CLINICAL RESEARCH STUDY

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Increased Prevalence of Coronary Artery Disease in Severe Psoriasis and Severe Atopic Dermatitis

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ABSTRACT

BACKGROUND: Psoriasis and atopic dermatitis (AD) are immuno-inflammatory diseases that can result in lifelong systemic inflammation. Unlike AD, psoriasis has been associated with cardiovascular disease. The aim of this study was to examine the prevalence, severity, and subtype of coronary artery disease (CAD) in psoriasis and AD patients without known cardiovascular disease.

METHODS: Consecutively enrolled patients (psoriasis n = 58, AD n = 31) and retrospectively matched controls (n = 33) were examined using cardiac computed tomography angiography (CCTA) and assessed using an 18-segment model of the coronary tree.

RESULTS: The prevalence of a coronary artery calcium score >0 was 29.8% in psoriasis and 45.2% in AD, vs 15.2% in controls ($P = .09$ and $P = .01$, respectively). More patients with psoriasis had a coronary artery calcium score ≥100 (psoriasis 19.3%, controls 2.9%; $P = .02$). CCTA showed the presence of plaques in 38.2% of psoriasis patients and 48.1% of AD patients, vs 21.2% of controls ($P = .08$ and $P = .03$, respectively). Psoriasis was associated with an increased prevalence of significant coronary stenosis (stenosis >70%) (psoriasis 14.6%, controls 0%; $P = .02$) and 3-vessel coronary affection or left main artery disease (psoriasis 20%, controls 3%; $P = .02$), whereas AD was associated with mild (AD 40.7%, controls 9.1%; $P = .005$) single-vessel affection.

CONCLUSIONS: These findings suggest that psoriasis and AD are associated with an increased prevalence of CAD. Patients with psoriasis have an increased prevalence of severe CAD.

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KEYWORDS: Atherosclerosis; Atopic dermatitis; Cardiac computed tomography angiography; Cardiovascular disease; Psoriasis

Psoriasis is a common inflammatory disease of the skin and joints with a prevalence of 1%-3% in the white population of Europe and North America.[1] The disease has a characteristic inflammatory pathogenesis based on T-helper (Th)1, Th17, and Th22 cell-mediated mechanisms[2,3] and is increasingly thought to be a systemic inflammatory disease linked to a range of comorbidities.[4]

While an increased prevalence of comorbidities such as diabetes, obesity, and heart disease has been suspected in psoriasis patients for several years,[5,6] research in the area accelerated following a landmark study in 2006.[7] The study documented an increased risk of myocardial infarction in patients with psoriasis compared with controls after adjusting for traditional risk factors. A large number of epidemiological registry and cohort studies have confirmed the

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association of psoriasis and traditional cardiovascular risk factors,[4,8] as well as the association between psoriasis and cardiovascular morbidity and mortality.[9,10] These findings have been somewhat contradicted by a retrospective study demonstrating increased all-cause but not cardiovascular mortality in psoriasis,[11] and a Dutch study, which did not reveal any increase in the risk of ischemic heart disease hospitalizations in predominantly mild psoriasis.[12]

Atopic dermatitis is another common, multifactorial Th2-driven inflammatory skin disease with a frequently chronic or chronically relapsing course. The disease usually manifests in infancy, but can occur throughout childhood and adolescence, and, in a subgroup of patients, persist into adulthood.[13-15]

In a subset of patients with severe disease, there is a lifelong constant inflammatory response in the skin with evidence of systemic inflammation.[16-18] One report indicated that atopic dermatitis may be a risk factor for ischemic stroke,[19] but traditionally atopic dermatitis has not been associated with an increased risk of cardiovascular disease.

Cardiac computed tomography (CT) is a well-established method for risk assessment and a diagnostic tool in suspected coronary artery disease. The low-radiation-dose noncontrast CT technique enables accurate measurements of the coronary artery calcium score, which is strongly associated with the risk of future cardiovascular events.[20-22] The absence of coronary artery calcium in asymptomatic patients is associated with excellent survival and predicts very low 10-year cardiovascular event rates.[23] In addition, coronary artery calcium scoring predicts future cardiovascular events more precisely than traditional cardiovascular risk-factor scoring.[24]

Contrast-enhanced cardiac CT angiography (CCTA) enables a detailed assessment of coronary anatomy[25] and the evaluation of noncalcified lesions.[25,26] Several studies have demonstrated that CT can distinguish between lipid-rich, fibrous, and calcified plaques,[27-29] and the presence of coronary artery disease on a coronary CT scan is strongly associated with an increased risk of future cardiovascular events.[30,31]

We aimed to examine the prevalence, severity, and subtype of coronary atherosclerosis as an indicator of cardiovascular risk in psoriasis and atopic dermatitis patients without known cardiovascular disease compared with age- and sex-matched subjects without known inflammatory diseases.

CLINICAL SIGNIFICANCE

- Severe psoriasis is associated with increased prevalence of coronary artery disease.
- Psoriasis patients had more proximal lesions and a higher prevalence of significant stenoses, as well as affection of 3 vessels and left main coronary artery disease.
- Severe atopic dermatitis is associated with increased prevalence of coronary artery disease.

PATIENTS AND METHODS

Study Design

The clinical study was conducted as a single-center observational case-control study. The Central Denmark Region Committees on Biomedical Research Ethics and the Danish Data Protection Agency approved the study protocol before patient enrollment commenced. All prospectively enrolled participants provided written informed consent before entering the study. The Committee on Research Ethics waived the requirement for informed consent regarding the retrospectively matched control group. This trial was registered with http://ClinicalTrials.gov, identifier NCT01356758.

Patients

Participants were consecutively recruited from a tertiary referral clinic at the Department of Dermatology, Aarhus University Hospital. Subjects considered for inclusion were either patients referred for treatment at the clinic or people who responded to a study notification in the member's magazine published by the Danish Psoriasis Association.

Eligible patients were men and women aged ≥18 years without symptoms of coronary artery disease, diagnosed with either severe psoriasis vulgaris or severe atopic dermatitis. The following criteria of severity were used: severe psoriasis group, severe plaque psoriasis with Psoriasis Area Severity Index (PASI) ≥10; severe atopic dermatitis group, diagnosis according to the criteria of Hanifin and Rajka,[32] body surface area of inflamed skin ≥10%, and one or more of the following sub-criteria: history of hospital admission for the treatment of atopic dermatitis, current use of potent topical corticosteroids (EU/UK class III-IV), and history or current use of systemic immunosuppressive treatment (prednisone/cyclosporine/methotrexate/azathioprine).

The exclusion criteria for both groups included: arterial hypertension, unless well controlled with antihypertensive medication for at least 3 months before inclusion (exclusion on blood pressure ≥180/100 mm Hg); lipid-lowering treatment, unless well controlled for at least 3 months before inclusion; plasma total-cholesterol ≥8 mmol/L; congestive heart failure (New York Heart Association group III and IV); reduced kidney function (estimated glomerular filtration rate below 60 mL/min); prior coronary artery intervention or coronary artery bypass grafting; prior myocardial infarction or stroke. For the patients suffering from psoriasis, additional exclusion criteria were: treatment with methotrexate, cyclosporin, acitretin, and fumarate esters within 6 months before inclusion unless less than a PASI-50% reduction had been observed during this treatment; ultraviolet type B phototherapy and psoralen ultraviolet type A photochemotherapy within 1 month before inclusion; prior or current treatment with biologic agents unless the treatment was discontinued due to insufficient