Autoinflammatory Pustular Neutrophilic Diseases

Haley B. Naik, MD, Edward W. Cowen, MD, MHSc*

KEYWORDS

• Pustular psoriasis • Palmoplantar pustulosis • Subcorneal pustular dermatosis
• Deficiency of IL-1 receptor antagonist (DIRA) • PAPA syndrome • SAPHO syndrome

KEY POINTS

- Deficiency of the interleukin 1 (IL-1) receptor antagonist (DIRA) is an autosomal-recessive autoinflammatory disease characterized by perinatal-onset pustular dermatosis resembling pustular psoriasis, multifocal aseptic osteomyelitis, and periostitis. It can be effectively treated with IL-1 receptor antagonists.
- Pyogenic arthritis, pyoderma gangrenosum, and acne compose PAPA syndrome, an autosomal-dominant autoinflammatory syndrome caused by mutations in the *PSTPIP1* gene.
- Synovitis, acne, pustulosis, hyperostosis, and osteitis compose the autoinflammatory syndrome known as SAPHO. Chronic recurrent multifocal osteomyelitis is likely a subtype of SAPHO that predominantly affects children.
- Pustular psoriasis constitutes a spectrum of inflammatory pustular dermatoses ranging from localized acrodermatitis continua of Hallopeau and palmoplantar pustulosis to generalized disorders including von Zumbusch pustular psoriasis and impetigo herpetiformis.
- The clinical similarities between defined autoinflammatory diseases with neutrophilic pustules and pustular psoriasis provides potential new mechanisms of treatment with biological agents targeting autoinflammatory pathways.

DEFICIENCY OF THE INTERLEUKIN 1 RECEPTOR ANTAGONIST

In 2009, Goldbach-Mansky and colleagues described an autosomal-recessive autoinflammatory disorder known as deficiency of the interleukin 1 (IL-1) receptor antagonist (DIRA) (**Fig. 1**).[1–6] DIRA is caused by homozygous loss of function mutations in *IL1RN*, the gene encoding the IL-1 receptor antagonist. Mutations lead to unopposed IL-1 signaling and resultant uncontrolled life-threatening systemic inflammation. Heterozygous carriers of loss of function mutations in *IL1RN* seem to be asymptomatic.[1–6] Fewer than 20 cases from the United States, Canada, the Netherlands, Brazil, and Puerto Rico have been described. First-generation mutations in these distinct geographic populations are believed to be founder mutations. The allele frequencies of the founder mutations in Newfoundland and Puerto Rico are estimated at 0.2% and 1.3%, respectively.

DIRA is characterized by perinatal-onset pustular dermatitis resembling pustular psoriasis, multifocal aseptic osteomyelitis, periostitis, leukocytosis, and increased acute-phase reactants. Affected individuals present between birth and 2.5 weeks of age with fetal distress, pustular rash, joint swelling, oral lesions, and pain with

Disclosures: None.
Dermatology Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Building 10, Room 12N238, 10 Center Drive, MSC 1908, Bethesda, MD 20892-1908, USA
* Corresponding author.
E-mail address: cowene@mail.nih.gov

Dermatol Clin 31 (2013) 405–425
http://dx.doi.org/10.1016/j.det.2013.04.001
0733-8635/13/$ – see front matter Published by Elsevier Inc.

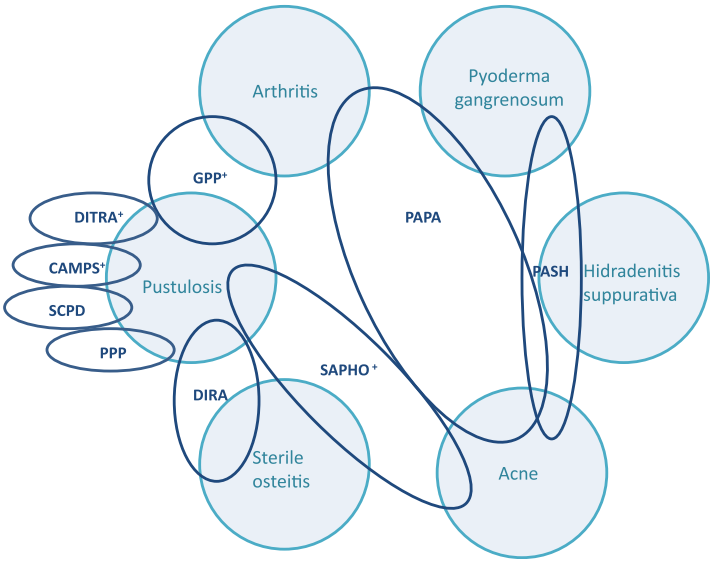

Fig. 1. Overlapping clinical features of pustular dermatoses. CAMPS, CARD 14-mediated pustular psoriasis; DIRA, deficiency of IL-1 receptor antagonist; DITRA, deficiency of the IL-36 receptor antagonist; GPP, generalized pustular psoriasis; PAPA, pyogenic arthritis, pyoderma gangrenosum, and acne; PASH, pyoderma, acne, and suppurative hidradenitis; PPP, palmoplantar pustulosis; SAPHO, synovitis, acne, pustulosis, hyperostosis, and osteitis; SCPD, subcorneal pustular dermatosis. '+' denotes presence of associated fevers.

movement. Premature birth is sometimes noted. Fever is typically absent. Cutaneous eruptions range from discrete crops of pustules to generalized pustulosis (**Fig. 2**). Ichthyosiform changes can be seen. Nail changes include pitting and onychomadesis. Respiratory insufficiency and thrombotic events have also been reported. Bony changes include epiphyseal ballooning of long bones, anterior rib-end widening, periosteal elevation of long bones, and multifocal osteolytic lesions. Less commonly, widening of the clavicles, metaphyseal erosions, and osteolytic skull lesions can be seen.[2] Mortality secondary to multiorgan failure in the setting of severe inflammatory response and pulmonary hemosiderosis with progressive interstitial fibrosis has been reported. Laboratory abnormalities include leukocytosis and marked increase of serum erythrocyte sedimentation rate and C-reactive protein levels. Cutaneous histopathology is characterized by epidermal acanthosis and hyperkeratosis and extensive neutrophilic infiltration of epidermis and dermis by neutrophils and pustule formation.[1]

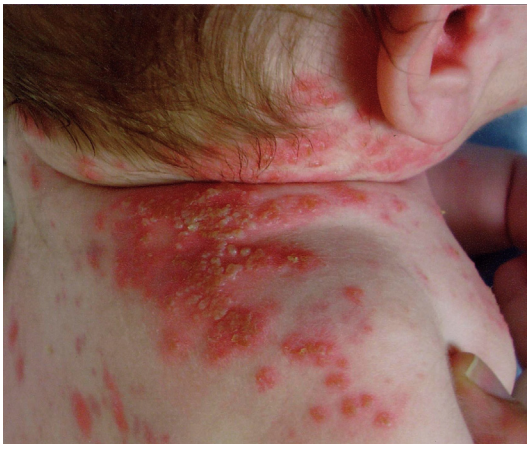

Fig. 2. DIRA. Bright red plaques studded with crops of pustules in an infant. (*Courtesy of* Raphaela Goldbach-Mansky.)

The differential diagnosis of DIRA includes bacterial osteomyelitis, infantile cortical hyperostosis, infantile pustular psoriasis, and chronic recurrent multifocal osteomyelitis (CRMO). Genetic sequencing is required for definitive diagnosis. DIRA can be effectively treated with the IL-1 receptor antagonist anakinra,[1,5,7] suggesting a potentially important role for IL-1 antagonism in the management of diseases with pustular phenotype. Individuals with less deleterious mutations have also been managed with corticosteroids and acitretin.[2] Given the severity of disease and availability of effective therapy, the key to successful management and reduced morbidity and mortality is early recognition of this condition and early implementation of anti-IL-1 therapy, before the development of irreversible bony lesions, respiratory disease, or other life-threatening events.

DEFICIENCY OF THE IL-36 RECEPTOR ANTAGONIST, A MONOGENIC FORM OF PUSTULAR PSORIASIS

Although most patients with pustular psoriasis lack a family history of similar disease, several familial cases have been reported, leading to a potential insight into common pathways of

Download English Version:

https://daneshyari.com/en/article/6062230

Download Persian Version:

https://daneshyari.com/article/6062230

Daneshyari.com