25). Malignant melanoma developed in cases who were exposed to minimum 250 sessions of therapy and who spent minimum 15 years following the first PUVA therapy (25).

In addition to the skin carcinoma, the incidence of lymphoma was found to be 7 times higher in patients exposed to the combination of PUVA therapy and MTX minimum for 36 months than in the patients less exposed to MTX in the previous study (26).

Cardiovascular Diseases

There are three important reasons for the risk profile in the pathogenesis of cardiovascular

diseases. The first reason is the systemic inflammation. Studies with mice have shown that myocardial inflammation may be present in psoriasis patients with increased TNF alpha levels in the lesional skin and serum, which may lead to heart failure. The second reason for the increased risk is the use of anti-inflammatory and systemic treatments that have atherogenic side effects. The third reason is related to the life-style factors such as smoking and obesity (27).

Psoriasis is a hyperproliferative and cutaneous disorder. It is characterized by the potential to lower levels of folate. As a result of this, homocysteine levels may raise, which is an independent risk factor for the development of cardiovascular disease (28).

It was found that many TNF-α mediated mechanisms led to endothelial dysfunction. Polymorphonuclear leukocytes were found to accumulate in the vascular structures after the endothelial cells encountered TNF-α. Furthermore, it was understood that TNF-α enabled adhesion in the endothelium and vascular invasion of dendritic cells. Therefore, following the stimulation of these cells; T-cells, monocytes and macrophages are activated. This leads to vascular inflammation and cytokine production. Moreover, TNF-α mediated oxidative stress directly results in the apoptosis of the endothelial cells (18).

It is well known that the prevalence of CAD, pulmonary embolism and cerebrovascular disease increases significantly in patients with psoriasis characterized by raised levels of TNF-α (29- 31).

In another recent large-scale epidemiological study, patients with severe psoriasis were followed for 5.4 years on average and psoriasis was demonstrated to be an independent risk factor for myocardial infarction (MI). The risk of acute MI was claimed to be higher especially in younger patients with severe psoriasis (32).

Metabolic Syndrome

According to the guidelines of NHLBI (National Heart, Lung, and Blood Institute) and AHA (American Heart Association) patients that meet minimum three of the criteria presented in **Table I** are diagnosed with metabolic syndrome (33). Metabolic syndrome increases the risk of type 2 diabetes by 3 to 9-fold and the risk of coronary artery disease, stroke and myocardial infarction by 2 to 3-fold (34- 36). The risk of presence of metabolic syndrome and its components was shown to increase in patients with psoriasis (37, 38). The incidence of metabolic syndrome increased in patients with severe and treatment resistant psoriasis patients compared to the control group (37). This association was pronounced in the patients aged 40-49 years who were diagnosed with psoriasis, while predisposition to metabolic syndrome was correlated with the advanced age at diagnosis (37).

Components of Metabolic Syndrome

Table I: Criteria for metabolic syndrome.

- Fasting glucose ≥100 mg/dL (or receiving drug therapy for hyperglycemia)
- Blood pressure ≥130/85 mm Hg (or receiving drug therapy for hypertension)
- Triglycerides ≥150 mg/dL (or receiving drug therapy for hypertriglyceridemia)
- HDL-C < 40 mg/dL in men or < 50 mg/dL in women (or receiving drug therapy for reduced HDL-C)
- Waist circumference ≥102 cm (40 in) in men or ≥88 cm (35 in) in women; if Asian American, ≥90 cm (35 in) in men or ≥80 cm (32 in) in women

* A patient that has at least 3 of 5 conditions is diagnosed with metabolic syndrome.

In a study assessing the association between the components of metabolic syndrome and psoriasis; psoriasis patients (131.560 people) were found to have an increased likelihood to smoke, have diabetes mellitus, hyperlipidemia, and body mass index compared to the age, gender and other coronary artery disease risk adjusted individuals without psoriasis (479.317 people) (38).

Obesity

Psoriasis patients were shown to be twice fatter than the normal population (39). The risk of obesity was found to be higher by 1,27 and 1,79-fold in moderate and severe psoriasis patients, respectively (38). Naldi et al. compared the psoriasis patients with a disease duration of shorter than two years and patients with other dermatological diseases and they found an association between psoriasis and increased body mass index (40). In this study, they also found that the likelihood of psoriasis increased by 1,6 and 1,9 times in patients with body mass index of 26-29 kg/m2 and >29 kg/m2, respectively (40).

Insulin Resistance/ Diabetes

According to several studies, there exists a potential association between PsO and increased serum fasting glucose levels, hyperinsulinemia, insulin resistance and type 2 diabetes (6). There are many studies that have explored the association between psoriasis and insulin resistance as well as diabetes and found various results. In a cross-sectional study, 110 non-obese individuals were assessed; while 70 of them had psoriasis and 40 were in the control group. Insulin resistance was found to be higher in psoriasis patient group than in the control group. Patients were divided into early-onset and late-onset groups in this study. Patients in the late-onset group were more predisposed to develop insulin resistance (41).

Hypertension

Investigators have also reported a higher prevalence of hypertension in PsO patients compared to controls (37, 38) In another study, 22% of adult PsO patients (age >18 years) who had been hospitalized from 1996 to 2002 had hypertension compared to10% of controls (adjusted OR: 3.27; 95% CI: 2.41–4.43) (37).

Proinflammatory / Prothrombotic State

Association between PsO and a proinflammatory and/or prothrombotic state has not been thoroughly explored. However, plasma acute-phase proteins, such as CRP, fibrinogen, and PAI-1, were shown to be significantly elevated in psoriatic patients compared with healthy controls (42, 43) in several studies.

Inflammatory Bowel Diseases

Crohn Disease (CD) patients appear to have higher rates of psoriasis than the general population (44). Danese et al. found that the prevalence of psoriasis ranged from 7% to 11% in the IBD population, compared to 1%-2% in the general population (45). Yates et al. reported a higher prevalence of psoriasis in CD (11.2%) than in UC (5.7%) in their study (46).

Obstructive Sleep Apnea Syndrome

Obstructive sleep apnea syndrome (OSAS) is a sleep disorder that has an impact on all systems. OSAS is caused by intermittent episodes of partial or complete upper airway obstruction during sleep. Karaca et al. found a higher incidence of OSAS (54.5%) in psoriasis patients compared to normal population. They stated that physicians had to take account of the life style-related comorbidities in assessing psoriasis patients (47).

Based on the review of studies published in our country, a retrospective study performed in Konya area demonstrated that hypertension, diabetes mellitus, asthma/chronic obstructive pulmonary disease, coronary artery disease and epilepsy were the most common concomitant systemic diseases. It was found that 4.6% of patients had hypertension, 2.9% had diabetes mellitus, 2.8% had asthma/chronic obstructive pulmonary disease, 0.9% had coronary artery disease %0.9 had epilepsy (48).

Conclusionally, psoriasis is considered as a multisystem disease; therefore, risk factors must be assessed systematically as soon as they are identified; while any problem found must be followed up in coordination with a specialist.

KAYNAKLAR

1. Nevitt GJ, Hutchinson PE. Psoriasis in the community: prevalence, severity and patients beliefs and attitudes towards the disease. Br J Dermatol 1996;135(4):533–7.

2. Nickoloff BJ, Nestle FO. Recent insights into the immunopathogenesis of psoriasis provide new therapeutic opportunities. J Clin Invest 2004;113(12):1664-75.

3. Krueger JG. The immunologic basis for the treatment of psoriasis with new biologic agents. J Am Acad Dermatol 2002;46(1):1-23.

4. Christophers E. Comorbidities in psoriasis. Clin Dermatol 2007;25(6):529–34.

5. Flanders WD, Boyle CA, Boring JR. Bias associated with differential hospitalization rates in incident case-control studies. J Clin Epidemiol 1989;42(5):395–401.

6. Gottlıeb AB, Chao C, Dann F. Psoriasis comorbidities. Journal of Dermatological Treatment 2008;19(1):5–21.

7. Strohal R, Kirby B, Puig L; the Psoriasis Expert Panel. Psoriasis beyond the skin: an expert group consensus on the management of psoriatic arthritis and common co-morbidities in patients with moderate-to-severe psoriasis. J Eur Acad Dermatol Venereol 2013 Dec 24. doi: 10.1111/jdv.12350. [Epub ahead of print]

8. Jankowiak B, Sekmistrz S, Kowalewska B, et al. Satisfaction with life in a group of psoriasis patients. Postepy Dermatol Alergol 2013;30(2):85-90.

9. Gupta MA, Schork NJ, Gupta AK, et al. Suicidal ideation in psoriasis. Int J Dermatol 1993;32(3):188–90.

10. Sharma N, Koranne RV, Singh RK. Psychiatric morbidity in psoriasis and vitiligo: A comparative study. J Dermatol 2001;28(8):419–23.

11. Adamzik K, McAleer MA, Kirby B. Alcohol and psoriasis: sobering thoughts. Clin Exp Dermatol 2013;38(8):819-22.

12. Kirby B, Richards HL, Mason DL, et al. Alcohol consumption and psychological distress in patients with psoriasis. Br J Dermatol 2008;158(1):138-40.

13. Gerdes S, Zahl VA, Weichenthal M, et al. Smoking and alcohol intake in severely affected patients with psoriasis in Germany. Dermatology 2010;220(1):38–43.

14. Xiao J, Chen LH, Tu YT, et al. Prevalence of myocardial infarction in patients with psoriasis in central China. J Eur Acad Dermatol Venereol 2009;23(11):1311–5.

15. Davidsson S, Blomqvist K, Molin L, et al. Lifestyle of Nordic people with psoriasis. Int J Dermatol 2005;44(5):378–83.

16. The burden of skin diseases 2004. 2004 [cited March 7 2007]. URL:http://www.sidnet.org/pdfs/Burden%20of%20Skin%20Diseases%202004.pdf31.01.2014

17. Christophers E. Comorbidities in psoriasis.Clin Dermatol 2007;25(6):529-34.

18. Atakan N, Doğan S. Psoriazis sistemik bir hastalık mıdır? Turk J Dermatol 2012;6(3):119-22.

19. Kundakcı N, Tursen U, Babiker MO, et al. The evaluation of the sociodemographic and clinical features of Turkish psoriasis patients. Int J Dermatol 2002;41(4):220-4.

20. Boffetta P, Gridley G, Lindelof B. Cancer risk in a population-based cohort of patients hospitalized for psoriasis in Sweden. J Invest Dermatol 2001;117(6):1531–7.

21. Frentz G, Olsen JH. Malignant tumours and psoriasis: a follow-up study. Br J Dermatol 1999;140(2):237–42.

22. Olsen JH, Moller H, Frentz G. Malignant tumors in patients with psoriasis. J Am Acad Dermatol 1992;27(5 Pt1):716–22.

23. Gelfand JM, Shin DB, Neimann AL, et al. The risk of lymphoma in patients with psoriasis. J Invest Dermatol 2006;126(10):2194–201.

24. Gelfand JM, Berlin J, van Voorhees A, et al. 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(11):1425–9.

25. Stern RS, Nichols KT, Väkevä LH. Malignant melanoma in patients treated for psoriasis with methoxsalen (psoralen) and ultraviolet A radiation (PUVA). The PUVA Follow-Up Study. N Engl J Med 1997;336(15):1041-5.

26. Stern RS. Lymphoma risk in psoriasis: results of the PUVA follow-up study. Arch Dermatol 2006;142(9):1132-5.

27. Wakkee M, Thio HB, Prens EP. Unfavorable cardiovascular risk profiles in untreated and treated psoriasis patients. Atherosclerosis 2007;190(1):1-9.

28. Tobin AM, Hughes R, Hand EB, et al. Homocysteine status and cardiovascular risk factors in patients with psoriasis: a case-control study. Clin Exp Dermatol 2011;36(1):19-23.

29. Friedewald VE, Cather JC, Gordon KB, et al. The editor's roundtable: psoriasis, inflammation, and coronary artery disease. Am J Cardiol 2008;101(8):1119-26.

30. Friedewald VE, Cather JC, Gelfand J, et al. AJC editor's consensus: psoriasis and coronary artery disease. Am J Cardiol 2008;102(12):1631-43.

31. Mehta NN, Yu Y, Pinnelas R, et al. Attributable risk estimate of severe psoriasis on major cardiovascular events. Am J Med 2011;124(8):775.e1-6.

32. Gelfand JM, Neimann AL, Shin DB, et al. Risk of myocardial infarction in patients with psoriasis. JAMA 2006;296(14):1735-41.

33. Third report of the National Cholesterol Education Program (NCEP) Expert Panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III) final report. Circulation 2002;106(25):3143–421.

34. Ford ES. Risks for all-cause mortality, cardiovascular disease, and diabetes associated with the metabolic syndrome: A summary of the evidence. Diabetes Care 2005;28(7):1769–78.

35. Laaksonen DE, Lakka HM, Niskanen LK, et al. Metabolic syndrome and development of diabetes mellitus: Application and validation of recently suggested definitions of the metabolic syndrome in a prospective cohort study. Am J Epidemiol 2002;156(11):1070–7.

36. Isomaa B, Almgren P, Tuomi T, et al. Cardiovascular morbidity and mortality associated with the metabolic syndrome. Diabetes Care 2001;24(4):683–9.

37. Sommer DM, Jenisch S, Suchan M, et al. Increased prevalence of the metabolic syndrome in patients with moderate to severe psoriasis. Arch Dermatol Res 2006;298(7):321–8.

38. Neimann AL, Shin DB, Wang X, et al. Prevalence of cardiovascular risk factors in patients with psoriasis. J Am Acad Dermatol 2006;55(5):829–35.

39. Herron MD, Hinckley M, Hoffman MS, et al. Impact of obesity and smoking on psoriasis presentation and management. Arch Dermatol 2005;141(12):1527–34.

40. Naldi L, Chatenoud L, Linder D, et al. Cigarette smoking, body mass index, and stressful life events as risk factors for psoriasis: results from an Italian case–control study. J Invest Dermatol 2005;125(1):61–7.

41. Ucak S, Ekmekci TR, Basat O, et al. Comparison of various insulin sensitivity indices in psoriatic patients and their relationship with type of psoriasis. J Eur Acad Dermatol Venereol 2006;20(5):517-22.

42. Vanizor Kural B, Orem A, Cimşit G, Yandi YE, Calapoglu M. Evaluation of the atherogenic tendency of lipids and lipoprotein content and their relationships with oxidant-antioxidant system in patients with psoriasis. Clin Chim Acta 2003;328(1-2):71–8.

43. Nielsen HJ, Christensen IJ, Svendsen MN, et al. Elevated plasma levels of vascular endothelial growth factor and plasminogen activator inhibitor-1 decrease during improvement of psoriasis. Inflamm Res 2002;51(12):563–7.

44. Najarian DJ, Gottlieb AB. Connections between psoriasis and Crohn's disease. J Am Acad Dermatol 2003;48(6):805–21; quiz 822-4.

45. Danese S, Semeraro S, Papa A, et al. Extraintestinal manifestations in inflammatory bowel disease. World J Gastroenterol 2005;11(46):7227–36.

46. Yates VM, Watkinson G, Kelman A. Further evidence for an association between psoriasis, Crohn's disease and ulcerative colitis. Br J Dermatol 1982;106(3):323–30.

47. Karaca S, Fidan F, Erkan F, et al. Might psoriasis be a risk factor for obstructive sleep apnea syndrome? Sleep Breath 2013;17(1):275-80.

48. Turan H, Acer E, Aliağaoğlu C, et al. Psoriazisli hastaların klinik ve sosyodemografik özelliklerinin değerlendirilmesi. Turk J Dermatol 2013;7(2):76-80.