

Successful treatment of Alopecia Totalis with calcitriol and paricalcitol in two girls aged 3 and 7-years

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Background

Alopecia areata (AA) is a T cell mediated autoimmune disease directed at the hair follicle (HF):

- limited to patchy hair loss over the scalp (focalis)
- total loss of scalp hair (totalis)
- loss of both scalp and body hair (universalis).

HF is a micro organ with its own immune and hormonal microenvironment. During the anagen segment of hair cycle, HF epithelium generates and maintains an area of *immune privilege*, which is mainly characterized by:

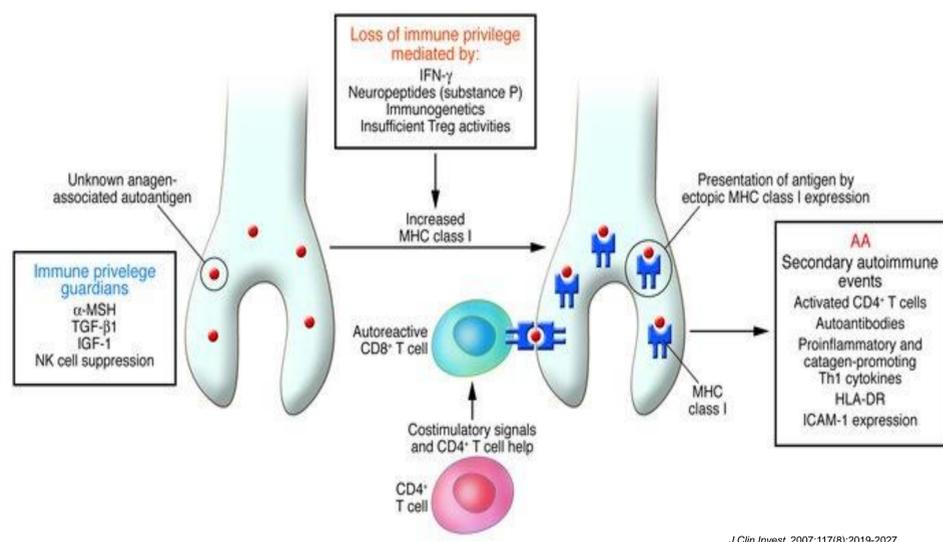
- low expression of MCH class Ia antigens,
- local production of immunosuppressive agents.

This HF immune privilege (HFIP) is important for the protection of the anagen and melanogenesis associated antigens from immune recognition by autoreactive CD8+ T cells.

Collapse of mechanisms that maintain the HFIP:

- renders the HF susceptible to inflammatory assault,
- is thought to contribute to development of AA

Growing evidence implicates the **INF γ** in triggering HFIP collapse.



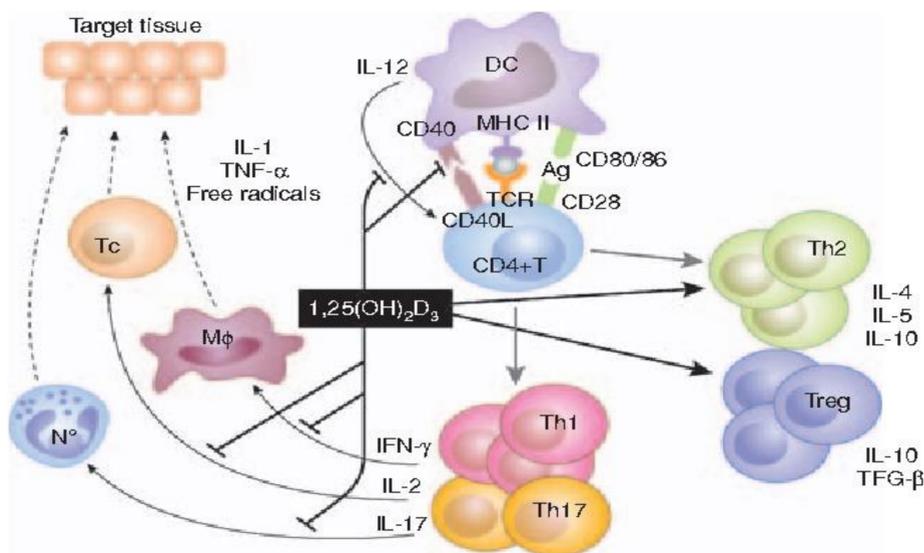
J Clin Invest. 2007;117(8):2019-2027

Figure 1. Alopecia Areata pathogenesis : " Hair follicle immune privilege" collapse model

Management can be challenging, and despite multiple treatment modalities, no therapy still stands.

- While localized AA may respond well to topical corticosteroids, many patients require more aggressive second-line therapy.
- Pediatric age and more extensive disease with resistance to initial therapies may sometimes benefit from a cocktail of established therapies,

The likelihood of complete spontaneous regrowth in AT/AU is <10%, but even then, relapses are common and frustrating.



Kidney Int. 2010 Jul;78(2):140-5

Figure 2. Vitamin D and immunomodulation

The functions of vitamin-D, far beyond calcium metabolism, related to autoimmune diseases are under continual investigation, because of the significant anti-inflammatory and immunomodulatory properties of this powerful nuclear receptor-activating hormone.

Cases

- Two girls with AT/AU, who experienced sudden and total hair loss at the age of 1 and 5 yrs and consulted in our pediatric endocrine unit at the age of 3 and 7 yrs.
- For 2 yrs, all approved treatments local and systemic including oral methotrexate had been tried from pediatric and adult specialized dermatology clinics with no results.
- Having published on the negativation of Type 1 associated autoantibodies with oral calcitriol (J Diabetes. 2013 PMID: 23302101) and recently on the cure of severe atopic dermatitis with calcitriol and it's analog paricalcitol (Case Reports in Pediatrics. 2018, <https://doi.org/10.1155/2018/9643543>),
- **we tried to induce immunomodulation by oral calcitriol**
- With 0.5 mcg/day **the 7-yr-old girl grew hair within 6m** (except from a small region at the rear of the scalp) and the result is maintained for 4.5 yrs now with normal calcium metabolism: Ca 10.1mg/dl, P 5.1mg/dl, ALP 318 IU/L, PTH 26 pg/ml, 25OHD3 41 ng/ml, 1-25(OH)₂ D3 30 ng/ml, 2hr Urine sample Ca/CR= 0.08.
- With 0.5 mcg x 3/day p.o. the 3-yr-old girl developed asymptomatic hypercalcemia at 3m (Ca 14 mg/dl, URINE Ca/CR= 1.37) and was switched to the equivalent and slightly higher dose of paricalcitol 2 mcg x 3/day p.o. Calcium metabolism normalized: Ca 9.8 mg/dl , P 3.8 mg/dl, ALP 146 IU/L, PTH 22.4 pg/ml, 25OHD3 61 ng/ml, 1-25(OH)₂ D3 38 ng/ml apart from mild hypercalciuria closely monitored 2hr Urine sample Ca/CR= 0.5.
- **Complete hair regrowth (scalp hair, eyebrows, eyelashes) was achieved by 6m of treatment.**



Figure 3. Hair regrowth in the 7-year old girl (top) and the 3-year old girl (bottom)

Conclusions

- **The active hormone calcitriol has immunomodulating properties that may even cure autoimmune diseases like Alopecia Totalis/Universalis.**
- **It's analog paricalcitol is a safe and effective alternative.**
- **Randomized controlled studies are required to prove the effectiveness and safety of this therapeutic approach, especially to establish the optimal dosage and type of Vit D administration.**

