The immune trumpet: reframing biologic-associated phenotype switching as functional pruritus phenotyping

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Background

Targeted biologics can suppress one inflammatory pathway while a clinically distinct eruption emerges along another[1,2]. In atopic dermatitis, IL-4/IL-13 and IL-31 signaling can directly amplify pruriceptive neuronal responses[3,4]. Whereas in psoriatic inflammation, IL-17A activates distinct sensory pathways implicated in itch and dysesthesia[5]. These treatment-associated phenotype shifts are usually classified as paradoxical eruptions, but their relationship to changing pruritic circuitry has not been systematically conceptualized[2].

Objective

To describe the "immune trumpet" model, in which treatment-induced morphologic transitions serve as bedside evidence of changing cytokine dominance and generate testable hypotheses about itch phenotype.

Methods

We reviewed patients from a single dermatology practice who developed a new inflammatory morphology while receiving cytokine-targeted therapy between January 2020 and December 2023. From more than 40 observed transitions, five representative cases were selected to

illustrate bidirectional movement between type 2–predominant and type 17–predominant disease. For each case, serial clinical photographs and records were used to compare pre- and post-treatment morphology, anatomic distribution, therapeutic modification, and subsequent clinical response.

Observations

New eruptions did not simply reproduce the original disease pattern. During suppression of type 2 signaling, patients developed type 17–pattern findings at sites including the extensor elbows and knees, scalp, umbilicus, nail unit, or intertriginous surfaces. Conversely, suppression of type 17 signaling could reveal eczematous disease with flexural lichenification and facial involvement. Several patients showed overlapping rather than mutually exclusive patterns, supporting a model in which multiple inflammatory programs may coexist but differ in relative dominance. Management was directed toward the newly apparent phenotype through biologic switching, addition of a second targeted agent, or adjunctive conventional therapy; clinical control could be restored without abandoning pathway-selective treatment.

Conclusions

The immune trumpet model treats cytokine-selective therapy as both intervention and physiologic perturbation. Here, suppressing one inflammatory program may expose another previously subclinical program whose morphology provides a visible readout of the prevailing immune state. For itch, this framework yields a prospective prediction rather than a retrospective assumption. A morphologic switch toward type 2 disease should be accompanied by an itch phenotype characteristic of eczematous inflammation, whereas a switch toward type 17 disease may be accompanied by greater burning, stinging, or dysesthetic qualities[5–8]. Prospective collection of Pruritus Numerical Rating Scale, 5-D Itch Scale, and qualitative itch descriptors

before and after morphologic transition in patients receiving biologic therapies could determine whether itch character changes in parallel with cytokine-axis switching and whether those changes precede visible disease.

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