

Predicting response to anti-TNF- α treatment in Hidradenitis suppurativa

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ORIGINAL ARTICLE, p 311

Hidradenitis suppurativa (HS) is comparatively common, frequently causes impairment and almost always presents a therapeutic challenge. In spite of this, it remains an understudied disease, and studies linking existing knowledge and experience are therefore particularly valuable as they provide insight and perspective.

Using flow cytometry, in 2007, Giamarellos-Bourboulis *et al.*¹ described an altered immune response in patients with HS, suggesting a role for tumour necrosis factor (TNF)- α and the innate immune system in the pathogenesis of the disease. Later, increased amounts of circulating, as well as lesional, TNF- α were found, supporting the previous observations.^{2–4} In parallel, the use of TNF- α blockers for the treatment of HS was being studied in case series.⁵ In consequence of these observational studies, small investigator-initiated randomized controlled trials were published indicating a positive treatment effect of TNF- α blockers on HS.^{6,7}

Not all patients however respond, and other immune mechanisms such as an excessive T helper 17 response, a lack of interleukin-22 and abnormalities of the innate immune system have been studied.^{8–10} For the innate immune system both low and high expression of various markers have been described, making the interpretation of the findings more complex.^{4,9,11} In spite of the increased interest in HS, the underlying reasons for these immunological abnormalities remain obscure, but leave the reader with the impression that early suggestions of immune dysregulation are gradually gaining support.¹²

In their article in this issue of BJD, Giamarellos-Bourboulis' group links genetic polymorphisms in the promoter region of the TNF gene to both disease severity and response to anti-TNF- α treatment, suggesting a genetic background for the inflammatory consequences of the immunological abnormalities of HS as well as response to therapy.¹³ Many questions remain to be answered, but this paper begins to link some of the known islands in the sea of unknown.

Conflicts of interest

None declared.

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References

- 1 Giamarellos-Bourboulis EJ, Antonopoulou A, Petropoulou C *et al.* Altered innate and adaptive immune responses in patients with hidradenitis suppurativa. *Br J Dermatol* 2007; **156**:51–6.
- 2 Matusiak L, Bieniek A, Szepietowski JC. Increased serum tumour necrosis factor- α in hidradenitis suppurativa patients: is there a basis for treatment with anti-tumour necrosis factor- α agents? *Acta Derm Venereol* 2009; **89**:601–3.
- 3 van der Zee HH, de Ruiter L, van den Broecke DG *et al.* Elevated levels of tumour necrosis factor (TNF)- α , interleukin (IL)-1 β and IL-10 in hidradenitis suppurativa skin: a rationale for targeting TNF- α and IL-1 β . *Br J Dermatol* 2011; **164**:1292–8.
- 4 Emelianov VU, Bechara FG, Gläser R *et al.* Immunohistological pointers to a possible role for excessive cathelicidin (LL-37) expression by apocrine sweat glands in the pathogenesis of hidradenitis suppurativa/acne inversa. *Br J Dermatol* 2012; **166**:1023–34.
- 5 Haslund P, Lee RA, Jemec GB. Treatment of hidradenitis suppurativa with tumour necrosis factor- α inhibitors. *Acta Derm Venereol* 2009; **89**:595–600.
- 6 Grant A, Gonzalez T, Montgomery MO *et al.* Infliximab therapy for patients with moderate to severe hidradenitis suppurativa: a randomized, double-blind, placebo-controlled crossover trial. *J Am Acad Dermatol* 2010; **62**:205–17.
- 7 Miller I, Lynggaard CD, Lophaven S *et al.* A double-blind placebo-controlled randomized trial of adalimumab in the treatment of hidradenitis suppurativa. *Br J Dermatol* 2011; **165**:391–8.
- 8 Schlapbach C, Hänni T, Yawalkar N, Hunger RE. Expression of the IL-23/Th17 pathway in lesions of hidradenitis suppurativa. *J Am Acad Dermatol* 2011; **65**:790–8.
- 9 Wolk K, Warszawska K, Hoeflich C *et al.* Deficiency of IL-22 contributes to a chronic inflammatory disease: pathogenetic mechanisms in acne inversa. *J Immunol* 2011; **186**:1228–39.
- 10 Hunger RE, Surovy AM, Hassan AS *et al.* Toll-like receptor 2 is highly expressed in lesions of acne inversa and colocalizes with C-type lectin receptor. *Br J Dermatol* 2008; **158**:691–7.
- 11 Dréno B, Khammari A, Brocard A *et al.* Hidradenitis suppurativa: the role of deficient cutaneous innate immunity. *Arch Dermatol* 2012; **148**:182–6.
- 12 Kurzen H, Kurokawa I, Jemec GB *et al.* What causes hidradenitis suppurativa? *Exp Dermatol* 2008; **17**:455–6.
- 13 Savva A, Kanni T, Damoraki G *et al.* Impact of Toll-like receptor-4 and tumour necrosis factor gene polymorphisms in patients with hidradenitis suppurativa. *Br J Dermatol* 2013; **168**:311–317.

Atopic dermatitis, filaggrin mutations and irritant contact dermatitis

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It is well known by dermatologists that individuals with childhood atopic dermatitis (AD) have an increased risk of develop-

ing occupational hand eczema later in life.^{1–3} Patients and their parents should therefore be advised to pursue professional careers without excessive irritant exposure. Interestingly, before it was possible to test for the common filaggrin gene (FLG) mutations that are observed in about 10% of Northern Europeans,⁴ a Swedish study including 955 patients aged 24–44 years with AD in childhood showed that severe disease, involvement of the hands before 15 years of age and xerosis, as well as irritant exposure, were strongly associated with the occurrence of hand eczema in adulthood.⁵ Since then, numerous studies have shown that, for example, hair-dressing, healthcare and food handling can be problematic occupations, especially for individuals with AD, often resulting in sick-leave and job change due to irritant contact dermatitis (ICD).

In this issue of the *BJD*, Visser et al.⁶ show that both FLG mutations and AD increase the risk of occupational ICD on the hands. Pertinently, individuals with concurrent FLG mutations and AD had the strongest risk. As FLG mutations are associated with xerosis⁷ and severe childhood AD,⁴ as well as hand eczema in childhood,⁸ it is likely that a considerable proportion of the patients who developed hand eczema in the pioneering Rystedt study⁵ were also FLG mutation carriers. As these individuals can be identified through either genotyping or by clinical inspection of the hallmarks of ichthyosis vulgaris,⁹ i.e. palmar and plantar hyperlinearity, xerosis, keratosis pilaris and scaly skin, it is possible to identify this subgroup of particularly susceptible individuals. This should be a mandatory part of the routine work-up when seeing patients with AD as it may benefit the patient and our societies. One may even argue that healthcare providers should warn FLG mutation carriers without AD against excessive wet work. The importance is highlighted by the poor prognosis of patients with ICD who have atopy and FLG mutations.¹⁰ Fortunately, FLG mutation carriers who have experienced hand eczema during childhood seem to avoid professions with irritant exposure, possibly due to information provided by healthcare providers, or due to self-selection (manuscript in preparation). ICD often precedes allergic contact dermatitis,¹¹ and a general population study showed that FLG mutation carriers who reported dermatitis at some point, had a fivefold increased risk of being contact sensitized.¹² With the important new findings from the Dutch–German group, it is evident that dermatologists should help to limit the morbidity of hand eczema by advising FLG mutation carriers against future excessive occupational irritant (and allergic) exposure.

Conflict of interests

None declared.

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References

- 1 Rystedt I. Atopic background in patients with occupational hand eczema. *Contact Dermatitis* 1985; **12**:247–54.
- 2 Hald M, Agner T, Blands J et al. Clinical severity and prognosis of hand eczema. *Br J Dermatol* 2009; **160**:1229–36.
- 3 Dickel H, Bruckner TM, Schmidt A et al. Impact of atopic skin diathesis on occupational skin disease incidence in a working population. *J Invest Dermatol* 2003; **121**:37–40.
- 4 Irvine AD, McLean WH, Leung DY. Filaggrin mutations associated with skin and allergic diseases. *N Engl J Med* 2011; **365**:1315–27.
- 5 Rystedt I. Factors influencing the occurrence of hand eczema in adults with a history of atopic dermatitis in childhood. *Contact Dermatitis* 1985; **12**:185–91.
- 6 Visser MJ, Landeck L, Campbell LE et al. Impact of atopic dermatitis and loss-of-function mutations in the filaggrin gene on the development of occupational irritant contact dermatitis. *Br J Dermatol* 2013; **168**:326–32.
- 7 Sergeant A, Campbell LE, Hull PR et al. Heterozygous null alleles in filaggrin contribute to clinical dry skin in young adults and the elderly. *J Invest Dermatol* 2009; **129**:1042–5.
- 8 Thyssen JP, Carlsen BC, Menné T et al. Filaggrin null mutations increase the risk and persistence of hand eczema in subjects with atopic dermatitis: results from a general population study. *Br J Dermatol* 2010; **163**:115–20.
- 9 Ezzedine K, Droitcourt C, Ged C et al. Usefulness of a global clinical ichthyosis vulgaris scoring system for predicting common FLG null mutations in an adult caucasian population. *Br J Dermatol* 2012; **167**:1165–9.
- 10 Landeck L, Visser M, Skudlik C et al. Clinical course of occupational irritant contact eczema of the hands in relation to filaggrin genotype status and atopy. *Br J Dermatol* 2012; **167**:1302–9.
- 11 Gittler JK, Krueger JG, Guttman-Yassky E. Atopic dermatitis results in intrinsic barrier and immune abnormalities: implications for contact dermatitis. *J Allergy Clin Immunol* 2012; (in press).
- 12 Thyssen JP, Linneberg A, Ross-Hansen K et al. Filaggrin mutations are strongly associated with contact sensitization in individuals with dermatitis. *Contact Dermatitis* 2013; (in press)

Atypical erythema multiforme is a prognostic indicator of severe hepatic dysfunction in Dress (Drug Reaction with Eosinophilia and Systemic Symptoms)

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ORIGINAL ARTICLE, p 391

Adverse reactions to drugs are important because they account for 5% of all admissions and arise in 10–20% of all hospital inpatients.¹ The majority of these reactions are predictable consequences of the known mechanism, for example overanticoagulation with warfarin. However, approximately 20% of adverse reactions are not pharmacologically predictable and a large proportion of these are due to drug allergy (syn. drug hypersensitivity) of which approximately 30% may be potentially life-threatening.² Skin manifestations are the commonest