CCL22 plasma levels correlate with disease severity and predict response to dithranol treatment in patients with psoriasis

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1. Introduction

- Dithranol is a potent topical treatment for psoriasis, leading to fast PASI reduction.
- Application of dithranol causes inflammation, but its mechanisms of action are still largely unclear and markers of treatment response are unknown.
- The aim of this study was to reveal any possible association between disease activity and/or response to dithranol treatment and plasma levels of selected cytokines/chemokines.
- CCL22 is chemotactic for dendritic cells, macrophages and natural killer cells. (1)
- CCL22 is induced by the Th2 cytokines IL-4 and IL-13 and is upregulated in psoriatic skin, although more commonly associated with atopic dermatitis. Its receptor CCR4 may be involved in T cell trafficking to lesional skin. (2)(3)(4)

3. Results

1. Dithranol treatment reduced PASI by a mean of 57% at the end of treatment and by 59% in the follow-up

Figure 2: PASI response in patients with chronic plaque-type psoriasis treated with dithranol. PASI score in patients with A) mild disease and B) moderate to severe disease.

2. Higher CCL22 plasma levels in patients with severe psoriasis

Figure 3: CCL22 plasma levels of patients with A) mild disease and B) moderate to severe disease. Patients with severe disease (PASI at baseline >10) have higher levels of CCL22. CCL22 concentrations further increased during dithranol treatment and decreased at end of therapy.

3. CCL22 levels correlate with disease severity and predict response to dithranol therapy

Figure 4: CCL22 correlation analysis. CCL22 significantly correlated with PASI score before (A), during (B and C) and after dithranol treatment (D) and pretreatment values of CCL22 inversely correlated with overall reduction in PASI (E). *r* Spearman correlation.

4. Conclusion

- Patients with severe psoriasis have higher CCL22 plasma levels, which further increased during dithranol treatment. Consistently, CCL22 is upregulated in (dithranol-treated) psoriatic skin compared to non-lesional skin.
- CCL22 plasma concentrations significantly correlated with PASI score before, during and after dithranol therapy, and pretreatment values of CCL22 inversely correlated with overall reduction in PASI. A persistent high level of CCL22 in plasma may be associated with poor response to dithranol treatment.
- How the increase of Langerhans cells after dithranol treatment is linked to CCL22 still needs to be determined.
- CCL22 could be a potential biomarker to predict therapy response to dithranol in psoriasis patients.

2. Patients & Methods

- 15 psoriasis patients (mean PASI score at baseline, 13.6±10.6) were enrolled in this study
- 65-Multiplex Immunoassay was used to analyze cytokine/chemokine concentrations in plasma
- CD1a immunohistochemistry (IHC) was performed to quantify Langerhans cells in the epidermis
- Correlations were performed using Spearman analysis. To predict PASI over time, Generalized Linear Mixed Model (GLMM) was used.
- Gene expression in skin biopsies was evaluated by using Affymetrix Human Gene 2.0 Arrays

Figure 1: Study chart of skin and blood sample collection from psoriasis patients (n=15).

Figure 5: CCL22 correlates with PASI over time. Scatterplot depicts relation between PASI (log10) and CCL22 plasma levels at the different time points before, during and after dithranol therapy.

4. Dithranol treatment leads to an increase in Langerhans cells in the epidermis

Figure 6: CD1a immunohistochemistry. In the upper panel, representative images of CD1a IHC are shown. Epidermal CD1a+ mean cell count increased during dithranol treatment and was significantly increased at follow-up (A). Comparison of area of CD1a staining with total area of epidermis showed similar results. (B)

5. CCL22 and CCR4 gene expression is upregulated in dithranol-treated lesional skin

Figure 7: CCL22 and CCR4 Fold change comparisons. CCL22 and its receptor CCR4 are upregulated in lesional skin (L) compared to non-lesional (NL) skin (FC=3.47, FC=3.07). Dithranol treatment was associated with a decrease in CCL22 and CCR4 gene expression at the end of therapy (FC = -1.66, FC=-1.43). *Students' t-test* p<0.05

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