

Co-morbidities in atopic dermatitis

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Atopic dermatitis is well known for its association to other atopic diseases including asthma, rhinitis and food allergy. This association is often described as the atopic march which is a serial occurrence of atopic conditions including food allergies, asthma and allergic rhino conjunctivitis, after the debut of atopic dermatitis.¹ The atopic march may be due to the decreased skin barrier function in atopic dermatitis patients, which in approximately 1/3 is due to mutations in the filaggrin gene (FLG). Filaggrin expression may however also be down regulated by the inflammatory reaction itself, thus patients with AD, without mutations in FLG, may actually have 'a functional mutation' in the gene.² Studies suggest that careful replenishment of the skin barrier may actually inhibit the development of AD and of type I allergies stressing the importance of the skin barrier function.³

Over the last decade the concept of systemic inflammation has led to studies into cardiovascular risks, cancer risks and risks of neuro-psychiatric diseases.

There seems to be an increased risk for myocardial infarctions in individuals with severe atopic dermatitis, but as is the case with other systemic inflammatory diseases the causal relationship is very difficult to evaluate. Two cohort studies performed through the Danish national registries have yielded two similar results that having severe AD in an early age increases the risk of myocardial infarction (MI) later in life.⁴ In one of the studies however, a statistical model to approximate tobacco smoking was used. This would suggest that AD patients smoked more than healthy controls, matched on age and gender, and when correcting for this the difference in the risk of developing MI between healthy controls and AD patients was eliminated.⁴ In contrast to this, a study of the degree of atherosclerotic lesions in the coronary arteries of patients with psoriasis, AD, and healthy controls revealed that independent of smo-

king habits psoriasis patients had the most severe atherosclerotic lesions, but surprisingly AD patients had the most widespread atherosclerotic lesions.⁵ Taken together these results demonstrate that there is an increased risk of MI's in AD patients but it is still unclear if it is due to common pathogenic mechanisms or common risk factors.⁶

Studies suggest that there may be a small but increased risk of lymphoma in atopic dermatitis with severity of AD as a risk factor. This may however be biased by systemic immune suppressant treatments, immune skewing, and genetic predispositions. Also use of topical immunosuppressive drugs has been suggested as a cause of lymphomas,⁷ although a recent prospective study has not been able to show this.⁸

A very strong association with attention deficit/hyperactivity disorder (ADHD) has been established over the last 10 years. ADHD is the most common behavioural disorder in children and adolescents affecting 5-8% worldwide. ADHD is a pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development. The consequences of the condition are profound for both the family and the patient on social, psychological and economical levels. Several cross-sectional studies from Europe and the US have shown an increased odds ratio for ADHD among patients suffering from AD, and the one co-factor that seems to increase this is inadequate sleep and sleep quality. In addition, cohort studies in Denmark and Taiwan have shown that early debut AD increases the OR of developing ADHD. Three explanatory models have been suggested for the association between these diseases: (1) release of inflammatory cytokines which interfere with the prefrontal cortex, (2) increased psychological stress and (3) common risk factors including genetics, prenatal stress, and environmental exposure.⁹

Depression, suicidal behavior and anxiety has also been described in atopic dermatitis patients. Whether it is due to the constant itch, sleep loss or lack of social life is unknown and the association may also be bidirectional since psychological stress is also known to induce AD symptoms.¹⁰



All of these results suggest to the clinician that although the main symptoms of the atopic dermatitis patient is from the skin, care and attention to the patients physical and psychological health must be part of any dermatological consultation.

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