Netherton syndrome

Netherton syndrome, an autosomal recessive hereditary disorder associated with mutations in the SPINK5 gene encoding a serine protease inhibitor, is featured by ichthyosis-like chronic skin inflammation, universal pruritus, severe dehydration and stunted growth. The pediatric patients may have a hair shaft defect or “bamboo hair” (trichorrhexis invaginata). The disrupted skin barrier function mediated by the increased serine protease activity presents a high susceptibility to infection and allergy, leading to the development of scaly, reddish skin similar to atopic dermatitis. The atopic manifestations persist throughout life, and post-natal mortality rates are high. In less severe cases, milder ichthyosis linearis circumflexa may occur. Netherton syndrome belongs to a primary immunodeficiency, straddling the innate and acquired immune system. Netherton patients may have altered immunoglobulin levels (high IgE and low IgG) and immature NK cells. The NK cells have a reduced lytic function. The patients are prone to recurrent skin infections with staphylococcus. Intravenous immunoglobulin administration is effective to improve and even resolve the skin and hair abnormalities.

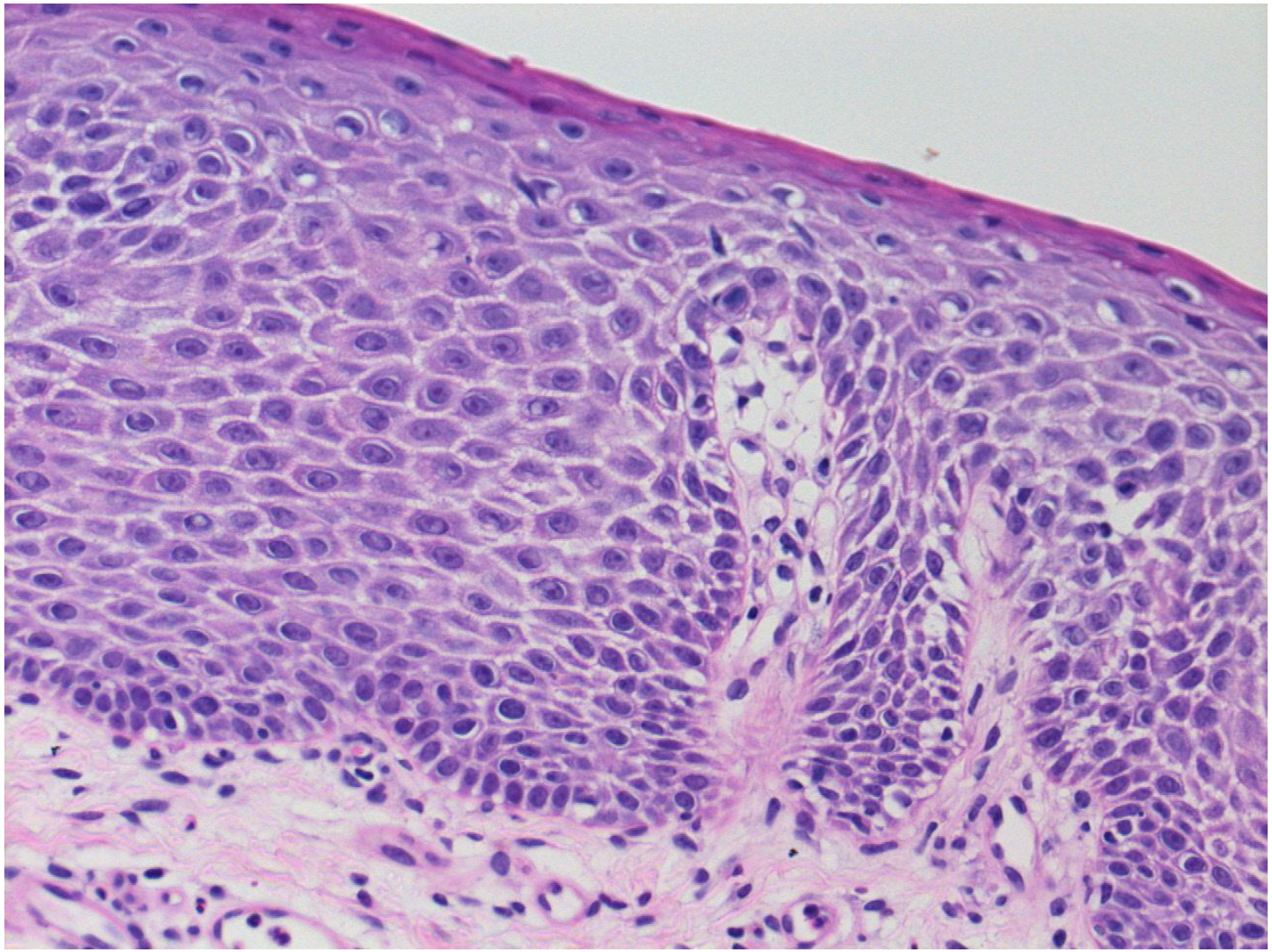
Lamellar bodies are secreted from the upper stratum spinosum and stratum granulosum layers of the epidermis, resulting in the formation of an impermeable, lipid-containing membrane serving as a water barrier and functioning for correct skin barrier. The lamellar bodies contain lipids (glucosylceramides), hydrolytic enzymes and proteins such as corneodesmosin. Lamellar body secretion and lipid structure are ultrastructurally abnormal in the epidermis of patients with Netherton syndrome.

Ref.-1: Barbati F, et al. Netherton syndrome in children: management and future perspectives. Front Pediatr 2021; 9: 645259. doi: 10.3389/fped.2021.645259

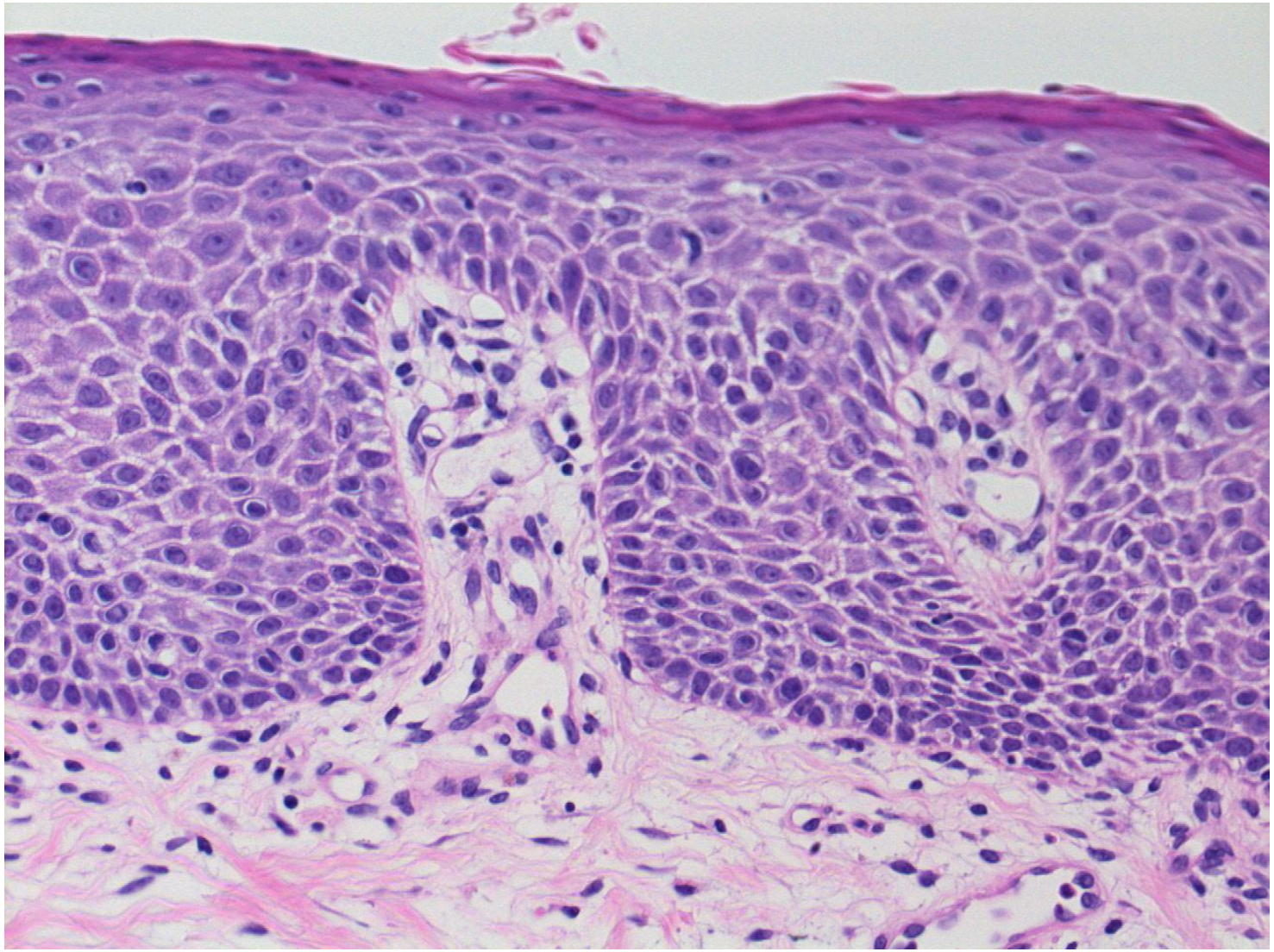
Ref.-2: Mahanty S, Setty SRG. Epidermal lamellar body biogenesis: insight into the roles of Golgi and lysosomes. Front Cell Dev Biol 2021; 9. doi: 10.3389/fcell.2021.701950

Case presentation

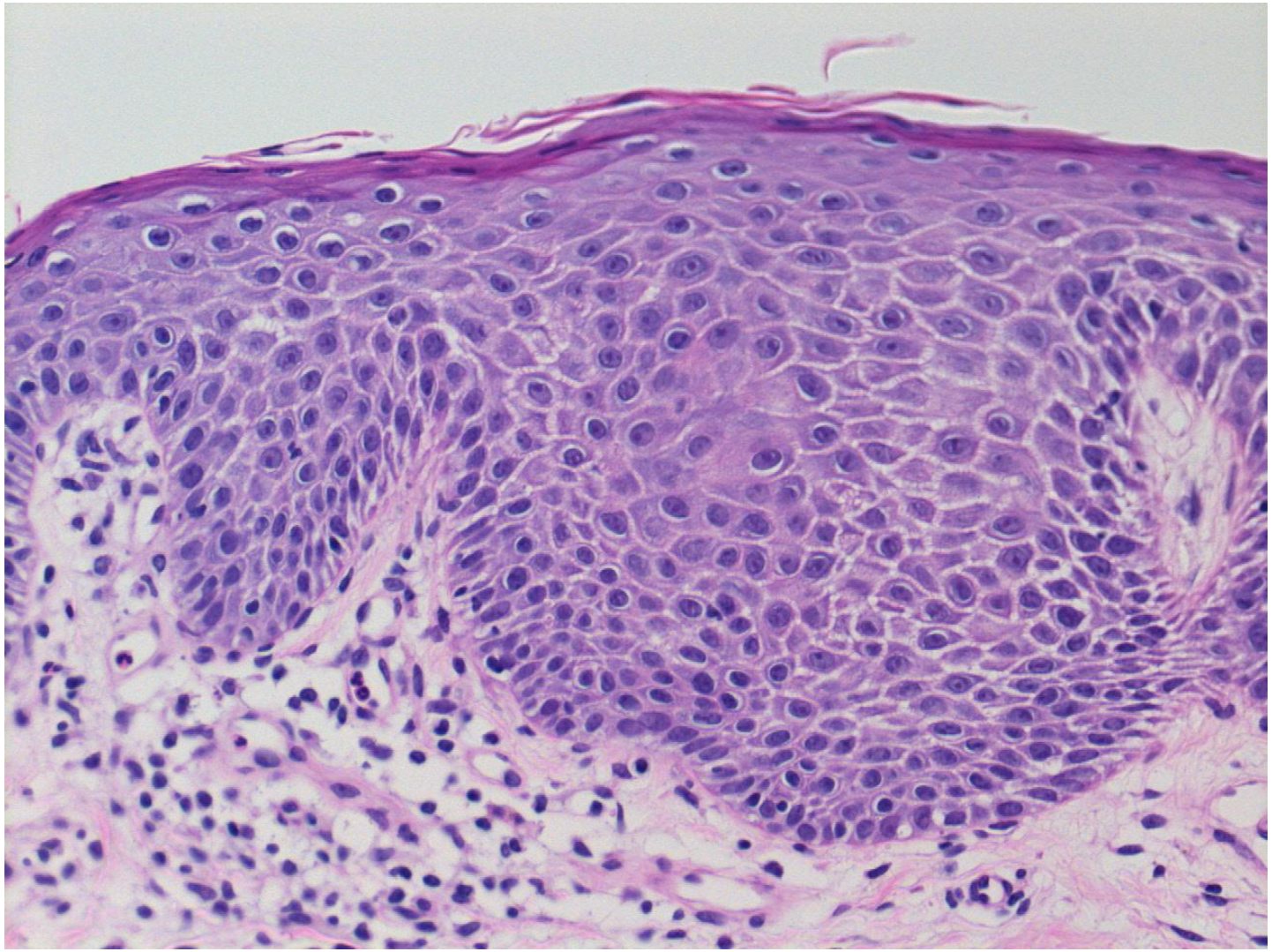
A 4-months-old girl complained of persistent erythroderma with erosive changes and repeated skin infections. The hair was thin and sparse. At birth, the skin was mildly covered with a collodion membrane. Clinically, non-bullous congenital ichthyosiform erythroderma was suspected. The possibility of Netherton syndrome was also considered.



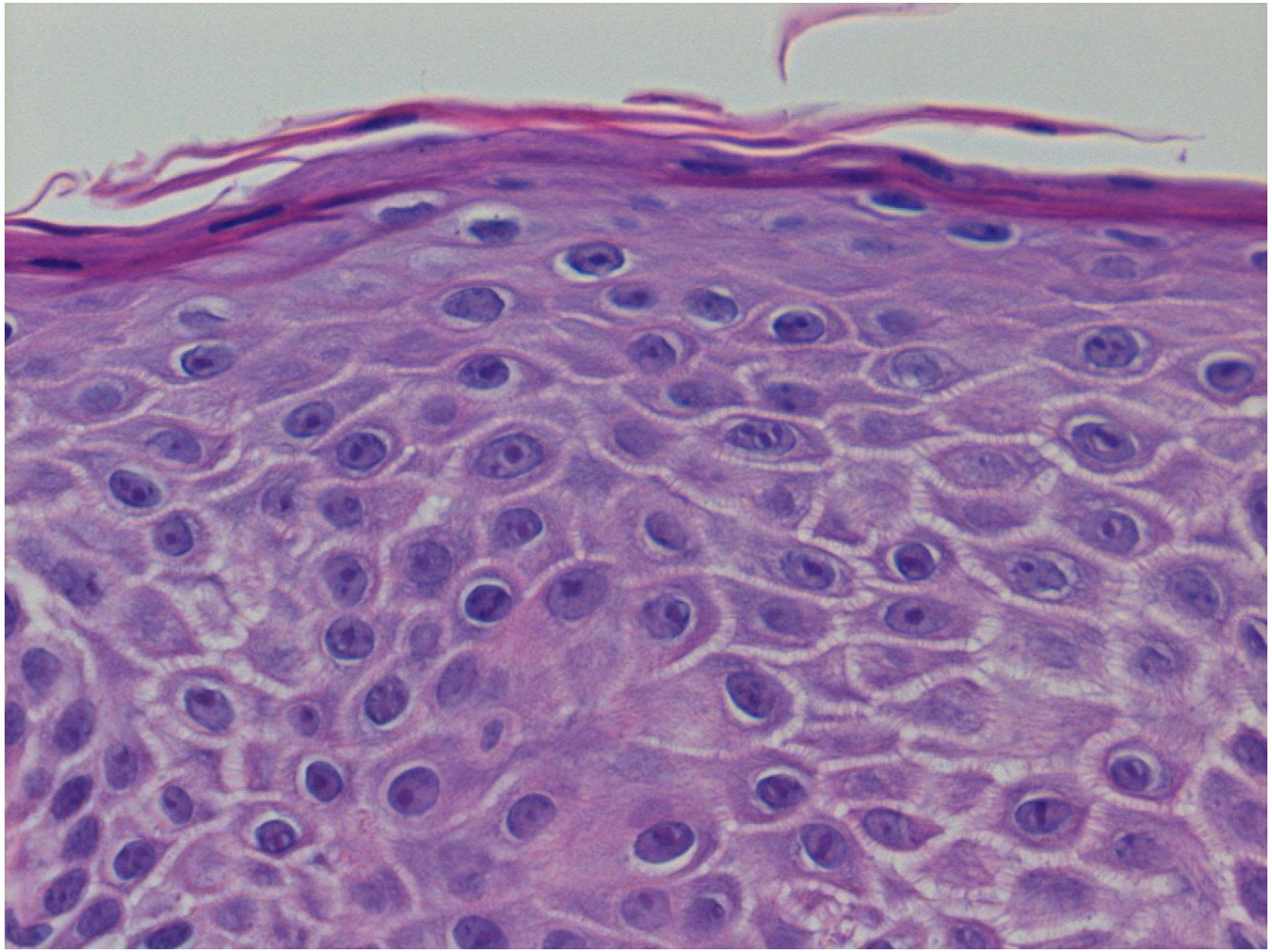
Netherton syndrome seen in a 4 months-old girl manifesting persistent ichthyosiform skin lesions. Biopsy taken from the forearm skin reveals a psoriatic skin reaction with acanthosis. intercellular edema and parakeratosis (H&E-1).



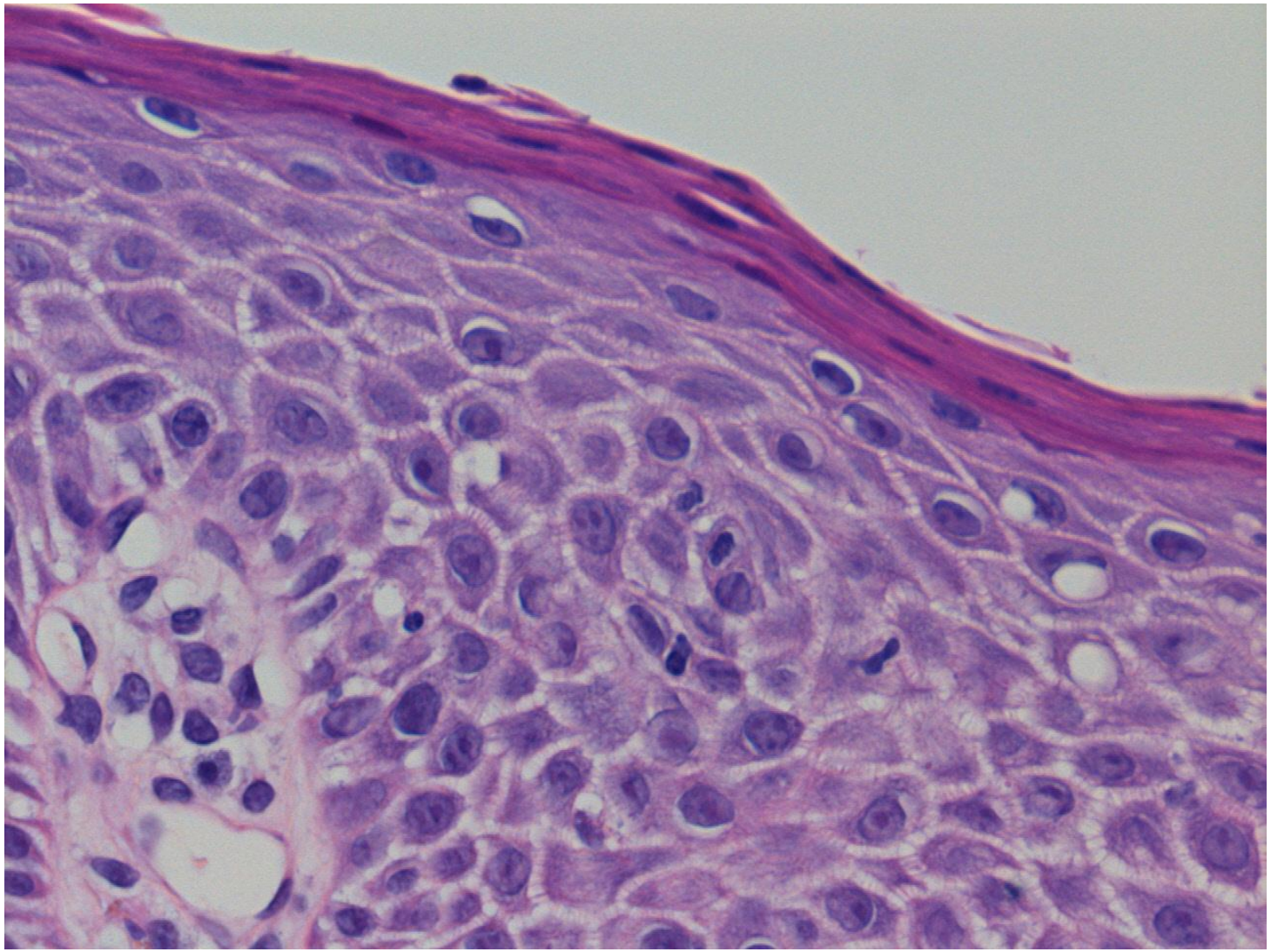
Netherton syndrome seen in a 4 months-old girl manifesting persistent ichthyosiform skin lesions. Biopsy taken from the forearm skin reveals a psoriatic skin reaction with acanthosis. intercellular edema and parakeratosis (H&E-2).



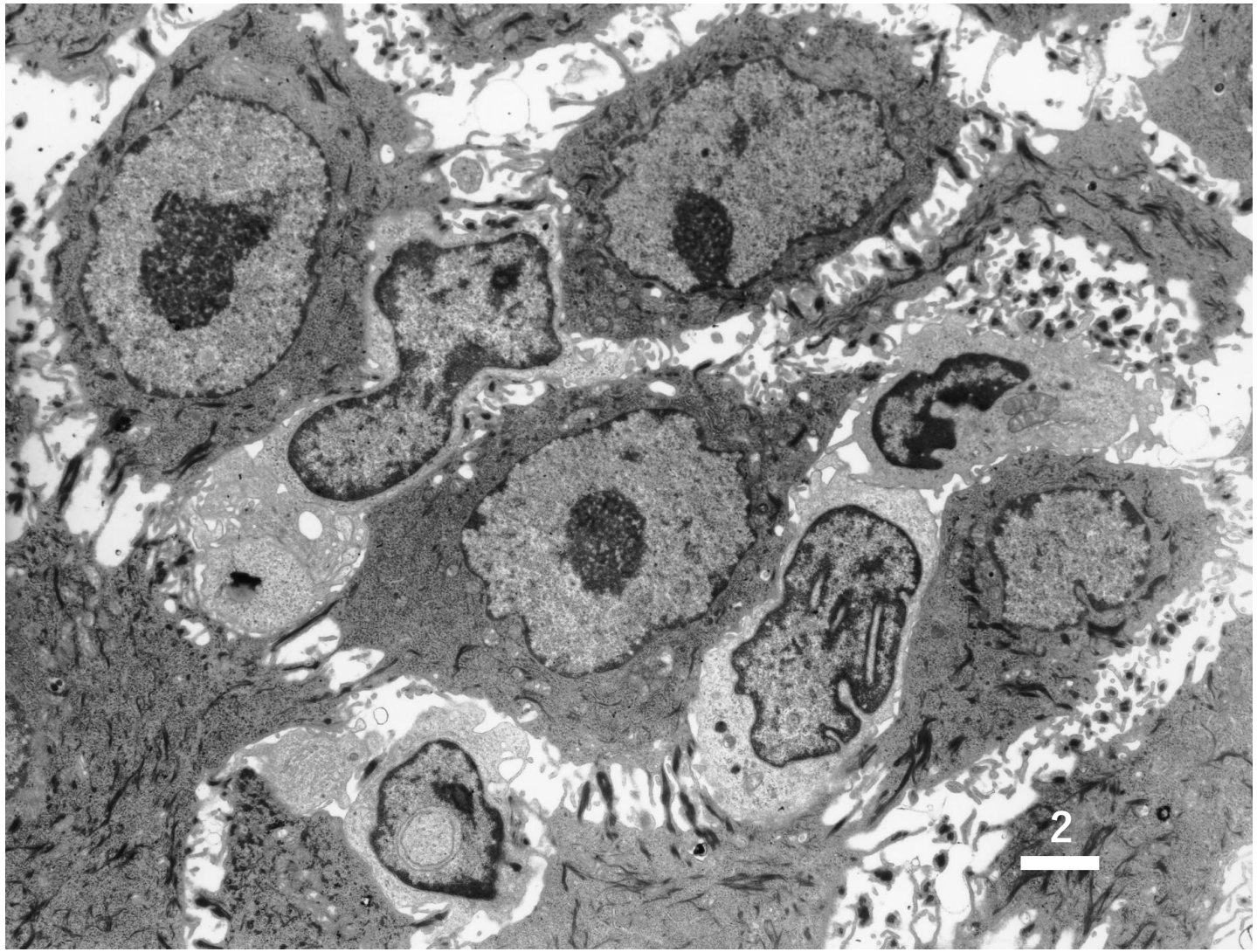
Netherton syndrome seen in a 4 months-old girl manifesting persistent ichthyosiform skin lesions. Biopsy taken from the forearm skin reveals a psoriatic skin reaction with acanthosis. intercellular edema and parakeratosis (H&E-3).



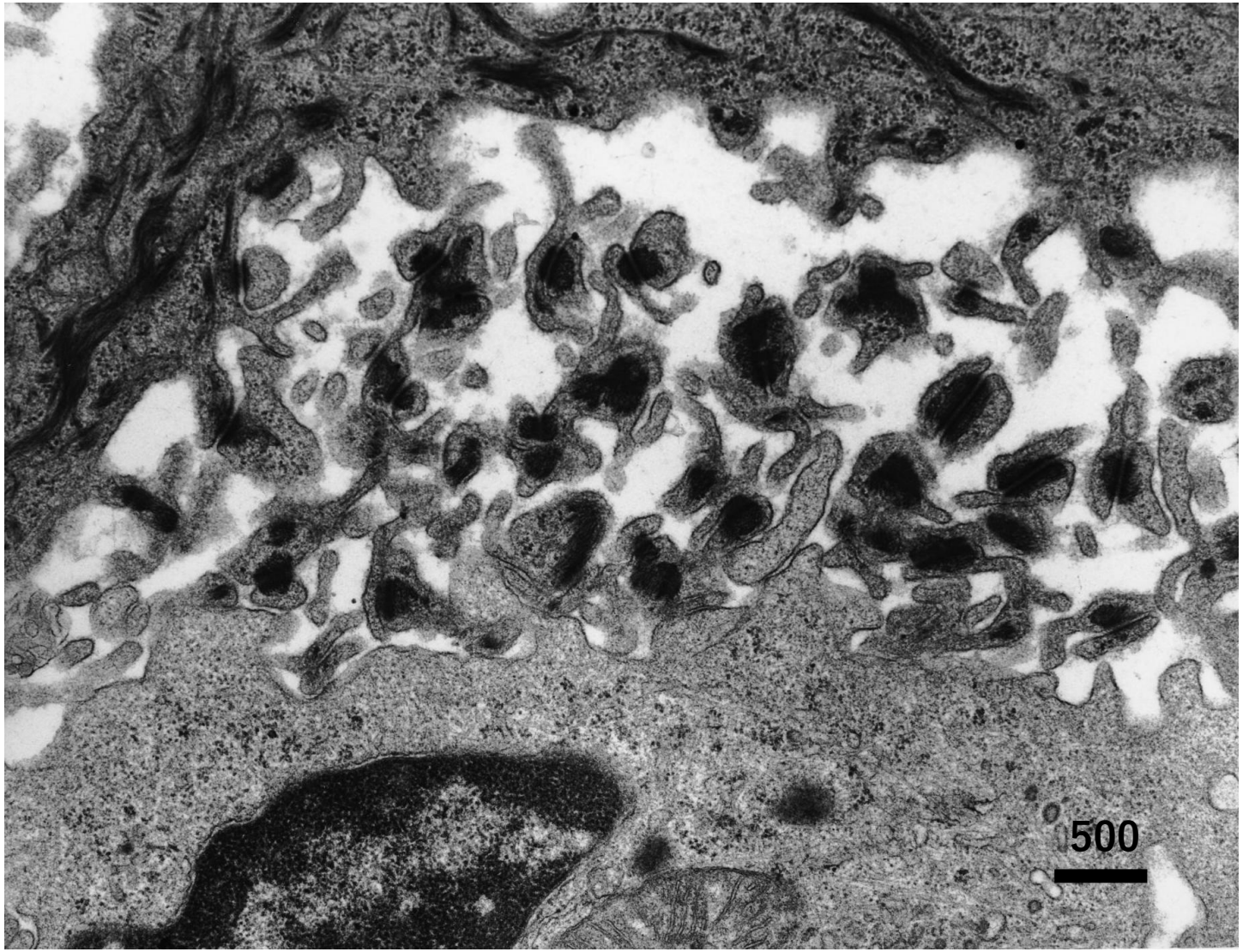
Netherton syndrome seen in a 4 months-old girl manifesting persistent ichthyosiform skin lesions. Biopsy taken from the forearm skin reveals a psoriatic skin reaction with acanthosis, intercellular edema and parakeratosis (H&E-4).



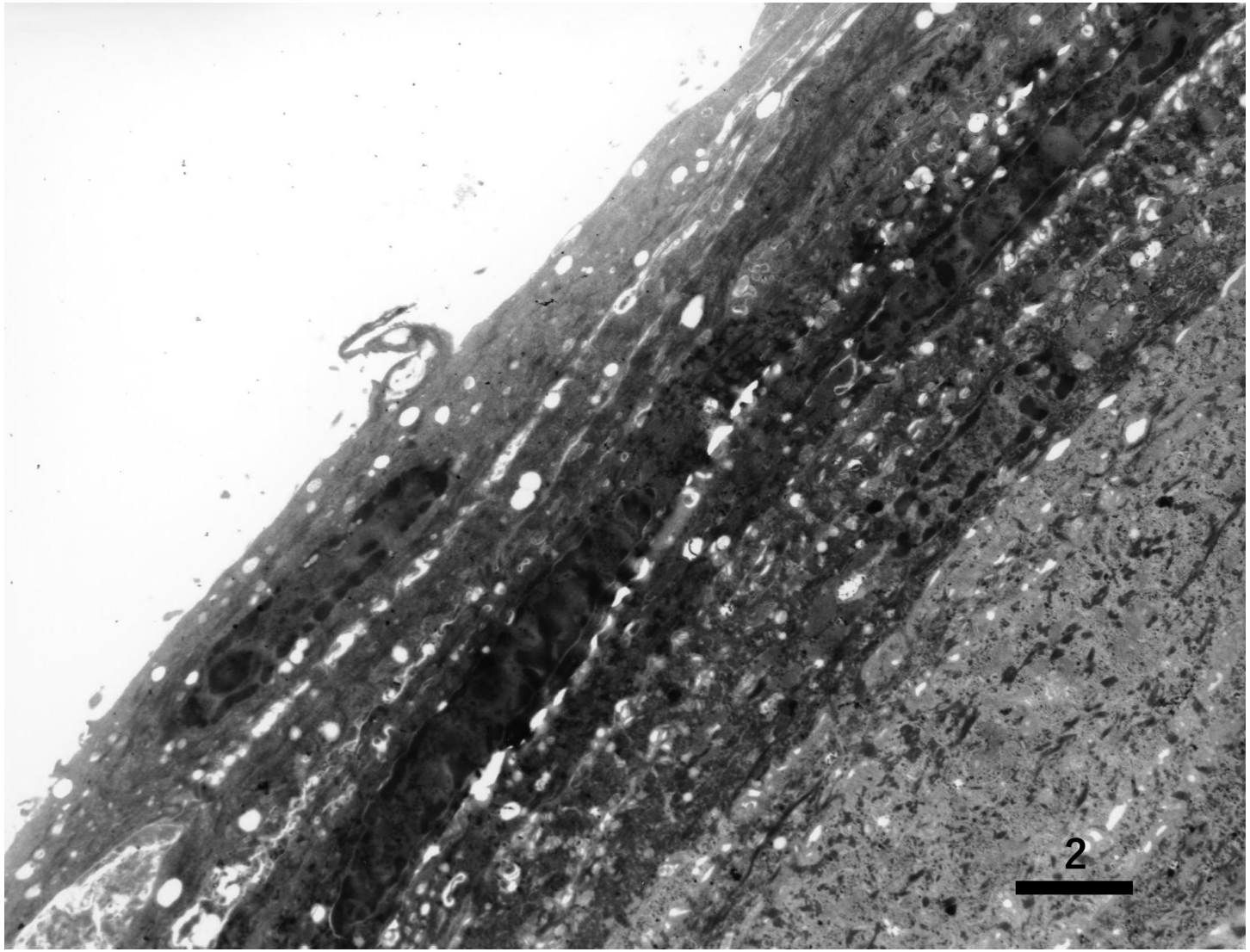
Netherton syndrome seen in a 4 months-old girl manifesting persistent ichthyosiform skin lesions. Biopsy taken from the forearm skin reveals a psoriatic skin reaction with acanthosis, intercellular edema and parakeratosis. Lymphocytic exocytosis is mildly noted (H&E-5).



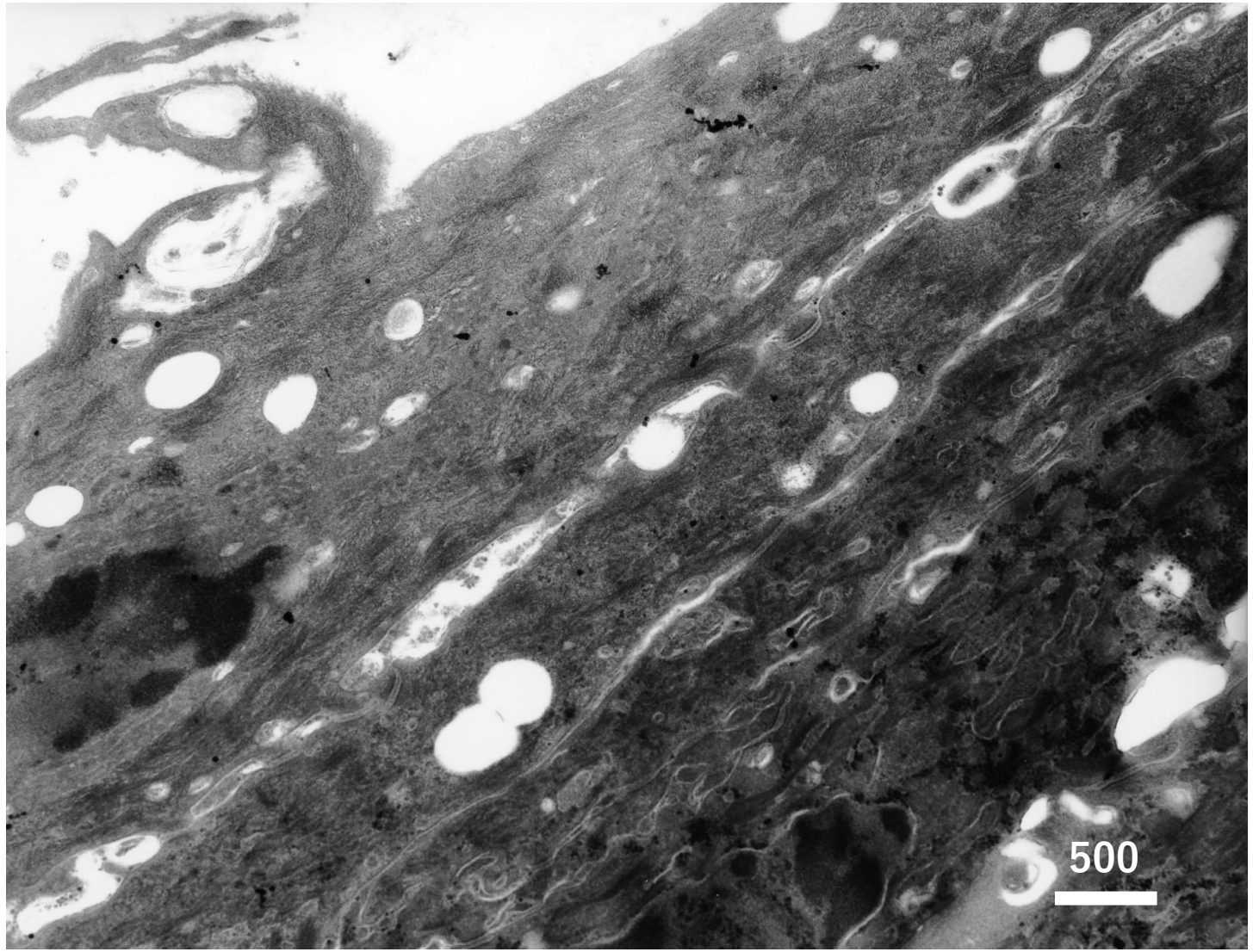
Ultrastructure of Netherton syndrome seen in a 4 months-old girl manifesting persistent ichthyosiform skin lesions. The keratinocytes show well-developed desmosomes. Lymphocytic exocytosis is noted among the keratinocytes (TEM-1).



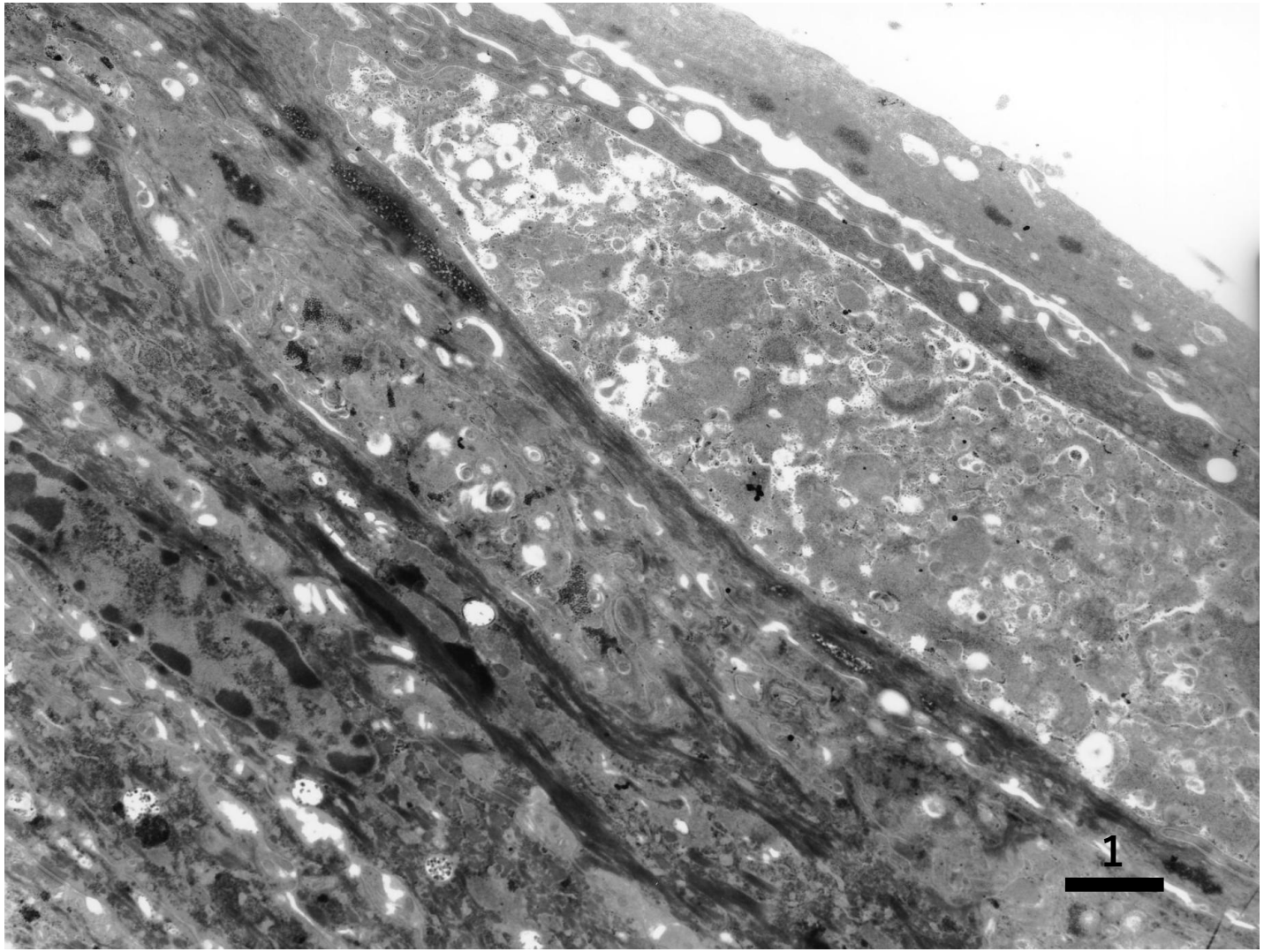
Ultrastructure of Netherton syndrome seen in a 4 months-old girl manifesting persistent ichthyosiform skin lesions. The keratinocytes show well-developed desmosomes. Intercellular edema is noted (TEM-2).



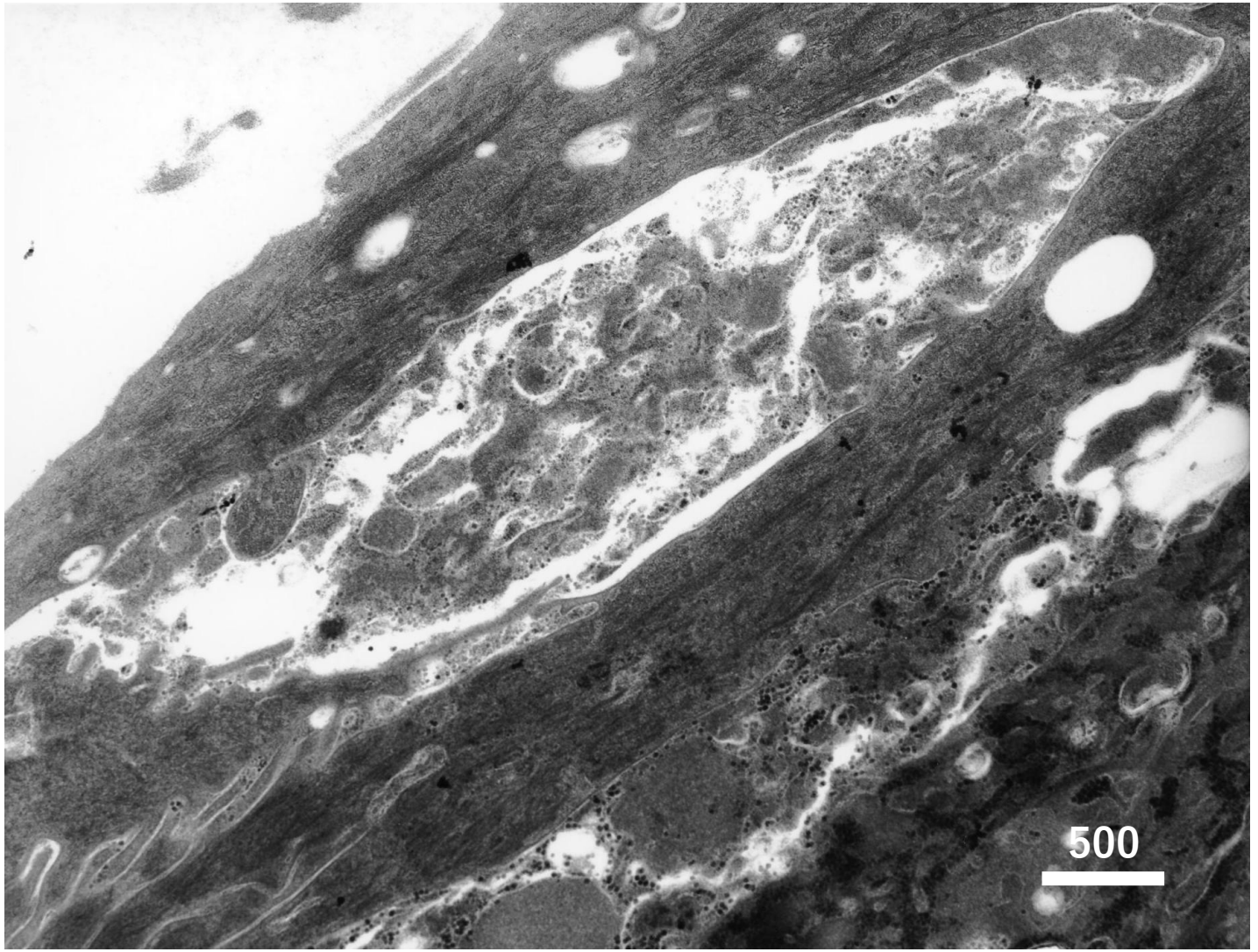
Ultrastructure of Netherton syndrome seen in a 4 months-old girl manifesting persistent ichthyosiform skin lesions. The parakeratotic layer keratinocytes show increased electron density with electron-lucent vacuoles (lamellar bodies) (TEM-3).



Ultrastructure of Netherton syndrome seen in a 4 months-old girl manifesting persistent ichthyosiform skin lesions.　The parakeratotic layer keratinocytes show increased electron density with electron-lucent vacuoles (lamellar bodies) (TEM-4).



Ultrastructure of Netherton syndrome seen in a 4 months-old girl manifesting persistent ichthyosiform skin lesions. In the parakeratotic layer, intercellular accumulation of amorphous and granular (lipoid) materials is observed, suggesting an altered lamellar body secretion (TEM-5).



Ultrastructure of Netherton syndrome seen in a 4 months-old girl manifesting persistent ichthyosiform skin lesions. In the parakeratotic layer, intercellular accumulation of amorphous and granular (lipoid) materials is observed, suggesting an altered lamellar body secretion (TEM-6).