PSORIASIS
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Pathogenesis

- Autoantigens: ADAMTSL5, cathelicidin (LL37)

- GWAS -> different genes involved in multiple affected pathways (innate + adaptative)

- Adaptative / autoimmune + innate / autoinflammatory responses in psoriasis.

- Although IL36RN, CARD14 cause/contribute to pustular “psoriasis”, the genetic basis for most patients with pustular skin disease remains elusive.
European Consensus Statement on Phenotypes of Pustular Psoriasis

• **Generalized pustular psoriasis (GPP):**
  • Primary, sterile, macroscopically visible pustules on non-acral skin (excluding cases where pustulation is restricted to psoriatic plaques).
  • With/without systemic inflammation
  • With/without psoriasis vulgaris
  • Either relapsing (>1 episode) or persistent (>3 months) condition.

• **Acrodermatitis continua of Hallopeau (ACH):**
  • Primary, persistent (>3 months), sterile, macroscopically visible pustules affecting the nail apparatus.
  • With/without psoriasis vulgaris

• **Palmoplantar pustulosis (PPP):**
  • Persistent (>3 months), sterile, macroscopically visible pustules on palms and/or soles and can occur
  • With/without psoriasis vulgaris.
Paradoxical psoriasiform reactions

- Possible with all TNF blockers (1-30 months)
- Incidence: 1-5 / 100 patients/year
- Three main clinical presentations
  - Psoriasis / eczema overlap
  - Generalized
  - Palmo-plantar
- Risk of recurrence with a different TNFi: 50%
- Treatment
  - Grade I (mild to moderate): continue TNFi + topical treatments +/- MTX, CyA (antibiotics)
  - Grade II (severe): switch to different class (ustekinumab)
Autoimmune skin diseases and biologicals

- Unknown pathogenesis
  - Possible dual antagonist-agonist effect on mTNF by antiTNF
  - IFN-alpha mediated Th1 response in predisposed individuals
- Vitiligo de novo
  - 70% on TNFi therapy
  - Potential reversibility
- Alopecia areata
  - Only described during antiTNF therapy
  - Plaque type >>> totalis > diffuse
  - Potential reversibility but risk of AA autonomisation if extensive involvement
  - 24% other autoimmune manifestations (vitiligo, paradoxal psoriasis, thyroiditis)
- Others
  - Exacerbation of inflammatory bowel disease with IL-17 antagonists
  - Eczematous eruption with IL-17 antagonists
Anti-TNFs

- Treatment of systemic inflammation in psoriasis
  - Possible prevention of cardiovascular disease
- Anti-TNFs remains de gold Standard for:
  - Psoriasis and:
    - Psoriatic arthritis
    - Inflammatory bowel disease
    - Uveitis
  - Children 4-11 yo

- Certolizumab
  - Maintenance of response at w48 in PsO trials
    - 400mg Q2W (PASI-75 81-87%) vs 200mg Q2W (PASI-75 67-78%) vs placebo (MI)
  - Lack of placental transfer of certolizumab pegol during pregnancy
Anti-IL17

- Secukinumab
  - Sustained efficacy and favourable safety profile through 5 years
    - PASI 75, 90, 100 (LOCF) 79.2%, 59.5%, 37.5%
  - Real world data

- Ixekizumab
  - Sustained complete to near complete skin clearance up to 5 years without new safety signals
    - PASI 75, 90, 100 (LOCF) 83%, 68%, 45%
  - Efficacy in patients previously treated with IL-17
  - SPIRIT-P1/P2: efficacy in PsA

- Brodalumab
  - Complete clearance (60%) is sustained during long-term (5y) treatment with brodalumab in moderate-to-severe psoriasis