INFLAMMATORY SKIN DISEASES (OTHER THAN ATOPIC DERMATITIS & PSORIASIS)

A CASE OF NEUTROPHILIC DERMATOSIS ASSOCIATED WITH AN NFKB2 GENE MUTATION

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Background: Nuclear factor-kappa B (NF-κB) signaling is involved in numerous biological processes of nearly all cells including inflammation and immunity. NF-κB is activated through two signalling cascades, the canonical and noncanonical pathways. The canonical pathway, which involves NF-κB1, primarily mediates broad inflammatory responses, whereas the noncanonical pathway, which involves NF-κB2, affects secondary lymphoid organogenesis, B-cell maturation and survival, and T-cell differentiation. Germline mutations in NFKB2 were identified in patients with common variable immunodeficiency. The patients with NFKB2 mutations also exhibited autoimmune skin disorders such as alopecia and vitiligo, however, there has been no report of neutrophilic dermatoses (NDs) associated with NFKB2 mutations.

Observation: The patient was a 12-year-old boy presenting an erythema nodosum-like eruption on his lower legs, accompanied by pyrexia, fatigue and general lymphadenopathy. A high dose of prednisolone was effective, however, tapering of PSL led to symptom flares. The patient was found to have a low serum level of IgG after the administration of systemic corticosteroid. At the age of 16, the indurated and painful erythema on his extremities worsened even with high doses of PSL and immunosuppressive agents. A histopathology of his skin and blood examination suggested ND. After a while, he developed encephalopathy due to an unknown cause. Finally, he developed serious infection resulting in death. Exome sequencing identified a heterozygous c.2557C>T (p.R853X) mutation in the NFKB2. Serum cytokine analysis of the patient showed elevated pro-inflammatory cytokines such as IL-1, 6, and 8.

Key message: Serum cytokine profile of our patient was consistent with that of patients with

common NDs. Positive and negative interplays between canonical and noncanonical pathways have been described. We speculated that our patient's autoinflammatory condition, through the aberrant regulation of both pathways based on the NFKB2 mutation, resulted in the skin and brain lesions.