Revie paper

Evaluation of pancreatic function in patients with plaque psoriasis

Agnieszka Białecka

Department of Dermatology and Venereology, Faculty of Medicine in Bydgoszcz, Nicolaus Copernicus University in Torun, Poland

Adv Dermatol Allegol 2023; XL (3): 372–376
DOI: https://doi.org/10.5114/ada.2023.129400

Abstract

Psoriasis is a chronic inflammatory dermatosis with periods of exacerbation and remission. Prevalence of psoriasis is estimated at 1–3% of the population of Europe and the United States of America. The disease process may affect the skin, nails and joints. Perception of psoriasis as not only a skin disease, but a systemic inflammatory disease that affects the functioning of the entire body has changed over the years. Patients suffering from psoriasis more often than the general population suffer from many comorbidities. Little data is available on the comorbidity of psoriasis and pancreatic diseases. The relationship between the coexistence of psoriasis and chronic pancreatitis seems to the most interesting and worth further studies.

Key words: psoriasis, pancreas, pancreatitis.

Psoriasis is a chronic inflammatory dermatosis with periods of exacerbation and remission. The disease process may affect the skin, nails and joints. In its classical form, psoriasis vulgaris (PV) is characterized by the appearance of red papules covered with silvery scales on the skin, typically affecting the elbows, knees and scalp, which is referred to as plaque psoriasis [1].

Prevalence of psoriasis is estimated at 1–3% of the population of Europe and the United States of America [2]. The incidence of psoriasis in Europe is estimated at 120–140/100,000/year [3]. The prevalence of psoriasis among children increases with age from 13.5/100,000/year in the 0–3 age group to 53.1/100,000/year in the 14–18 age group [4]. Undoubtedly however, current data indicate an increasing incidence of psoriasis [4, 5]. Perhaps this is related to the greater prevalence of risk factors exacerbating the course of psoriasis, but also to better access to health care systems and more accurate diagnostics or collection of epidemiological data [4].

First symptoms of psoriasis may occur at any age, but two onset peaks are most common – at the age of 15–20 and at the age of 55–60. This age differentiation at diagnosis corresponds to two clinical models of psoriasis that differ in age of onset, course, and prognosis [2, 3, 4–6].

Originally, psoriasis was considered a disease caused by excessive epidermal proliferation. The exact aetiology of psoriasis is still not fully understood. It is known, however, that psoriasis is the result of a complex reaction of many factors, including genetic, environmental and immunological conditions.

Psoriasis is a chronic and incurable disease. Most patients are diagnosed with mild to moderate psoriasis [7]. However, approximately 20% of patients suffering from psoriasis will require systemic treatment or hospitalization during their lives because of an unstable course of the disease [8, 9]. Bacterial, viral and fungal infections, emotional stress, stimulants and some medications are known factors that trigger episodes of exacerbations [9].

Perception of psoriasis as not only a skin disease, but a systemic inflammatory disease that affects the functioning of the entire body has also changed over the years. We now know, for example, that psoriasis may be an important risk factor for the development of cardiovascular diseases [10].

We also know that patients suffering from psoriasis more often than the general population suffer from such comorbidities as arterial hypertension, dyslipidaemias, obesity, diabetes, non-alcoholic fatty liver disease (NAFLD) and finally full-blown metabolic syndrome [6].

Little data are available on the comorbidity of psoriasis and pancreatic diseases. Previous studies on the coexistence of psoriasis and diseases of the digestive system have focused on the relationship between psoriasis and Crohn's disease or ulcerative colitis [11].

Address for correspondence: Agnieszka Białecka PhD, Department of Dermatology and Venereology, Faculty of Medicine, Nicolaus Copernicus University, 9 Sklodowskiej-Curie St, 85-094 Bydgoszcz, Poland, phone/fax: +48 525853867, e-mail: agnieszka_bialecka@wp.pl
Received: 18.06.2023, **accepted:** 20.06.2023.

However, the assessment of pancreatic function in patients suffering from psoriasis was the subject of interest of scientists more than 100 years ago. At the beginning of the 20th century, it was believed that the onset or exacerbation of psoriasis may be related to certain disorders of the exocrine function of the pancreas. It has been assumed that lipocaic, a product extracted from the pancreas, possibly a hormone, inhibits fat formation and, when injected in dogs after pancreatectomy, prevents the fatty liver that usually follows pancreatectomy. Becker *et al*. published two series of studies with lipocaic in patients suffering from psoriasis [12, 13]. The authors believed that successful treatment of psoriasis would depend on maintaining serum lipid levels at the lower limit of normal. In the first series of studies, they noted improvement in 4 patients after administration of lipocaic, and no improvement in 2 [12]. Lipocaic was administered orally to patients in a second series of studies with 23 patients who were followed for 2 to 18 months. Remission occurred in 7 patients, some improvement in 12, but no changes were noted in 4. The assumed reduction in serum lipid levels did not occur, but the authors noted that the improvement occurred faster in patients with low blood lipid values [13].

Deproteinized extracts from the pancreas, without insulin, histamine and acetylcholine, were used in the studies by Downing *et al*., who reported improvement in 50% of treated patients [14].

In 1953, Ingels studied the clinical response in 36 patients suffering from psoriasis while using a pancreatic extract called Entozyme [15]. In 24 patients, refractory to all previous therapies, this extract was the only treatment used and a good clinical response occurred in 19 patients within 4 weeks to 3 months, with complete remission observed in 4 patients. In 11 of the 12 patients, Entozyme was added to topical therapy and improvement occurred within 2 weeks to 3 months or more. In these patients, previous treatments also proved ineffective. Ingels in his work noted that a good response to the applied treatment was associated with a serum cholesterol value below 300 mg/dl.

In the studies cited above, the emphasis was on supplementing and replacing key enzymes for fat metabolism.

In their studies, Madden and Karon did not show any variability in the exocrine function of the pancreas in patients suffering from psoriasis [16]. However, they used only an indirect measurement by measuring faecal nitrogen, faecal fat, and serum lipase and amylase levels.

Farber, on the other hand, conducted a study on 30 patients with psoriasis compared to a control group and used a direct measurement of the level of bile, trypsin, chymotrypsin, lipase and amylase in the fluid obtained from the duodenum [17]. However, the obtained data did not show any significant differences in the exocrine function of the pancreas in patients suffering from psoriasis compared to the healthy population. According to the author of the paper, replacement therapies with pancreatic enzymes did not seem to be recommended.

All these papers currently have only a historical aspect. However, it is worth noting the significant interest in the values of the lipid profile in the serum of patients. Today, we know that patients with psoriasis have been shown to have a variety of abnormalities in serum lipid levels, most commonly with elevated triglyceride (TG) values, decreased high-density lipoprotein (HDL) values, and elevated total cholesterol (TC) and low-density lipoprotein fraction (LDL) [18–21]. Salihbegovic *et al.* also confirmed the relationship between dyslipidaemia and psoriasis, with the incidence of dyslipidaemia correlated with the severity of the disease as measured by the Psoriasis Area and Severity Index (PASI) [22]. Disorders of the oxidative-antioxidant balance in psoriasis lead to oxidation of LDL cholesterol particles and formation of oxidized LDL (ox-LDL), which damage endothelial cells, increase the influx of inflammatory cells to the vascular wall and promote formation of reactive oxygen species (ROS), which results in the development of atherosclerotic lesions [19, 23]. Additionally, patients with psoriasis showed increased values of autoantibodies against oxidized LDL particles (AuAb-oxLDL), which can be used to assess cardiovascular risk and confirm the important role of ox-LDL in the pathogenesis of atherosclerotic lesions [24, 25]. The level of AuAb-oxLDL seems to be positively correlated with the severity of psoriasis [25]. Studies conducted so far have also shown an association between the apolipoprotein (Apo) E4 allele and chronic plaque psoriasis and small-follicular psoriasis, suggesting a possible role of ApoE in the pathogenesis of psoriasis. The ApoE4 isoform is strongly associated with hyperlipidaemia, and thus with the development of atherosclerosis [26]. However, exact mechanisms of these interactions are not known and certainly require further research. Also currently used systemic drugs, such as cyclosporin A and retinoids, may induce dyslipidaemia [27]. Therefore, during therapy, it is recommended to closely monitor parameters of lipid metabolism and use a low-fat diet. In turn, a positive effect of the therapy on the lipid profile values was observed in the case of tumor necrosis factor α (TNF-α) inhibitors, during which an increase in HDL values was demonstrated [19]. The current recommendations on the treatment and management of patients with psoriasis already include the target lipid parameters that clinicians should aim for in their patients [28].

Pancreatitis is a significant medical problem due to the severity of the clinical course and uncertain prognosis. Acute pancreatitis is an inflammation of the pancreas, which is most often caused by gallstones and alcohol abuse. Other, less popular, risk factors are also known, such as hypercalcemia, hypertriglyceridemia, certain medications, smoking, and type 2 diabetes [29, 30].

Patients most often report to the hospital because of severe epigastric pain radiating to the back and more than three times elevated levels of lipase and amylase in the blood serum or urine [29]. Acute pancreatitis may be mild as a self-limiting disease in 80% of cases, but in 20% it is accompanied by serious complications and the risk of death [31].

In 2007, Amouzougan *et al.* described the case of a patient with psoriatic arthritis and recurrent acute pancreatitis [32]. The authors excluded coexistence of other possible risk factors for acute pancreatitis, such as gallbladder lithiasis, history of chronic alcohol consumption, or dyslipidaemia. The patient was treated with TNF-α inhibitors. The authors noted that acute pancreatitis could be a rare visceral complication of psoriatic arthritis.

In 2013, Clayton *et al.* described a very interesting case of a patient with psoriasis, chronic alcoholic pancreatitis, with frequent exacerbations, treated with anti-TNF-α inhibitors [33]. The authors focused on the role of TNF in the development and treatment of acute and chronic pancreatitis. TNF is one of the main mediators of acute pancreatitis. Elevated levels of TNF are observed in the serum of animals with experimentally induced acute pancreatitis [34] and in patients with acute pancreatitis [35].

Sahu *et al.* described the case of a psoriasis patient with acute triglyceridaemia-induced pancreatitis caused by adalimumab [36]. According to the authors, TNF-α blockade by adalimumab may increase the production of other cytokines affecting lipogenesis. Previously, only two cases of TNF-α inhibitor therapy associated with acute pancreatitis have been described [37, 38].

Chronic pancreatitis is an inflammatory disease of the pancreas, characterized by chronic inflammation and cell degeneration. This chronic inflammatory process leads to a gradual loss of exocrine and endocrine function of the pancreas and subsequent fibrosis of the organ parenchyma [39]. Risk factors for chronic pancreatitis include alcohol abuse, smoking, genetic predisposition, pancreatic duct obstruction, hypertriglyceridemia and chronic kidney disease. Patients with chronic pancreatitis may experience chronic pain and reduced quality of life, and their life expectancy is shortened [40].

A large study comparing the prevalence of chronic pancreatitis in patients with psoriasis compared to a healthy population was published only in 2016 by scientists from Taiwan [41]. In their work, the authors used data obtained from the Taiwan National Health Insurance Research Database on 48,430 patients with psoriasis and 193,720 patients without psoriasis. Based on statistical analysis, the authors showed that the prevalence of chronic pancreatitis was 0.61 in patients with psoriasis and 0.34 in those without psoriasis per 1,000 person-years during a 6.6-year follow-up period. All groups of patients with psoriasis had a statistically higher risk of chronic pancreatitis, with the exception of patients with arthritis, and the risk increased with the severity of psoriasis. The authors also showed that patients treated with methotrexate and nonsteroidal anti-inflammatory drugs had a lower risk of chronic pancreatitis. As scientists indicate, psoriasis and chronic pancreatitis have similar risk factors, such as hyperlipidaemia, chronic renal failure and cigarette smoking [39, 42]. In addition, inflammatory mediators in psoriasis, such as TNF-α, IL-1, IL-17 and IL-18, are also elevated in chronic pancreatitis [43–45]. Systemic treatment of patients with psoriasis and the relationship with the incidence of chronic pancreatitis seem to be extremely interesting. Methotrexate turned out to be a drug that alleviates the course of acute pancreatitis and reduces the levels of pro-inflammatory cytokines [46]. The authors did not show an increase in the incidence of chronic pancreatitis and the use of cyclosporine or acitretin, drugs that may increase serum lipid levels. So far, one case of fatal pancreatitis associated with the use of acitretin has been reported [47]. Perhaps this is related to the close monitoring of lipid parameters during systemic acitretin treatment in psoriasis and the early initiation of treatment with fibrates or statins.

Assessment of the incidence of pancreatic cancer in the population of patients suffering from psoriasis seems to be equally interesting. Solid pancreatic tumours are mainly pancreatic ductal adenocarcinoma (PDAC), which accounts for 90% of pancreatic neoplasms [48].

As it is the case with almost all malignancies, PDAC risk factors are divided into modifiable and non-modifiable. The first group includes: alcohol, smoking, specific diet, diabetes, obesity, and exposure to certain chemicals. The second group includes age, sex, ethnicity, family history and genetic factors, diabetes, chronic pancreatitis, blood type other than "0" [49].

The peak incidence of pancreatic cancer occurs between the age of 60 and 80. Pancreatic cancer is more common in men and its symptoms include a history of acute pancreatitis, chronic pancreatitis, *de novo* diabetes, poor diabetes control, dyspepsia, gallstones, abdominal pain, weight loss or jaundice [49].

Pancreatic cancer has a low 5-year survival rate ranging from 2 to 9%, depending on the country studied [50]. This is due to the aggressiveness of the disease and its initially clinically silent course.

Brauchli *et al.* in their paper published in 2009 presented a study of a population of 73,404 patients, including 36,702 with psoriasis and 36,702 patients without a diagnosis of psoriasis [51]. After excluding patients with a history of cancer or HIV, the remaining study population consisted of 67,761 patients, including 33,760 with psoriasis and 34,001 without psoriasis. In this population, 1703 patients diagnosed with cancer were identified. The IR was 5.83 (95% confidence interval (CI): 5.47–6.22) per 1,000 person-years in patients with psoriasis, and 5.18 (95% CI: 4.83–5.55) per 1,000 person-years in patients without psoriasis. Among 1,703 cases of patients diag-

nosed with cancer, 54% also had a diagnosis of psoriasis. Patients with psoriasis have been shown to have a statistically significant increased risk of developing malignancies of the lymphatic system and the gastrointestinal tract (especially pancreatic cancer). The diagnosis of malignancies correlated with the duration of the disease and possibly the severity of the disease. The increased incidence of pancreatic cancers was also confirmed by Boffett's 2001 study [52].

The reason for the increased incidence of pancreatic cancer may be the fact that chronic inflammation affects the initiation of a neoplastic process [53]. Patients with psoriasis receive many immunosuppressive drugs, although the data obtained so far show mainly an increased risk of nonmelanoma skin cancers in patients receiving cyclosporine A [54]. Pancreatic cancer and psoriasis also share many common risk factors, such as smoking, obesity, type 2 diabetes and chronic pancreatitis [49].

A relationship between psoriasis and pancreatic diseases has not been well understood so far, in recent years scientists have focused on the links between psoriasis and cardiovascular disorders. It seems crucial to conduct further research, which may make it possible to include the assessment of pancreatic function in permanent algorithms of care for patients suffering from psoriasis, and thus avoid the development of serious complications.

Conflict of interest

The author declares no conflict of interest.

References

1. Brandon A, Mufti A, Gary Sibbald R. Diagnosis and management of cutaneous psoriasis: a review. Adv Skin Wound Care 2019; 32: 58-69.
2. Parisi R, Symmons DP, Griffiths CE, et al. Global epidemiology of psoriasis: a systematic review of incidence and prevalence. J Invest Dermatol 2013; 133: 377-85.
3. Huerta C, Rivero E, Rodriguez LA. Incidence and risk factors for psoriasis in the general population. Arch Dermatol 2007; 143: 1559-65.
4. Tollefson MM, Crowson CS, McEvoy MT, et al. Incidence of psoriasis in children: a population-based study. J Am Acad Dermatol 2010; 62: 979-87.
5. Icen M, Crowson CS, McEvoy MT, et al. Trends in incidence of adultonset psoriasis over three decades: a population-based study. J Am Acad Dermatol 2009; 60: 394-401.
6. Vena GA, Altomare G, Ayala F, et al. Incidence of psoriasis and association with comorbidities in Italy: a 5-year observational study from a national primary care database. Eur J Dermatol 2010; 20: 593-8.
7. Gelfand JM, Feldman SR, Stern RS, et al. Determinants of quality of life in patients with psoriasis: a study from the US population. J Am Acad Dermatol 2004; 51: 704-8.
8. Naldi L, Colombo P, Placchesi EB, et al. Study design and preliminary results from the pilot phase of the PraKtis study: self-reported diagnoses of selected skin diseases in a representative sample of the Italian population. Dermatology 2004; 208: 38-42.
9. Naldi L, Gambini D. The clinical spectrum of psoriasis. Clin Dermatol 2007; 25: 510-8.
10. Białecka A, Białecki M, Serafin Z, et al. Atherosclerosis attacks in patients with psoriasis vulgaris but without a relationship with the severity and course of the disease. Adv Dermatol Allergol 2021; 38: 673-81.
11. Fu Y, Lee C, Chi C. Association of psoriasis with inflammatory bowel disease: a systematic review and meta-analysis. JAMA Dermatol 2018; 154: 1417-23.
12. Becker SW, Clark DE, Dragstedt LR, et al. The experimental use of lipocaic in the treatment of psoriasis. J Invest Derm 1939; 2: 218.
13. Becker SW, Clark DE, Dragstedt LR, et al. Further observations on the use of lipocaic in the treatment of psoriasis. J Invest Derm 1941; 4: 59-67.
14. Downing JG, Glicklich EA, Messina SJ. Deproteinated pancreatic extract in treatment of psoriasis. Arch Derm Syph 1942; 45: 1125-7.
15. Ingels AE. Entozyme in treatment of psoriasis. California Med 1953; 79: 437.
16. Madden JF, Karon IM. Pancreatic function and X-ray studies in psoriasis. AMA Arch Derm Syphilol 1953; 67: 66-76.
17. Farber EM, Johnson RE, Shwachman H. The exocrine function of the pancreas in psoriasis. AMA Arch Derm 1957; 76: 236-8.
18. Pietrzak A, Lecewicz-Toruń B. Activity of serum lipase (EC 3.1.1.3) and the diversity of serum lipid profile in psoriasis. Med Sci Monit 2002; 8: 9-13.
19. Wakkee M, Thio HB, Prens EP, et al. Unfavorable cardiovascular risk profiles in untreated and treated psoriasis patients. Atherosclerosis 2007; 190: 1-9.
20. Rocha-Pereira P, Santos-Silva S, Rebelo I, et al. Dislipidemia and oxidative stress in mild and in severe psoriasis as a risk for cardiovascular disease. Clin Chim Acta 2001; 303: 33-9.
21. Tekin NS, Tekin IO, Barut F, et al. Accumulation of oxidized low-density lipoprotein in psoriatic skin and changes of plasma lipid levels in psoriatic patients. Mediators Inflamm 2007; 2007: 78454.
22. Salihbegovic EM, Hadzigrahic N, Suljagic E, et al. Psoriasis and dyslipidemia. Mater Sociomed 2015; 27: 15-7.
23. Madamanchi NR, Hakim ZS, Runge MS. Oxidative stress in atherogenesis and arterial thrombosis: the disconnect between cellular studies and clinical outcomes. J Thromb Haemost 2005; 3: 254-67.
24. Vanizor Kural B, Orem A, Cimşit G, et al. Plasma homocysteine and its relationships with atherothrombotic markers in psoriatic patients. Clin Chim Acta 2003; 332: 23-30.
25. Sunitha S, Rajappa M, Mohan Thappa D, et al. Is the ratio of antibodies against oxidized LDL to oxidized LDL an indicator of cardiovascular risk in psoriasis? Oman Med J 2016; 31: 390-3.
26. Campalani E, Allen MH, Fairhurst D, et al. Apolipoprotein E gene polymorphisms are associated with psoriasis but do not determine disease response to acitretin. Br J Dermatol 2006; 154: 345-52.
27. Neimann AL, Shin DB, Wang X, et al. Prevalence of cardiovascular risk factors in patients with psoriasis. J Am Acad Dermatol 2006; 55: 829-35.
28. Reich A, Adamski Z, Chodorowska G, et al. Psoriasis. Diagnostic and therapeutic recommendations of the Polish Dermatological Society. Part 1. Dermatol Rev 2020; 107: 92-108.

29. Lankisch PG, Apte M, Banks PA. Acute pancreatitis. Lancet 2015; 386: 85-96.
30. Wang GJ, Gao CF, Wei D, et al. Acute pancreatitis: etiology and common pathogenesis. World J Gastroenterol 2009; 15: 1427-30.
31. Lund H, Tønnesen H, Tønnesen MH, Olsen O. Long-term recurrence and death rates after acute pancreatitis. Scand J Gastroenterol 2006; 41: 234-8.
32. Amouzougan A, Chopin F, Patouillard B, et al. Recurrent acute pancreatitis in psoriatic arthritis. Joint Bone Spine 2007; 74: 513-5.
33. Clayton H, Flatz L, Vollenweider-Roten S, et al. Anti-TNF therapy in the treatment of psoriasis in a patient with acute-on-chronic pancreatitis. Dermatology 2013; 227: 193-6.
34. Malleo G, Mazzon E, Siriwardena AK, et al. Role of tumor necrosis factor- in acute pancreatitis: from biological basis to clinical evidence. Shock 2007; 28: 130-40.
35. Malmstrom ML, Hansen MB, Andersen AM, et al. Cytokines and organ failure in acute pancreatitis: inflammatory response in acute pancreatitis. Pancreas 2012; 41: 271-7.
36. Sahu KK, Lal A, Mishra AK, et al. Adalimumab-related hypertriglyceridemia and acute pancreatitis. QJM 2020; 113: 298-99.
37. Werlang ME, Lewis MD, Bartel MJ. Tumor necrosis factor alpha inhibitor-induced acute pancreatitis. ACG Case Rep J 2017; 4: e103.
38. Gunawan F, Fayyaz B, Mihardja TO. Etanercept – a culprit agent in acute pancreatitis? J Community Hosp Intern Med Perspect 2019; 9: 147-9.
39. Braganza JM, Lee SH, McCloy RF, et al. Chronic pancreatitis. Lancet 2011; 377: 1184-97.
40. Beyer G, Habtezion A, Werner J, et al. Chronic pancreatitis. Lancet 2020; 396: 499-512.
41. Chiu HY, Hsieh CF, Chiang YT, et al. The risk of chronic pancreatitis in patients with psoriasis: a population-based cohort study. PLoS One 2016; 11: e0160041.
42. Chiu HY, Huang HL, Li CH, et al. Increased risk of glomerulonephritis and chronic kidney disease in relation to the severity of psoriasis, concomitant medication, and comorbidity: a nationwide population-based cohort study. Br J Dermatol 2015; 173: 146-54.
43. Yuan BS, Zhu RM, Braddock M, et al. Interleukin-18: a pro-inflammatory cytokine that plays an important role in acute pancreatitis. Expert Opin Ther Targets 2007; 11: 1261-71.
44. Ni J, Hu G, Xiong J, et al. Involvement of interleukin-17A in pancreatic damage in rat experimental acute necrotizing pancreatitis. Inflammation 2013; 36: 53-65.
45. Sri Manjari K, Jyothy A, Shravan Kumar P, et al. A single-nucleotide polymorphism in tumor necrosis factor-alpha (-308 G/A) as a biomarker in chronic pancreatitis. Gene 2014; 539: 186-9.
46. Duan L, Ma Y, Chi J, et al. The regulatory role of immunosuppressants on immune abnormalities in acute pancreatitis. Biomed Rep 2014; 2: 193-8.
47. Katz HI, Waalen J, Leach EE. Acitretin in psoriasis: an overview of adverse effects. J Am Acad Dermatol 1999; 41: S7-12.
48. Jin C, Bai L. Pancreatic cancer–current situation and challenges. Gastroenterol Hepatol Lett 2020; 2: 1-3.
49. Hawksworth G, Hales J, Martinez F, et al. Pancreatic cancer tends in Europe: epidemiology and risk factor. Medical Studies 2019; 35: 164-71.
50. McGuigan A, Kelly P, Turkington RC, et al. Pancreatic cancer: a review of clinical diagnosis, epidemiology, treatment and outcomes. World J Gastroenterol 2018; 24: 4846-61.
51. Brauchli YB, Jick SS, Miret M, et al. Psoriasis and risk of incident cancer: an inception cohort study with a nested case-control analysis. J Invest Dermatol 2009; 129: 2604-12.
52. 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: 1531-7.
53. Krishnamoorthy S, Honn KV. Inflammation and disease progression. Cancer Metastasis Rev 2006; 25: 481-91.
54. Paul CF, Ho VC, McGeown C, et al. Risk of malignancies in psoriasis patients treated with cyclosporine: a 5 y cohort study. J Invest Dermatol 2003; 120: 211-6.