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CLINICAL LETTERS

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Prurigo-like atopic dermatitis in a child with CARD11-associated severe combined immunodeficiency successfully treated with dupilumab

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Abstract

A 12-year-old boy affected by severe combined immunodeficiency due to a heterozygous variant in the CARD domain of *CARD11*, c.169G>A; p.Glu57Lys, developed severe atopic dermatitis and alopecia areata. After failure of conventional systemic therapy, dupilumab was administered at a dose of 400 mg subcutaneously, followed by 200 mg every 14 days. The patient had an excellent clinical response after 1 month and complete remission after a year, with the absence of side effects, demonstrating good efficacy and safety profile.

KEYWORDS
atopic dermatitis, CARD11, dupilumab, immunodeficiency

1 | CASE REPORT

A 12-year-old boy, born to nonconsanguineous parents, developed severe atopic dermatitis (AD) at age 3 months. Six months later, due to continued flares, laboratory tests were performed, revealing a serum IgE of 2376 kU/L (normal range: 0–230 kU/L) with severe hypogammaglobulinemia (IgG: 65 mg/dL, IgA: <4 mg/dL, IgM: 18 mg/dL). B-cell evaluation showed reduced IgM memory B cells. The patient underwent immunoglobulin replacement therapy. At age 5 years, he developed an anaphylactic egg allergy that responded to oral immunotherapy. At age 9 years, his AD and pruritus worsened, and oral cyclosporine was introduced at 4 mg/kg/day, combined with twice daily use of emollients. After 1 year of disease control, his eczema worsened and cyclosporine was increased to 6 mg/kg/day, with addition of topical corticosteroids and oral antihistamines to control pruritus. He had poor treatment adherence due to lack of efficacy and development of gingival hypertrophy and hypertrichosis. He presented with severe, chronic, diffuse eczema with prurigo nodules involving face and limbs, and occipital alopecia areata, with severely impaired quality of life (Figure 1). Whole-exome sequencing was performed, revealing a novel de novo heterozygous pathologic dominant negative variant in the CARD domain of *CARD11*, c.169G>A p.Glu57Lys. The pathologic variant affected a highly conserved protein region, leading to an immunological phenotype of combined immunodeficiency (CID).

Dupilumab was started with a loading dose of 400 mg subcutaneously, followed by 200 mg every 14 days. Within 1 week, he reported rapid improvement in pruritus. At 1 month, there was a dramatic clinical response, with disappearance of eczema, prurigo nodules and alopecia at 2 months (Figure 2). The patient remained in remission at his 12-month follow-up visit and has not experienced any adverse events or infectious complications.

CARD11 is a membrane protein involved in T-cell receptor signaling through the nuclear factor κB pathway, a predisposition locus for severe atopy. Loss of function of CARD11, due to a dominant-negative effect of a *CARD11* variant, leads to severe AD associated with a defective T-cell response skewed toward a T-helper

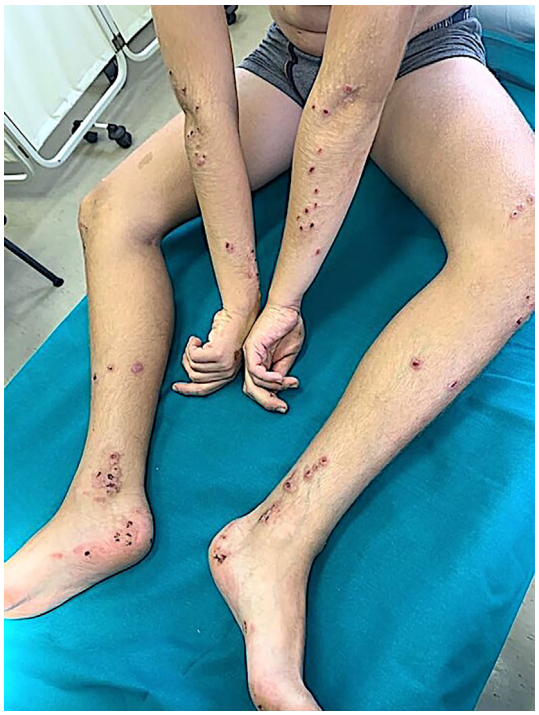

FIGURE 1 The patient prior the treatment with dupilumab.

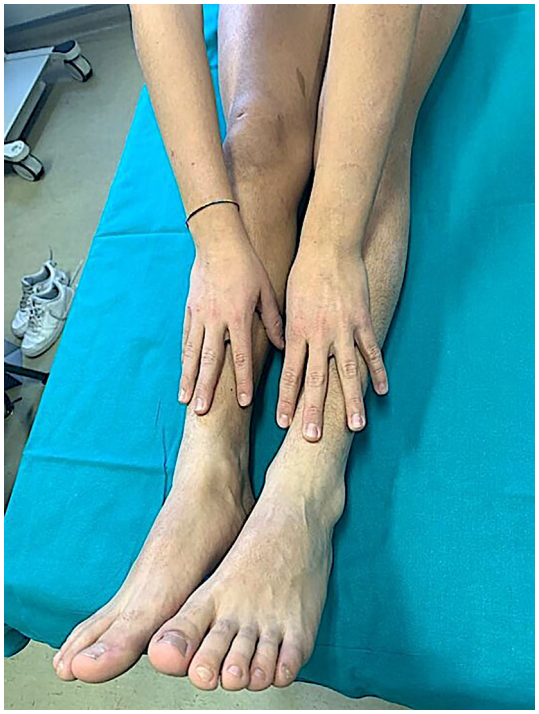

FIGURE 2 The patient after 8 weeks treatment with dupilumab.

(Th)2 phenotype. The phenotype of patients with germline variants of *CARD11* is broad, varying from severe forms of combined immunodeficiency to B-cell lymphoproliferative diseases. CARD11 deficiency-associated clinical features can vary, encompassing atopic diseases, autoimmune diseases, and infections of skin and respiratory tract. These may be associated with immunologic abnormalities, such as hypogammaglobulinemia, neutropenia, or abnormal T-cell proliferation and differentiation.[1,2]

Dupilumab, a humanized monoclonal antibody against IL-4Rα, is increasingly used in treatment-refractory AD, now approved for patients 6 months and older. The imbalance toward Th2 cytokine production in CARD11-associated AD patients suggested that dupilumab might help control AD in SCID with atopy. Recently, it has successfully treated AD in monogenic forms of hyper-IgE syndrome[3] and in an adult with a *CARD11* variant and atopic dermatitis.[4] Based on this case and our patient with CARD11-associated severe combined immunodeficiency and severe AD with prurigo nodularis and alopecia areata, we conclude that dupilumab is both effective and safe in this clinical setting.

AUTHOR CONTRIBUTIONS

All authors equally contributed to all stages of the article.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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