Heart Metab. (2013) 60:30-33

Psoriasis and risk of cardiovascular disease: case report and discussion

Catriona Maybury, Catherine H. Smith
St John's Institute of Dermatology, King's College, London, UK

Correspondence: Dr. Catriona Maybury, St John's Institute of Dermatology, King's College, London, UK
Tel: 020 7188 6412, fax: 020 7188 8050, e-mail: catriona.maybury@kcl.ac.uk

Abstract

Psoriasis is a common inflammatory disease affecting 2% of the population. People who have severe psoriasis (requiring a systemic therapy) have a marked increase in cardiovascular disease. This could be due to an increased prevalence of traditional cardiovascular risk factors in people with psoriasis, the effect of chronic inflammation or a combination of both factors. Patients with severe disease should be risk assessed for cardiovascular disease and co-morbidities actively managed. ■ Heart Metab; 2013;60:30–33

Keywords: Psoriasis; inflammation; skin disease; cardiovascular disease; anti-TNF therapy.

Introduction

A 40-year-old lawyer has been followed in our severe psoriasis clinic since 2002. He first developed psoriasis in his twenties. He has a past medical history of mild psoriatic arthritis and hypercholesterolemia. He is an ex-smoker and drinks a moderate amount of alcohol. He is overweight (body mass index 26) but has no history of diabetes. He has a family history of ischemic heart disease. After 5 years of using topical skin treatments and phototherapy, in 2001 he required systemic therapy. He was treated with methotrexate, acitretin and cyclosporin between 2001 and 2007, when despite cyclosporin therapy, his psoriasis deteriorated.

The psoriasis area and severity index (PASI) is a validated and widely used disease severity scoring tool employed by the UK's National Institute of Health and Clincal Excellence (NICE) to guide suitability for systemic therapy. In 2007, his PASI score was 30.5 (range 0–72) and he therefore met NICE criteria for TNF antagonist therapy. He responded rapidly to 8-weekly infliximab infusions at 5 mg/kg (PASI 3 in March 2008) with complete disease control for 2 years. In August 2009 his psoriasis started to flare between treatments and his regime was altered to 6-weekly infusions.

In september 2009 he developed chest pain and shortness of breath during a trip to the hairdresser. He was hospitalized with an acute coronary syndrome, a troponin rise and an ischemic ECG. Slight chest pains during the infliximab infusion 7 days before the infarct triggered a collective decision to avoid further infusions, although the etiological relevance of infliximab in relation to the subsequent coronary event was never clear. Two months later his psoriasis flared. The initiation of bisoprolol and ramipril post infarction may have contributed to this; both drugs may exacerbate psoriasis [1]. During the same period he developed recurrent chest pain. In-stent restenosis was diagnosed and treated by a second angioplasty and stent within stent. A difficult year followed: his psoriasis was poorly controlled; stenoses in the RCA and left anterior descending arteries required stenting to alleviate chest pain and he also experienced two minor transient ischemic attacks. He underwent percutaneous coronary intervention of the RCA. Further episodes of chest pain in 2012 resulted in a coronary artery bypass grafting procedure.

In 2011, another systemic agent was sought to help control his severe psoriasis. Options were limited given his previous poor response to standard sys-

Abbreviations

CVD: cardiovascular disease; **ECG:** elctrocardiogram; **FAE:** fumeric acid esters; **IL:** interleukin; **JAMA:** Journal of the American Medical Association; **MACE:** major adverse cardiovascular event; **MI:** myocardial infarction; **RCA:** right coronary artery; **TNF:** tumour necrosis factor; **UK:** United Kingdom

temic therapy, and reluctance by both the patient and his cardiologist to try another TNF antagonist drug. He was therefore prescribed FAE, which induce apoptosis causing a reduction in peripheral CD4 and CD8 T cells and are used as first-line systemic therapy for chronic plaque psoriasis in Germany but remain unlicensed in the UK [2]. He achieved excellent disease control with FAE (PASI 2). In early 2013 this treatment was complicated by mild renal impairment with proteinuria presumed secondary to FAE therapy. A switch to ustekinumab, a monoclonal antibody (mAb) directed against the p40 unit shared by IL-12 and IL-23 (licensed for use in UK by NICE since 2009) for severe psoriasis is being considered but may be relatively contraindicated, in view of the possible link between p40 mAb (briakinumab, ustekinumab) and MACE [3].

Psoriasis

Psoriasis is a common inflammatory disease with environmental and genetic etiology, which affects approximately 2% of the population. The pathophysiology involves T-cell activation and release of cytokines including TNFα. Cutaneous inflammation combined with hyperproliferation of the epidermis results in erythematous, raised plaques with overlying scale. Nails are frequently involved and up to 30% of patients also have psoriatic arthritis [4, 5] (*Figure 1* [please note—the images used to illustrate this case are not of the patient described in the case report]).

Psoriasis and cardiovascular risk

A Swedish study published in 2004 attracted widespread interest when it reported that patients with psoriasis requiring hospital admission had a significantly increased risk of death from CVD compared to the general population [6]. This was followed by a large population-based study published in the JAMA, which identified psoriasis as a possible independent risk factor for MI [7]. A recent systematic review and meta-analysis designed to investigate incident CVD in people with psoriasis concluded that people who have severe disease (requiring systemic therapy or hospitalization) have a marked increase in CVD: the risk ratio relative to the general population for CVD mortality was 1.37 (95% CI 1.17–1.60) and 3.04 (95% CI 0.65–14.35) for MI. The relative risks of CVD were highest in the younger, severe disease population (3.10 [95% CI 1.98-4.86] for MI at 30 years) [8]. As a result of such research, psoriasis was cited as an independent risk factor for MI in the 2012 European guidelines on CVD prevention, which also recognize that the relative risk of MI is greatest in young patients and those with severe disease [5]. UK NICE guidelines published in October 2012 recommend that adults with severe psoriasis of any type should undergo a cardiovascular risk assessment at presentation using a validated risk assessment tool. They also recommend clinicians "offer a further assessment every 5 years or more frequently if indicated" [9].

The relationship between psoriasis and CVD is complex. Patients with psoriasis have an increased prevalence of coronary risk factors including metabolic syndrome [10, 11]. Psoriasis patients also tend to smoke more than the general population [12]. These factors may account for some if not all of the increased incidence of CVD seen in this group.

Inflammation has been recognized as an independent cardiovascular risk factor and there is an argument that a marker to reflect inflammation (such as highly sensitive C-reactive protein) should be added to cardiovascular risk scoring [13]. In an animal study using mice with psoriasiform dermatitis (KC-Tie2 mice) and an absence of comorbidities, aortic root inflammation was present in 33% of the affected KC-Tie2 group compared with 0% of controls (P = 0.04). After treatment of skin inflammation, the aortic root lesions resolved. The study showed that in murine models, skin inflammation alone promotes vascular inflammation and thrombosis [14]. The mechanisms linking psoriasis, metabolic syndrome and CVD have not yet been established in human subjects; one hypothesis invokes chronic T helper type 1 (Th1) inflammation [10]. A Th1-driven immune response that includes activated monocytes, macrophages and Th1 proinflammatory cytokines (including interferon and TNFα) is the hallmark of active psoriasis and also plays a role in metabolic syndrome and atherogenesis [4, 15].

Heart Metab. (2013) 60:30-33

Anti-TNF therapy and CVD

If the relationship between psoriasis and CVD is causal – and currently this is not proved – then it can be hypothesized that treating psoriasis may abrogate the risk of CVD. With regard to older, oral systemic therapies for psoriasis (namely methotrexate, acitretin, cyclosporin), although it is accepted that certain drugs may increase individual cardiovascular risk factors (for example cyclosporin is linked to hypertension and dyslipidemia), the benefit of treating severe, active disease may decrease the overall incidence of MI [16–18].

Studies evaluating the effect of treatment with anti-TNFα therapies on the incidence of MI are ongoing. Published studies have shown mixed results; either lowering the risk or having no significant effect [18, 19]. There have been concerns that newer IL-12/23 agents (ustekinumab and briakinumab) may be associated with an increase in MACE. In 2011, after an elevated MACE rate was identified in a phase III briakinumab study, the sponsoring pharmaceutical company (Abbvie) withdrew the drug from further development. A JAMA meta-analysis [3] found no significant difference in the rate of MACE in patients with psoriasis treated with anti-TNFα/IL-12/23 agents compared to controls, although the study may have been underpowered and the authors advised clinicians to exercise caution in patients with identifiable cardiovascular risk factors when prescribing IL-12/23 agents. This year Papp et al [20] reviewed safety outcomes in patients treated with ustekinumab for up to 5 years and found no elevated risk of MACE. Although reassuring for clinicians, more comprehensive data from large, prospective registries are likely to give a clearer picture over the next 5–10 years.

Conclusion

Severe psoriasis is a risk factor for CVD. This could be due to an increased prevalence of traditional cardiovascular risk factors in people with psoriasis, the effect of chronic inflammation in patients with psoriasis or, more likely, a combination of both factors. Patients with severe disease should be risk-assessed for CVD and comorbidities should be actively managed. ■

REFERENCES

1. Basavaraj KH, Ashok NM, Rashmi R, Praveen TK (2010) The role of drugs in the induction and/or exacerbation of psoriasis. Int J Dermatol 49(12):1351-1361. PubMed PMID: 21091671. Epub 2010/11/26. eng

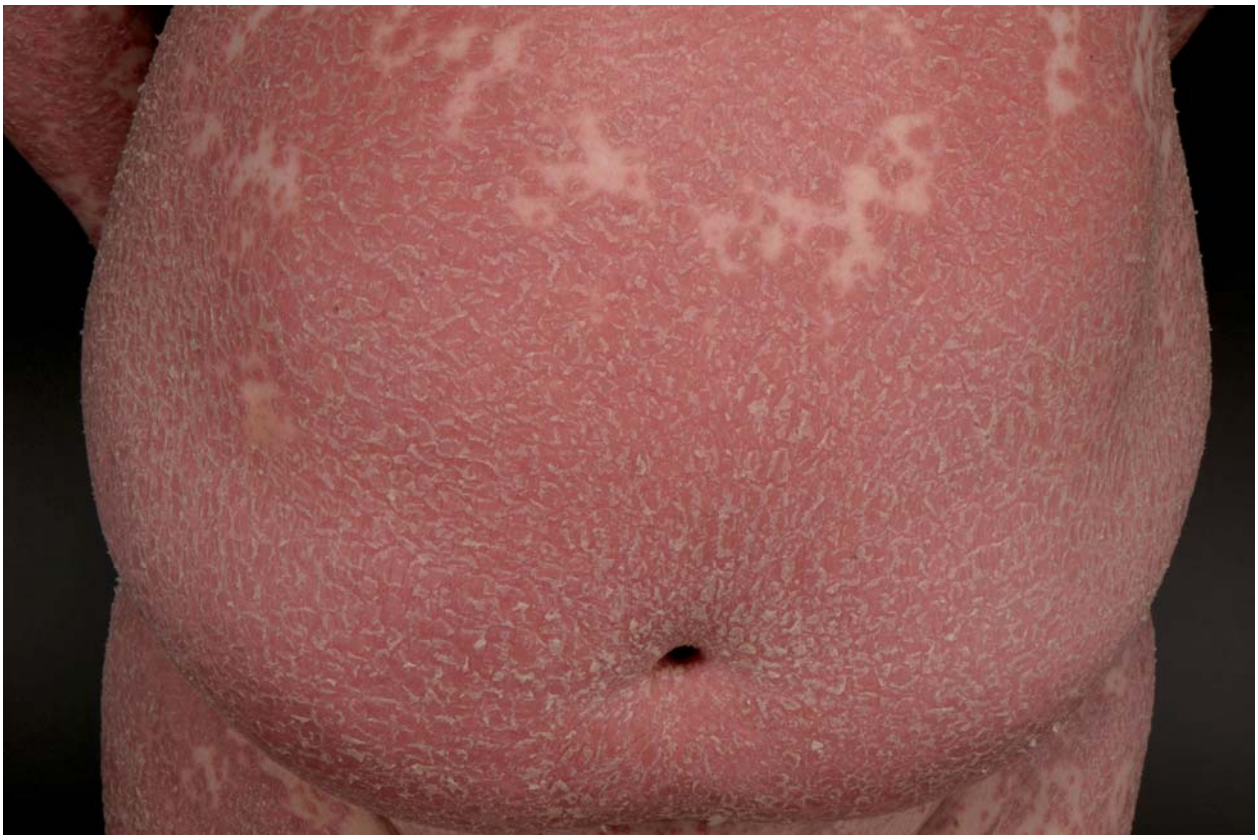

Fig. 1 *Patient with severe chronic plaque psoriasis.*

2. Wain EM, Darling MI, Pleass RD, Barker JN, Smith CH (2009) Treatment of severe, recalcitrant, chronic plaque psoriasis with fumaric acid esters: a prospective study. Br J Dermatol 162(2):427-434. PubMed PMID: 19519838. Epub 2009/06/13. eng
3. Ryan C, Leonardi CL, Krueger JG, Kimball AB, Strober BE, Gordon KB, et al (2011) Association between biologic therapies for chronic plaque psoriasis and cardiovascular events: a meta-analysis of randomized controlled trials. JAMA 306(8):864-871. PubMed PMID: 21862748. Epub 2011/08/25. eng
4. Nestle FO, Kaplan DH, Barker J (2009) Psoriasis. N Engl J Med 361(5):496-509. PubMed PMID: 19641206. Epub 2009/07/31. eng
5. Perk J, De Backer G, Gohlke H, Graham I, Reiner Z, Verschuren WM, et al (2012) European guidelines on cardiovascular disease prevention in clinical practice (version 2012): the fifth joint task force of the European Society of Cardiology and other societies on cardiovascular disease prevention in clinical practice (constituted by representatives of nine societies and by invited experts). Int J Behav Med 19(4):403-488. PubMed PMID: 23093473. Epub 2012/10/25. eng
6. Mallbris L, Akre O, Granath F, Yin L, Lindelof B, Ekbom A, et al (2004) Increased risk for cardiovascular mortality in psoriasis inpatients but not in outpatients. Eur J Epidemiol 19(3):225-230. PubMed PMID: 15117115. Epub 2004/05/01. eng
7. Gelfand JM, Neimann AL, Shin DB, Wang X, Margolis DJ, Troxel AB (2006) Risk of myocardial infarction in patients with psoriasis. JAMA 296(14):1735-1441. PubMed PMID: 17032986. Epub 2006/10/13. eng
8. Samarasekera EJ, Neilson JM, Warren RB, Parnham J, Smith CH (2013) Incidence of cardiovascular disease in people with psoriasis: a systematic review and meta-analysis. J Invest Dermatol . 2013. Feb 21 doi: 10.1038/jid.2013.149. [Epub ahead of print]
9. National Institute for Health and Clinical Excellence (2013) CG153. Psoriasis: The assessment and management of psoriasis. http://publications.nice.org.uk/psoriasis-cg153. Accessed 15 May 2013
10. Langan SM, Seminara NM, Shin DB, Troxel AB, Kimmel SE, Mehta NN, et al (2012) Prevalence of metabolic syndrome in patients with psoriasis: a population-based study in the United Kingdom. J Invest Dermatol 132(3 part 1):556-562. PubMed PMID: 2012095310
11. Ma C, Harskamp CT, Armstrong EJ, Armstrong AW (2013) The association between psoriasis and dyslipidaemia: a systematic review. Br J Dermatol 168(3):486-495. PubMed PMID: 23106411. Epub 2012/10/31. eng
12. Naldi L, Chatenoud L, Linder D, Belloni Fortina A, Peserico A, Virgili AR, et al (2005) Cigarette smoking, body mass index, and stressful life events as risk factors for psoriasis: results from an Italian case–control study. J Investig Dermatol 125(1):61-67. PubMed PMID: 15982303. Epub 2005/06/29. eng
13. Ridker PM, Buring JE, Rifai N, Cook NR (2007) Development and validation of improved algorithms for the assessment of global cardiovascular risk in women: the Reynolds Risk Score. JAMA 297(6):611-619. PubMed PMID: 17299196. Epub 2007/02/15. eng
14. Wang Y, Gao H, Loyd CM, Fu W, Diaconu D, Liu S, et al (2012) Chronic skin-specific inflammation promotes vascular inflammation and thrombosis. J Invest Dermatol 132(8):2067-2075. PubMed PMID: 22572815. Pubmed Central PMCID: PMC3402600. Epub 2012/05/11. eng
15. Libby P, Ridker PM, Hansson GK (2009) Inflammation in atherosclerosis: from pathophysiology to practice. J Am Coll Cardiol 54(23):2129-2138. PubMed PMID: 19942084. Pubmed Central PMCID: PMC2834169. Epub 2009/11/28. eng
16. Pietrzak A, Bartosinska J, Chodorowska G, Szepietowski JC, Paluszkiewicz P, Schwartz RA (2013) Cardiovascular aspects of psoriasis: an updated review. Int J Dermatol 52(2):153-162. PubMed PMID: 23347301. Epub 2013/01/26. Eng
17. Micha R, Imamura F, Wyler von Ballmoos M, Solomon DH, Hernan MA, Ridker PM, et al (2011) Systematic review and meta-analysis of methotrexate use and risk of cardiovascular disease. Am J Coll Cardiol 108(9):1362-1370. PubMed PMID: 21855836. Pubmed Central PMCID: PMC3196048. Epub 2011/08/23. eng
18. Wu JJ, Poon KY, Channual JC, Shen AY (2012) Association between tumor necrosis factor inhibitor therapy and myocardial infarction risk in patients with psoriasis. Arch Dermatol 148(11):1244-1250. PubMed PMID: 22911151. Epub 2012/08/23. eng
19. Abuabara K, Lee H, Kimball AB (2011) The effect of systemic psoriasis therapies on the incidence of myocardial infarction: a cohort study. Br J Dermatol 165(5):1066-1073. PubMed PMID: 21777216. Epub 2011/07/23. eng
20. Papp KA, Griffiths CE, Gordon K, Lebwohl M, Szapary PO, Wasfi Y, et al (2013) Long-term safety of ustekinumab in patients with moderate-to-severe psoriasis: final results from five years of follow-up. Br J Dermatol 2013 Apr;168(4):844-54. doi: 10.1111/bjd.12214.