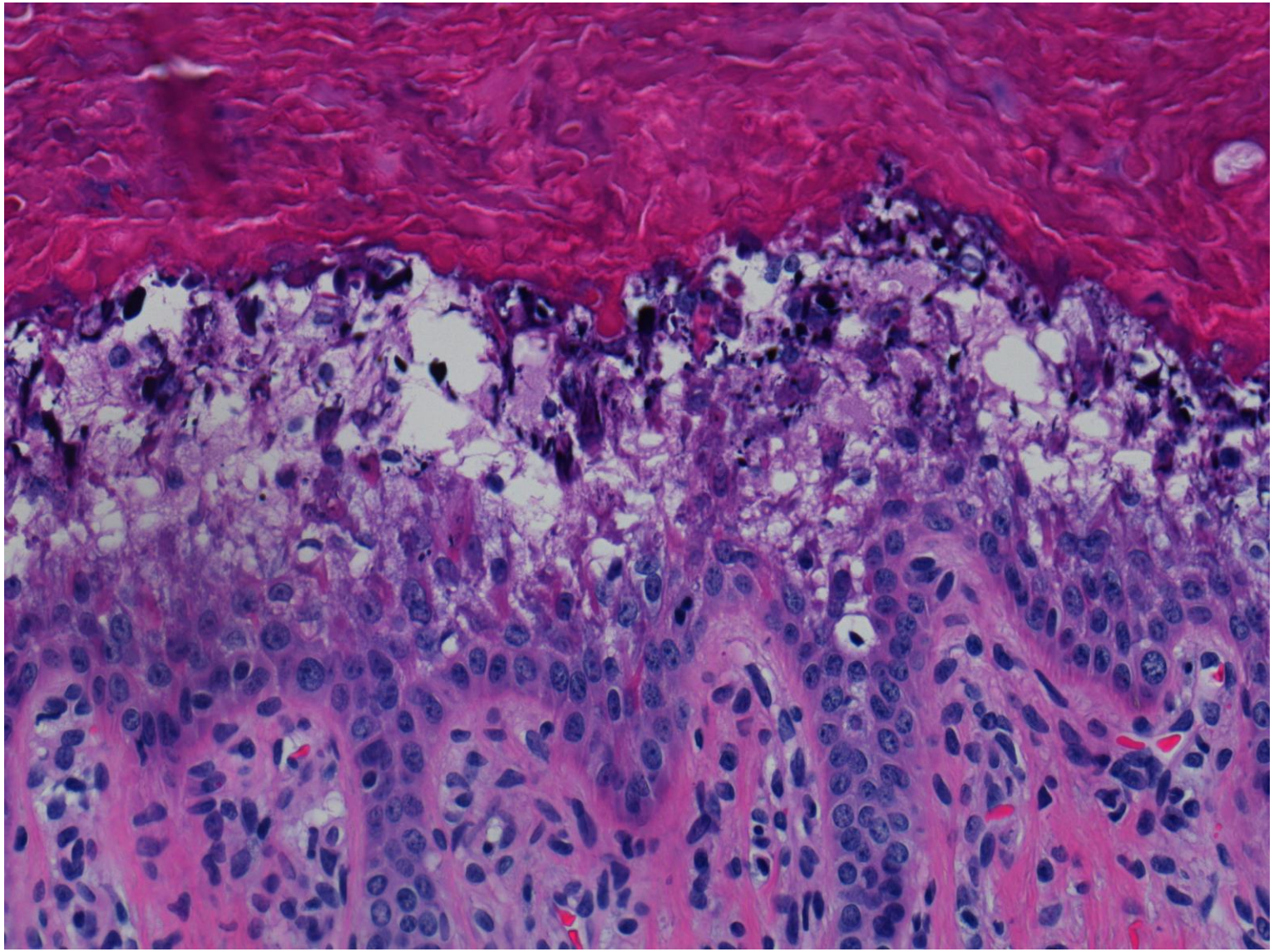
Panels of hereditary epidermolysis bullosa: light and electron microscopic features

Hereditary epidermolysis bullosa (EB) is featured by skin fragility and blistering on the skin and mucous membranes, in response to minimal trauma. EB is clinically and genetically heterogeneous, and is classified into four main types according to the blister-occurring layer of the skin: epidermolysis bullosa simplex (intraepidermal), junctional EB (within the lamina lucida of the basement membrane), dystrophic EB (below the basement membrane), and Kindler EB (mixed skin cleavage pattern). At least 16 genes encoding proteins essential for the integrity and adhesion of skin layers are involved in EB.

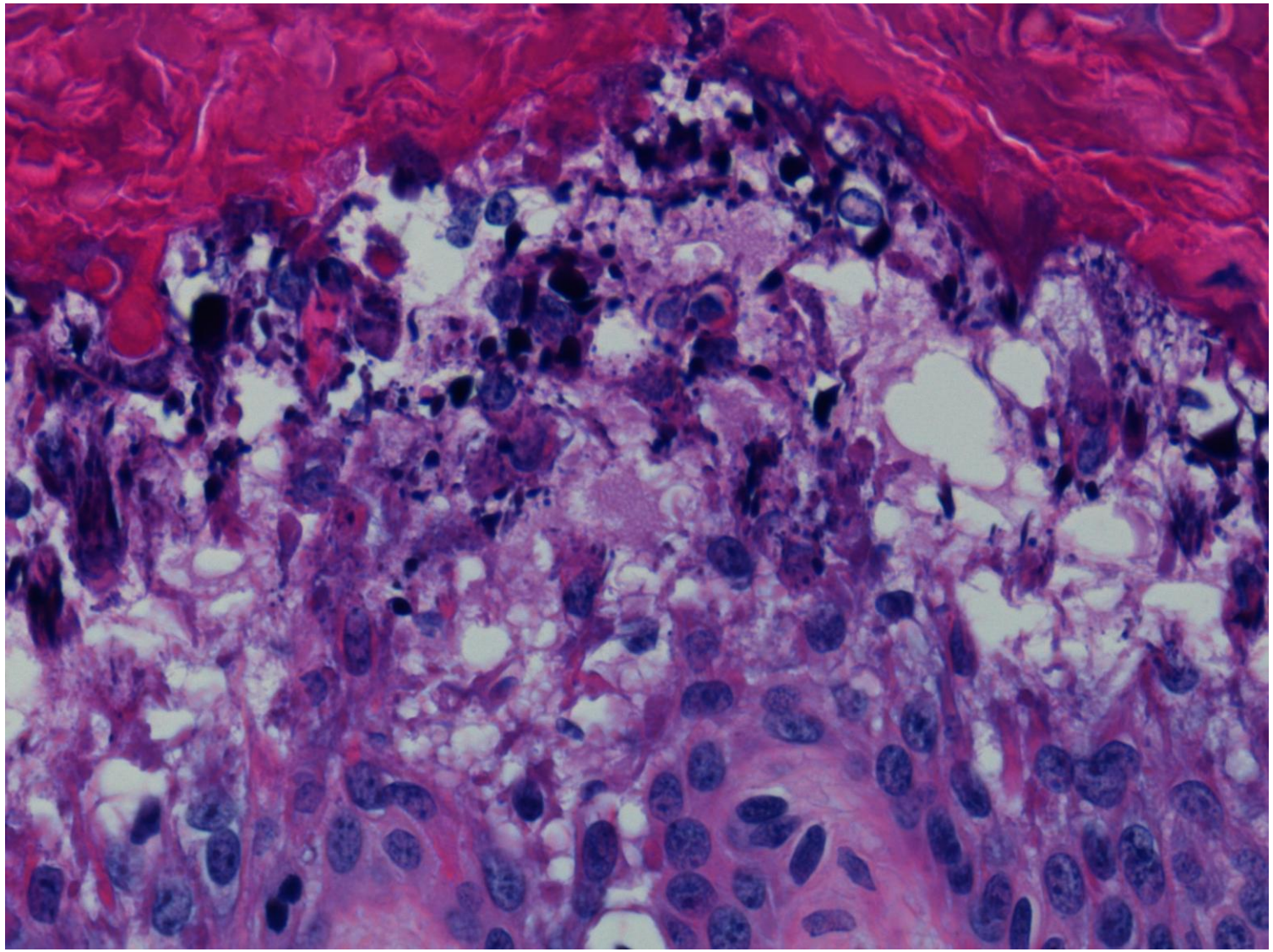
Ref.: Mariath LM, et al. Inherited epidermolysis bullosa: update on the clinical and genetic aspects. An Bras Dermatol 2020; 95(5): 551-569. doi: 10.1016/j.abd.2020.05.001

Classification of inherited epidermolysis bullosa (EB)

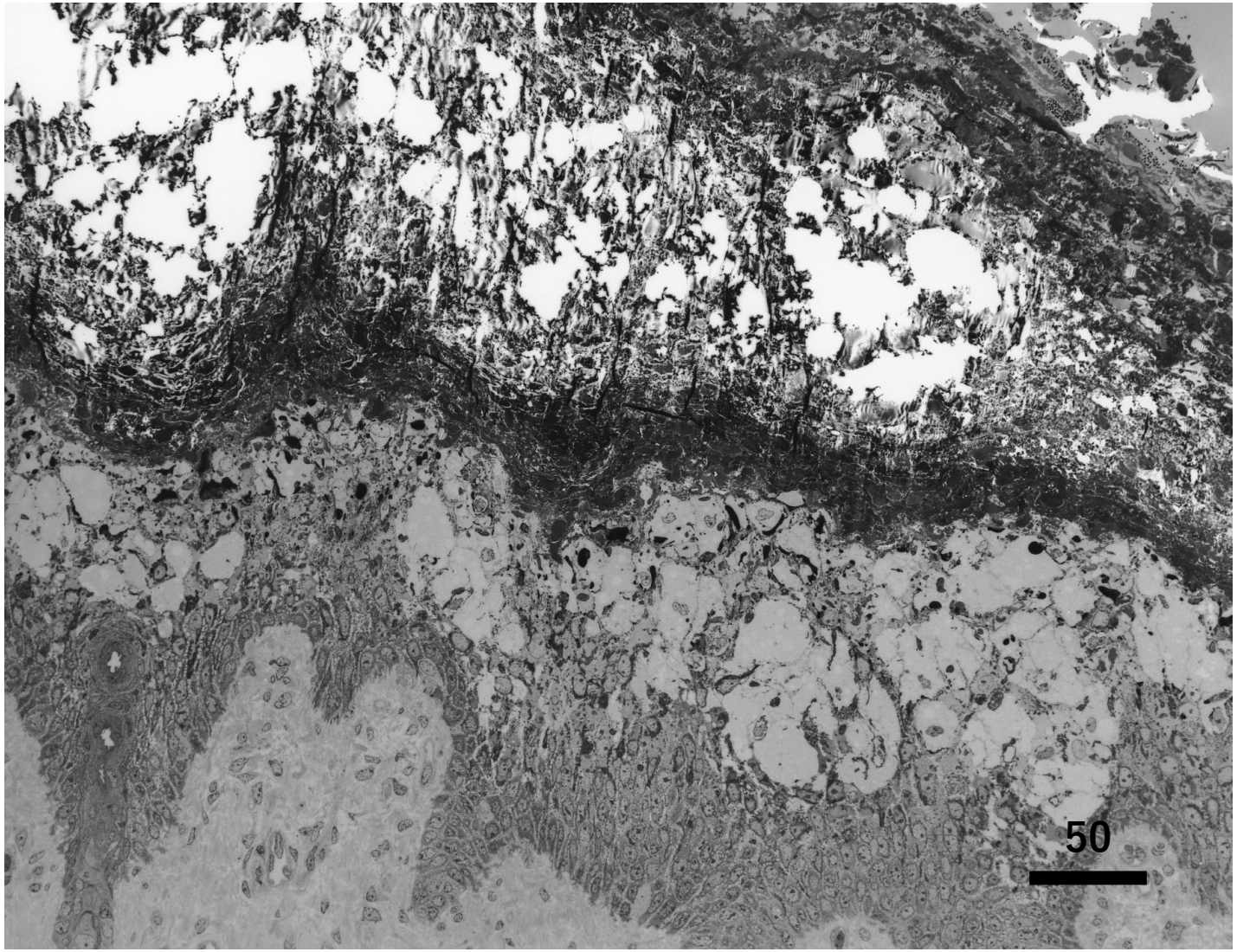
Type/subtype	gene defect	target protein
1) EB simplex (epidermolytic)		
a) Suprabasal type (lethal acantholytic)	DSP	desmoplakin
(plakophilin deficiency)	PKP1	plakophilin-1
b) Basal type (localized, Weber-Cockayne)	KRT5/KRT14	keratin-5/keratin-14
(generalized, Koebner)	KRT5/KRT14	keratin-5/keratin-14
(EB herpetiformis, Dowling-Meara)	KRT5/KRT14	keratin-5/keratin-14
2) Junctional EB (junctional)		
a) JEB gravis/Herlitz type (lethal)	LAMA3/B3/C2	laminin-5
b) JEB non-Herlitz type (non-lethal)	LAMA3/B3/C2	laminin-5
	COL17A1	collagen XVII
3) Dystrophic EB (dermolytic)		
a) DEB dominant type	COL7A1	collagen VII
b) DEB recessive type	COL7A1	collagen VII
4) Kindler EB (mixed skin cleavage pattern)	FERMT1	kindlin-1



Epidermolysis bullosa simplex, suprabasal granulolytic type, seen in the heel skin of a 1-day-old female baby. Epidermolytic vacuolation is seen in the suprabasal layer, particularly at the granular layer level. H&E-1

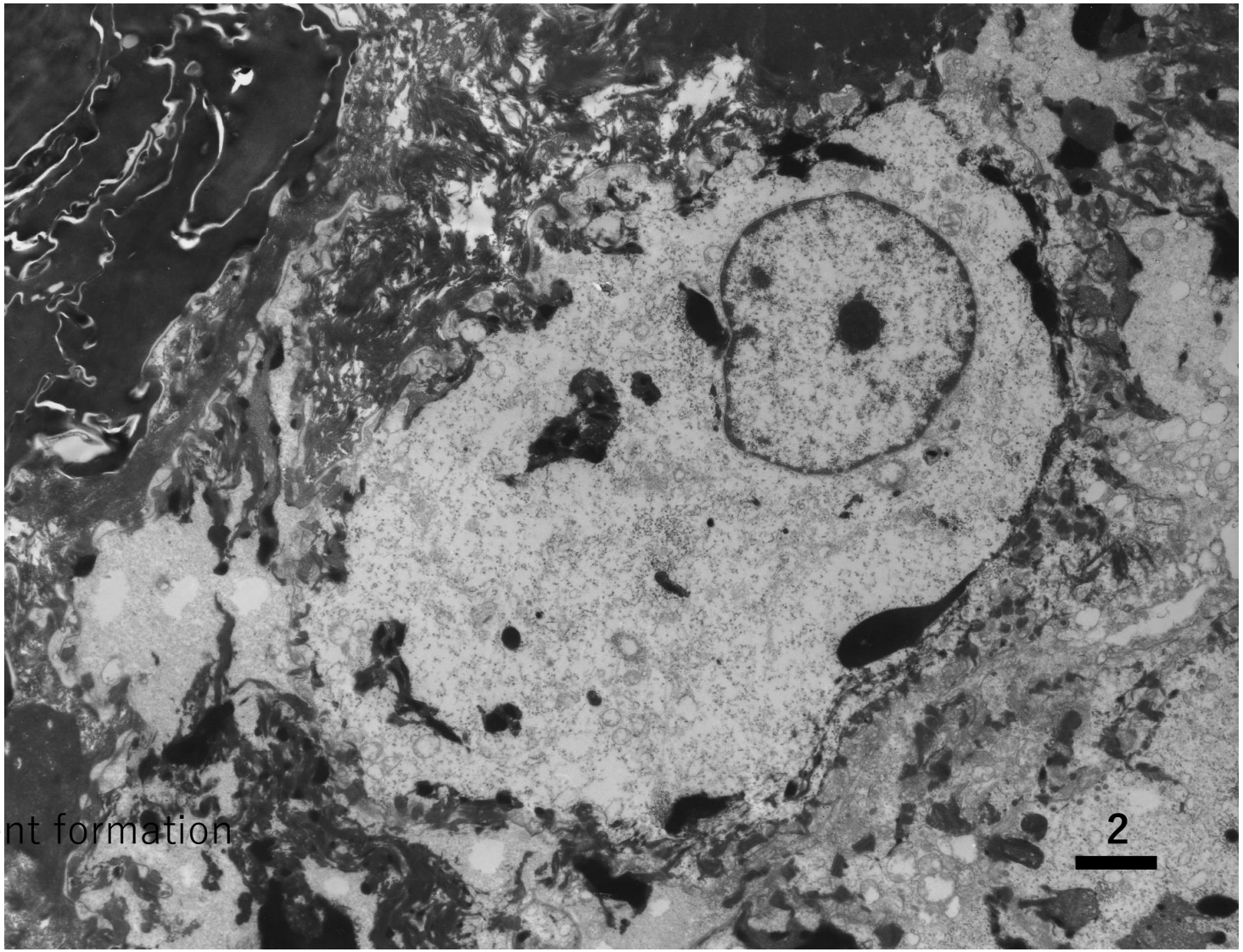


Epidermolysis bullosa simplex, suprabasal granulolytic type, seen in the heel skin of a 1-day-old female baby. Epidermolytic vacuolation is seen in the suprabasal layer, particularly at the granular layer level. H&E-2

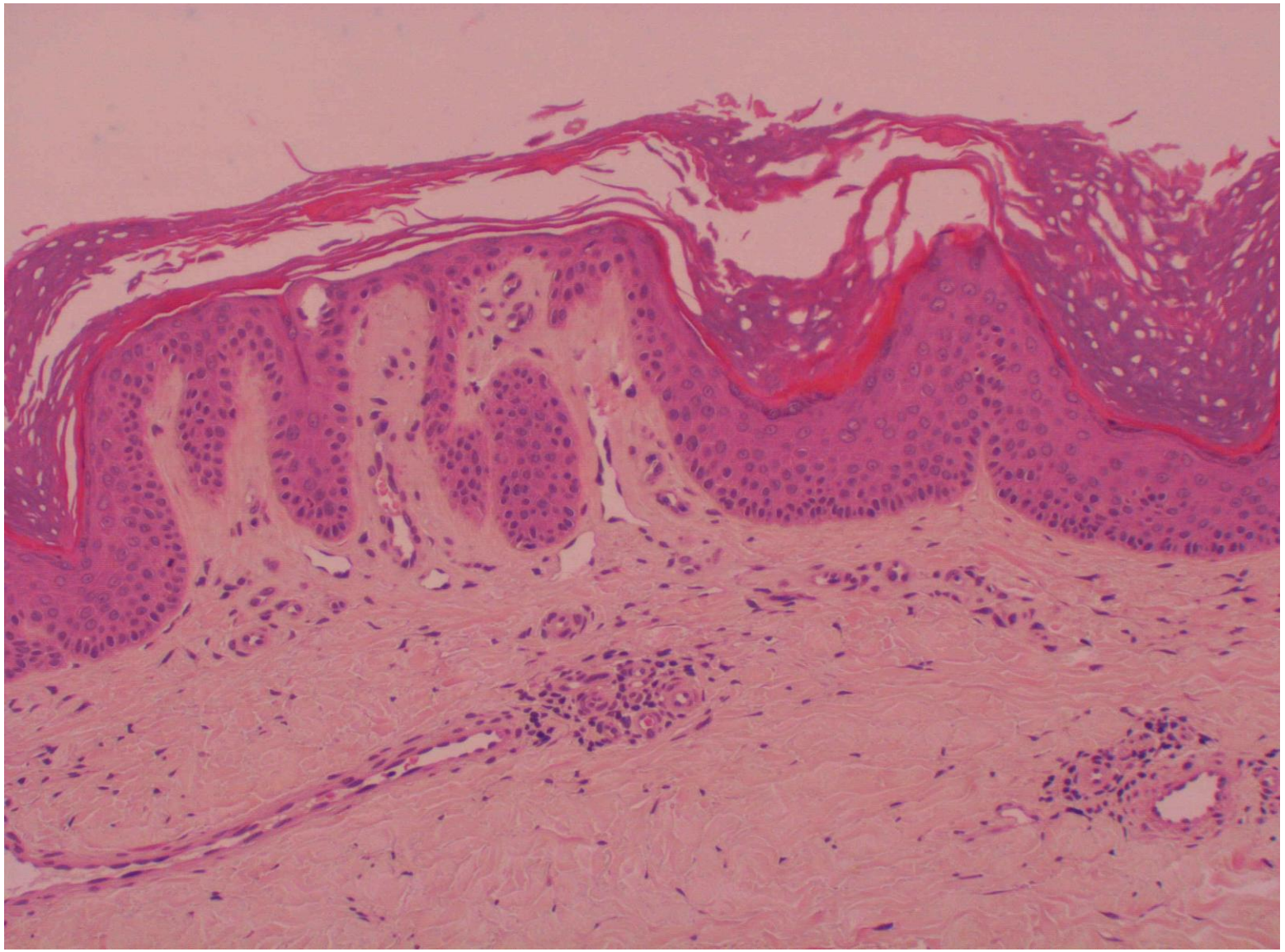


Epidermolysis bullosa simplex, suprabasal granulolytic type, seen in the heel skin of a 1-day-old female baby. Ultrastructurally, epidermolysis is evident in the suprabasal layer, particularly at the granular layer level. EM-1

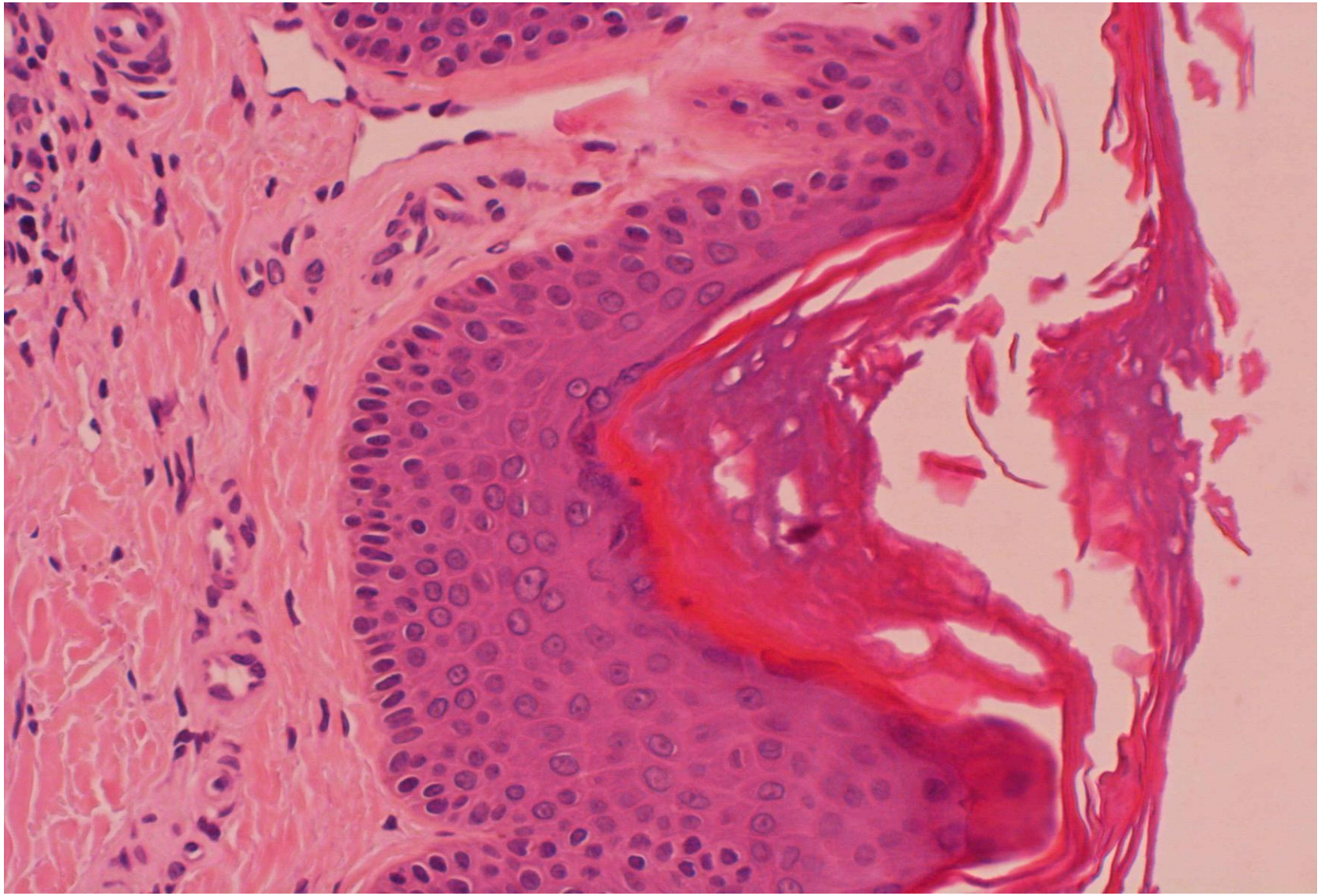
Poor tonofilament formation



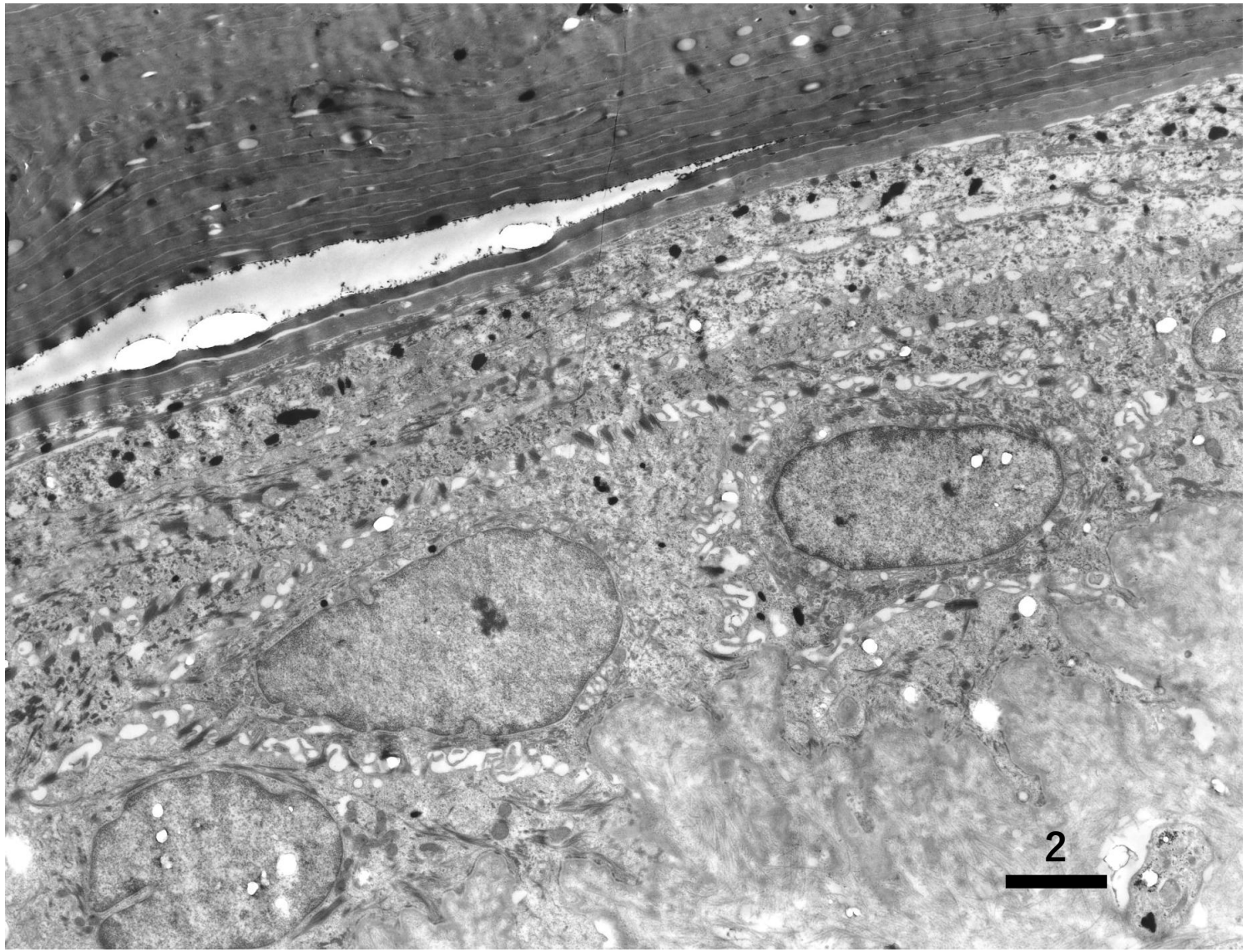
Epidermolysis bullosa (EB) simplex, suprabasal granulolytic type, seen in the heel skin of a 1-day-old female baby. Ultrastructurally, the keratinocyte reveals poor tonofilament formation with vacant perinuclear cytoplasm. EM-2



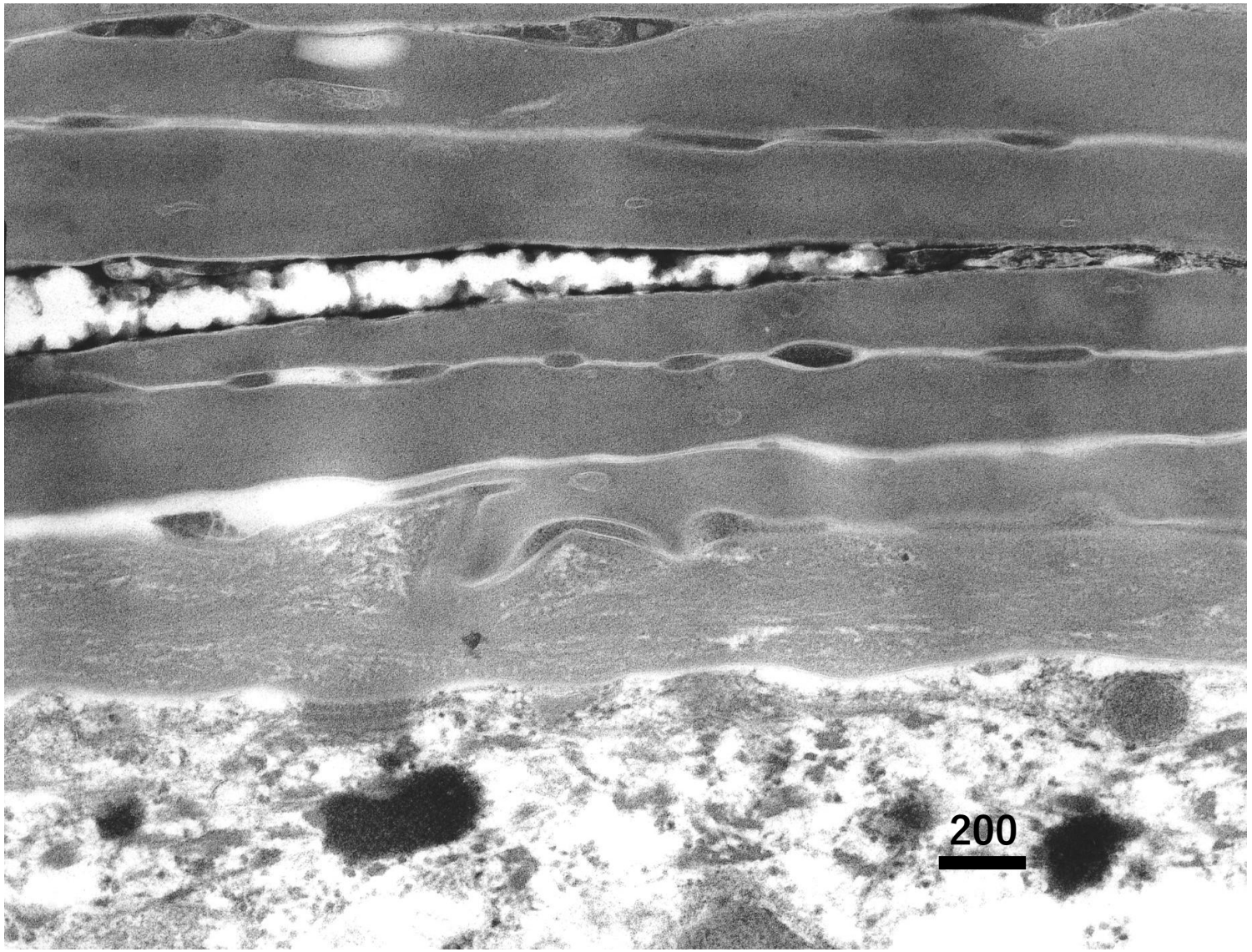
Epidermolysis bullosa simplex in the lower leg of a 37-year-old male patient. He has a family history of the bullous skin disease. The epidermolysis is seen in the cornified layer. H&E (1)



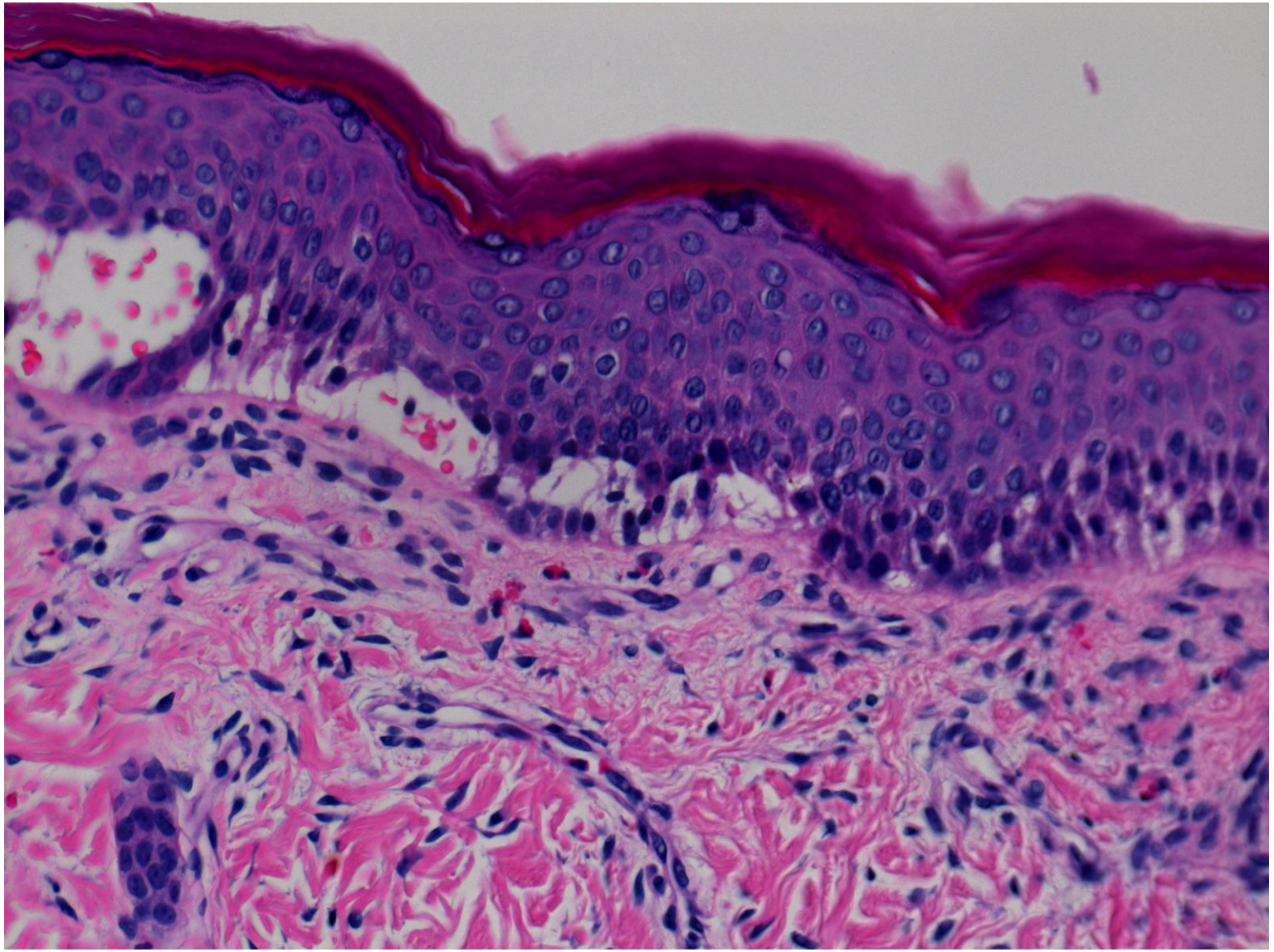
Epidermolysis bullosa simplex in the lower leg of a 37-year-old male patient. He has a family history of the bullous skin disease. The epidermolysis is seen in the cornified layer. H&E (2)



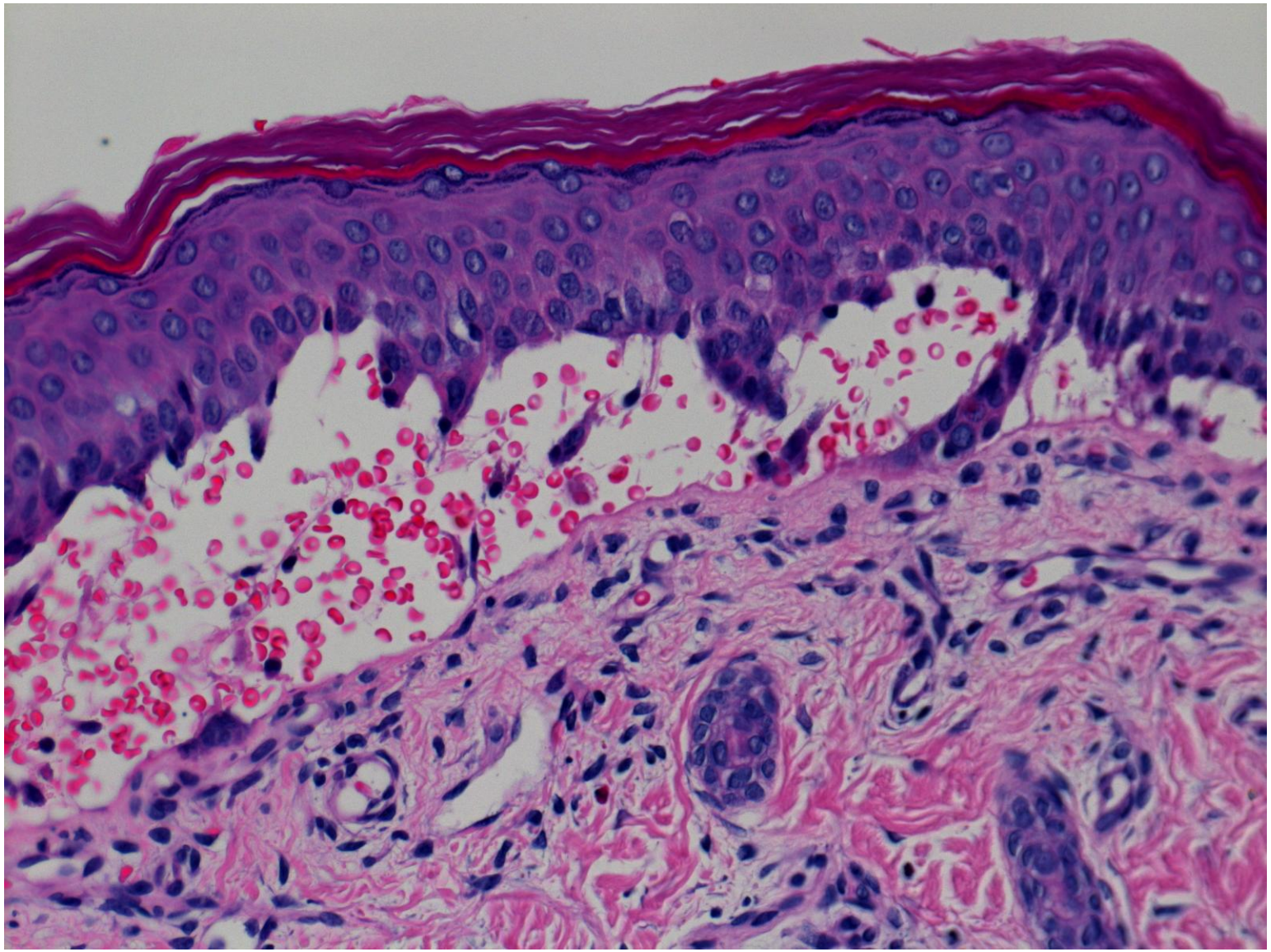
Epidermolysis bullosa simplex in the lower leg of a 37-year-old male patient. He has a family history of the bullous skin disease. Ultrastructurally, the epidermolysis is seen in the cornified layer just above the granular layer. EM (1)



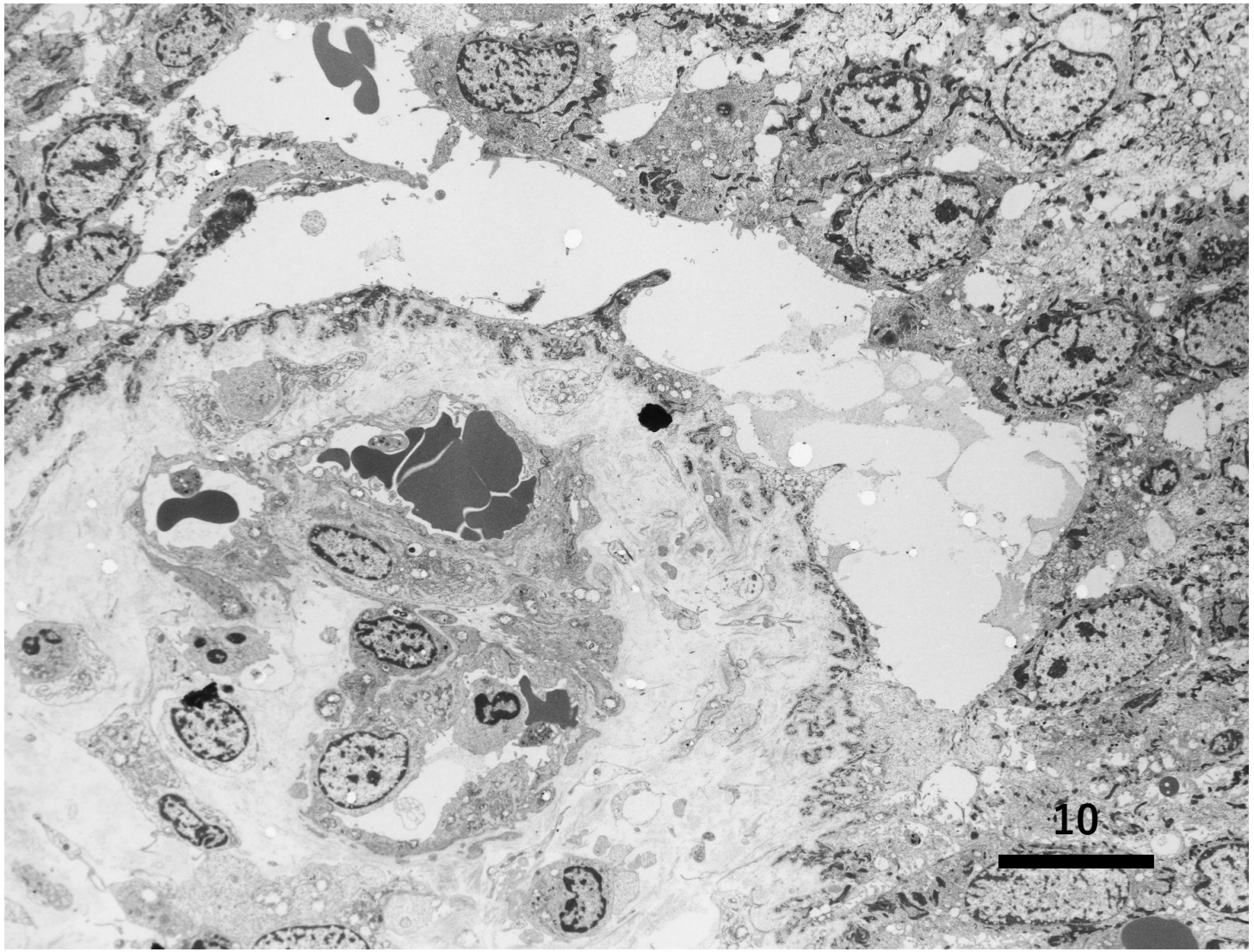
Epidermolysis bullosa simplex in the lower leg of a 37-year-old male patient. He has a family history of the bullous skin disease. Ultrastructurally, the epidermolysis is seen in the cornified layer. EM (2)



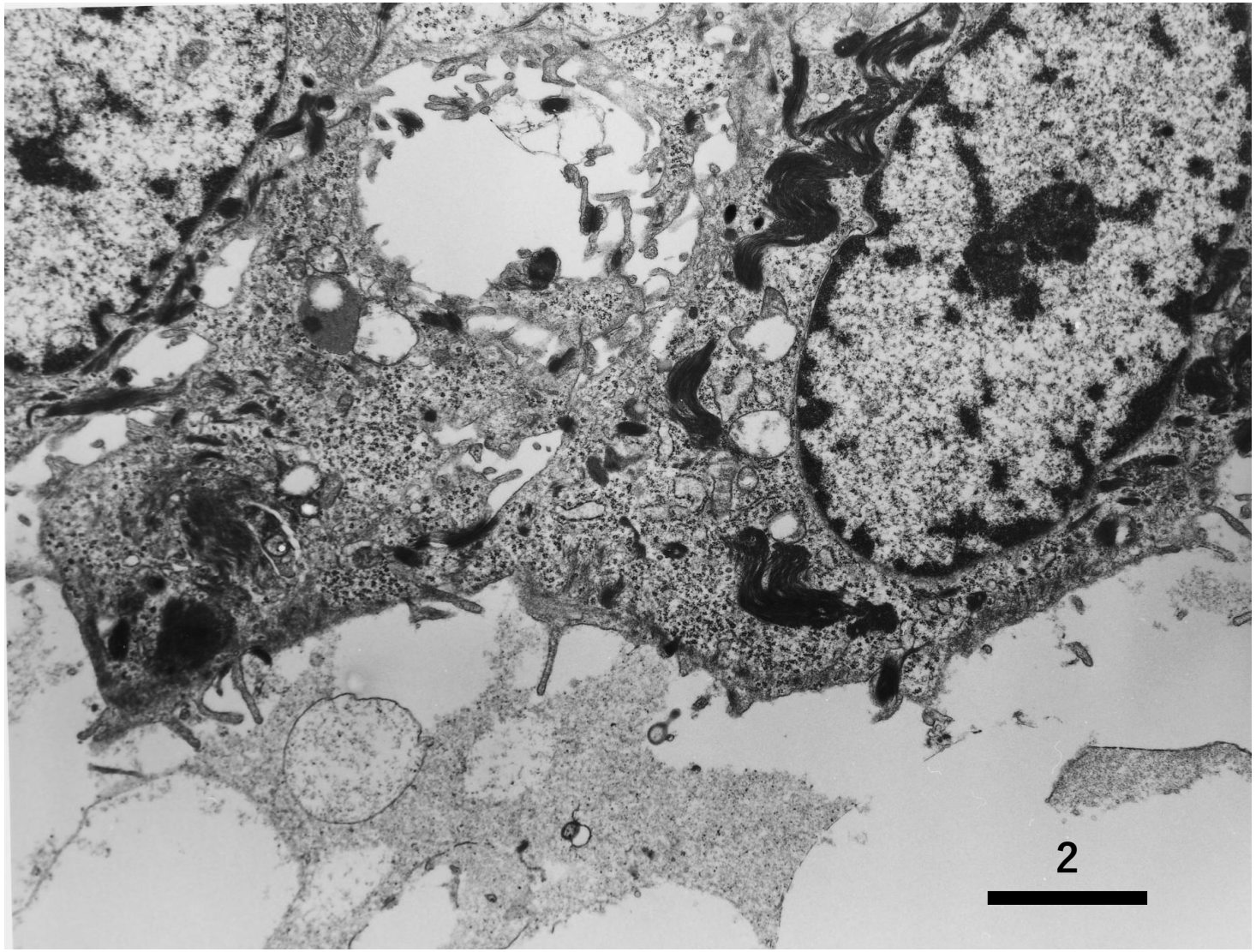
Epidermolysis bullosa simplex, basal type, in the leg of an 11-day-old male baby. Generalized, Koebner type is indicated. The epidermolysis is seen in the basal layer. H&E (1)



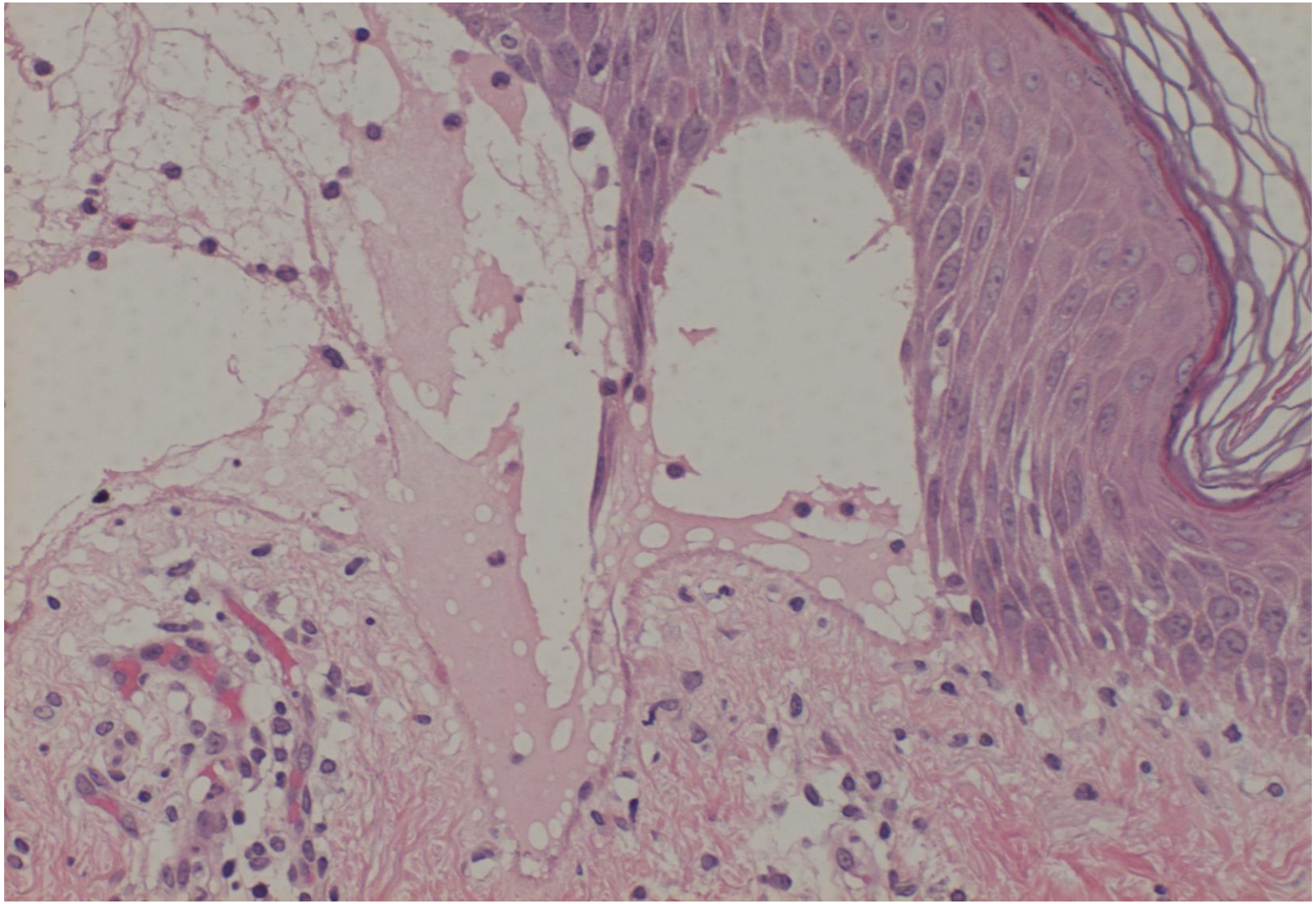
Epidermolysis bullosa simplex, basal type, in the leg of an 11-day-old male baby. Generalized, Koebner type is indicated. The epidermolysis is seen in the basal layer. H&E (2)



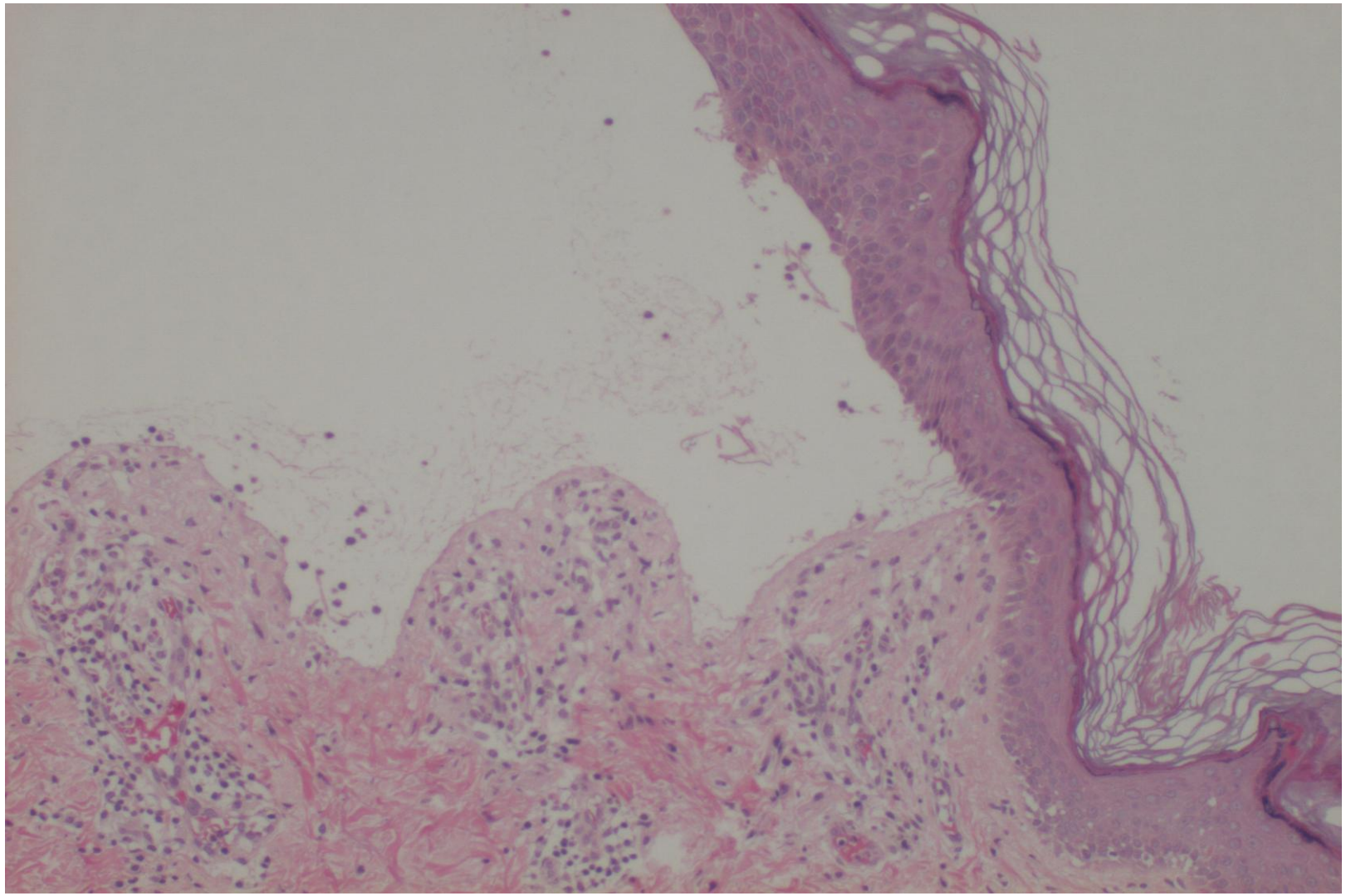
Epidermolysis bullosa simplex, basal type, in the leg of an 11-day-old male baby. Generalized, Koebner type is indicated. The epidermolysis is seen in the basal layer. The hemidesmosomes, basal lamina and anchoring fibrils remain intact. EM (1)



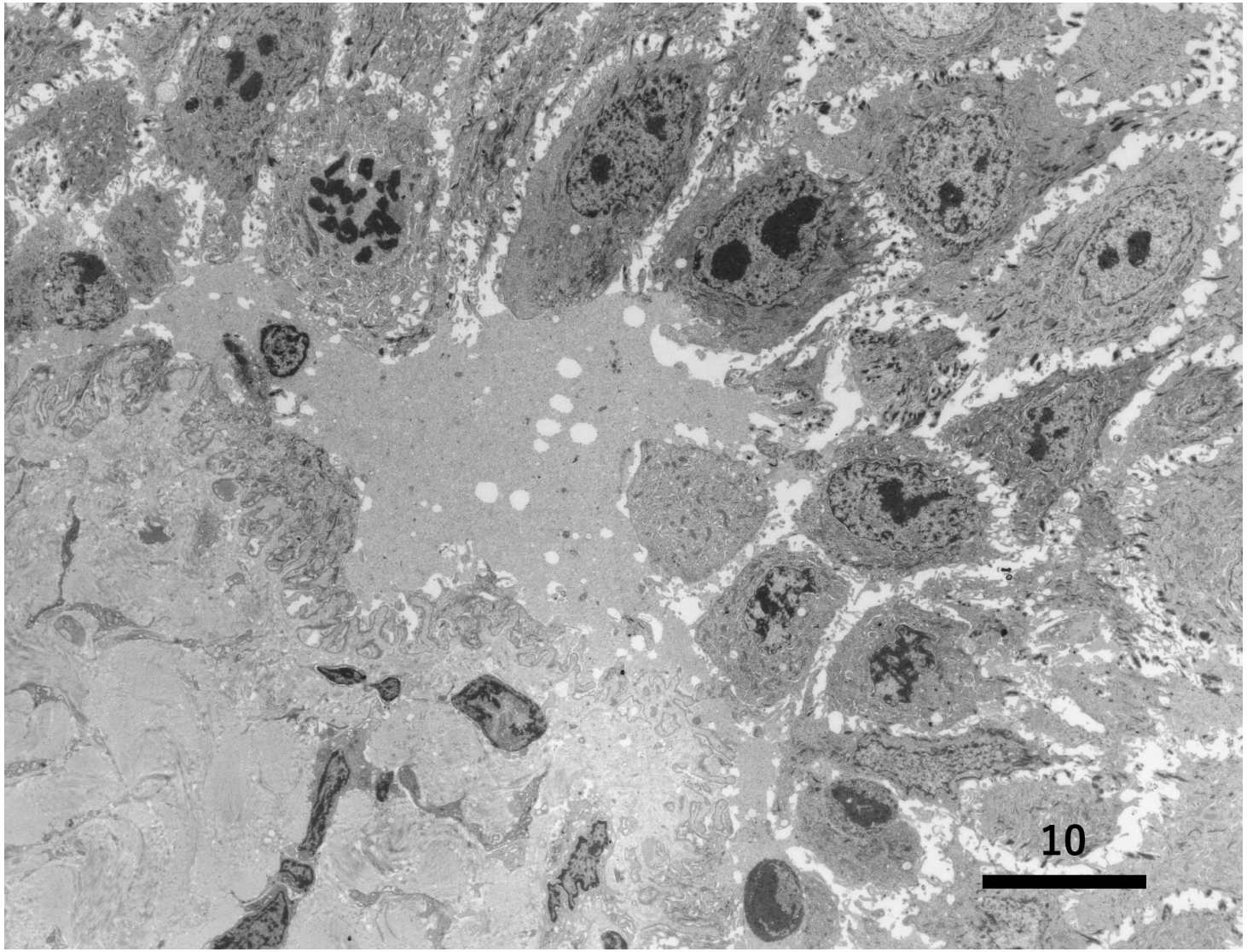
Epidermolysis bullosa simplex, basal type, in the leg of an 11-day-old male baby. Generalized, Koebner type is indicated. At the roof of the basal epidermolysis, the plasma membrane of the detached basal cell possesses microvilli. Tonofilaments are poorly developed and distorted. EM (2)



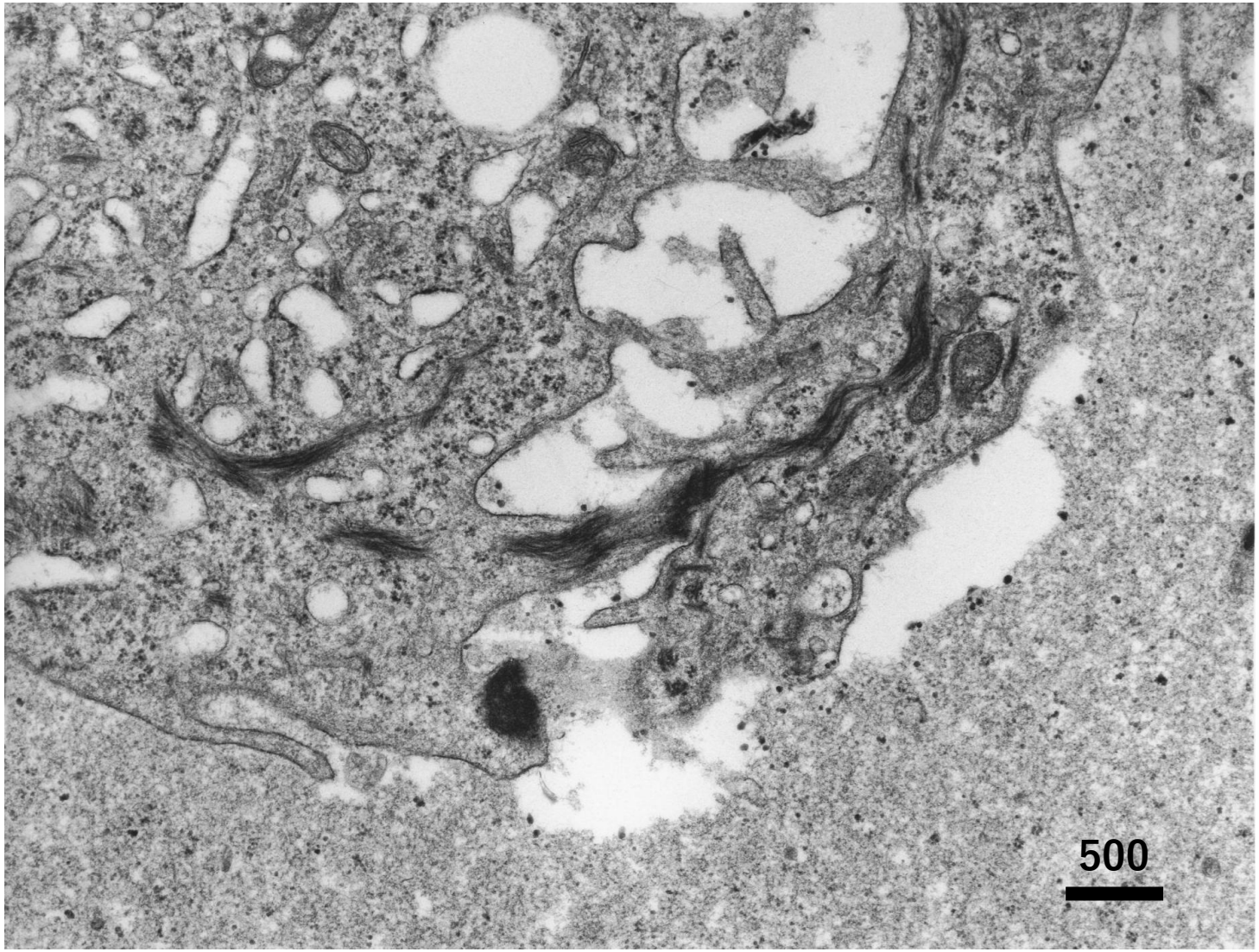
Epidermolysis bullosa herpetiformis, Dowling-Meara type, seen in a 29-year-old female patient. In this special subtype of EB simplex, formation of herpes-like large bullae is seen at the basal cell level. H&E (a)



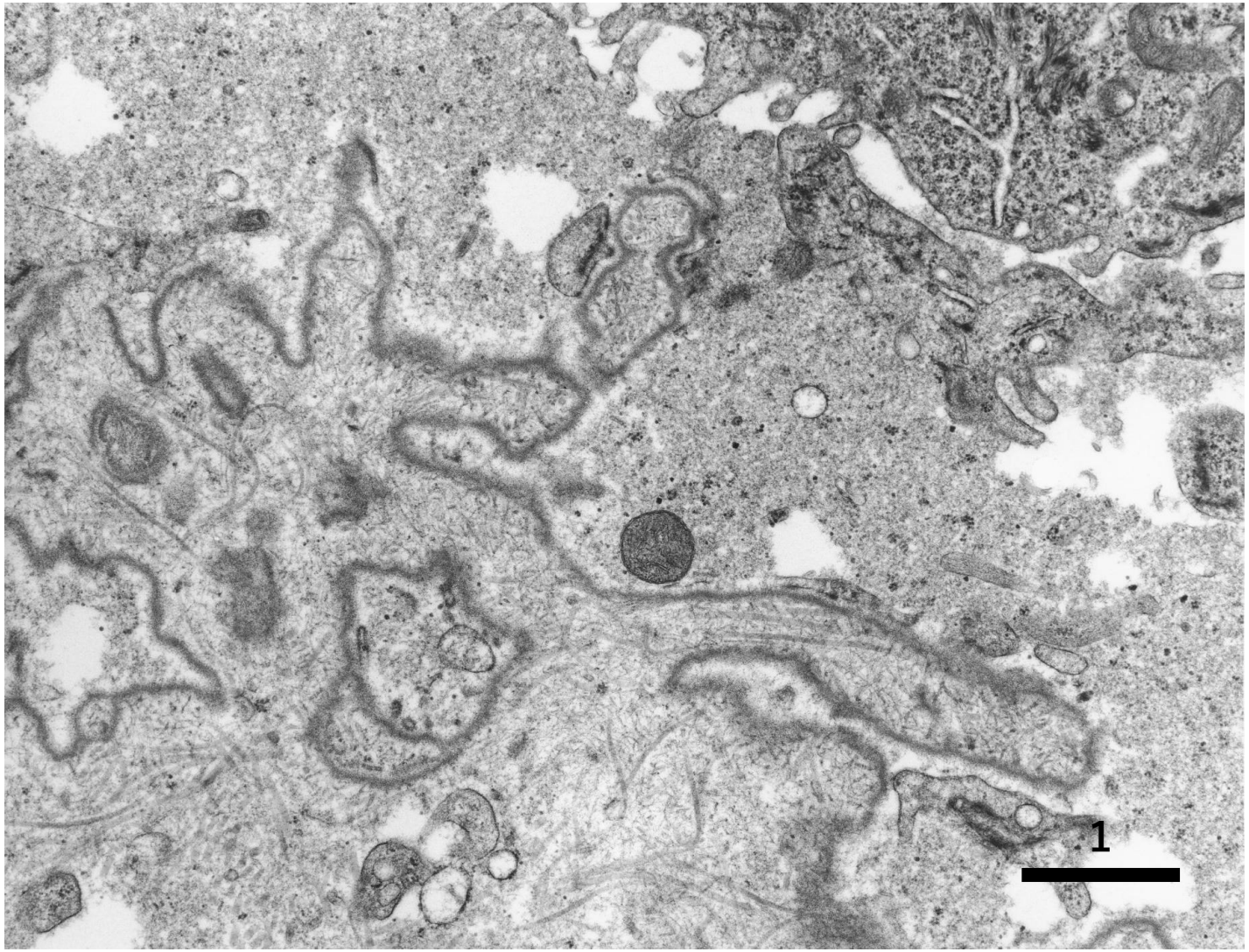
Epidermolysis bullosa herpetiformis, Dowling-Meara type, seen in a 29-year-old female patient. In this special subtype of EB simplex, formation of herpes-like large bullae is seen at the basal cell level. H&E (b)



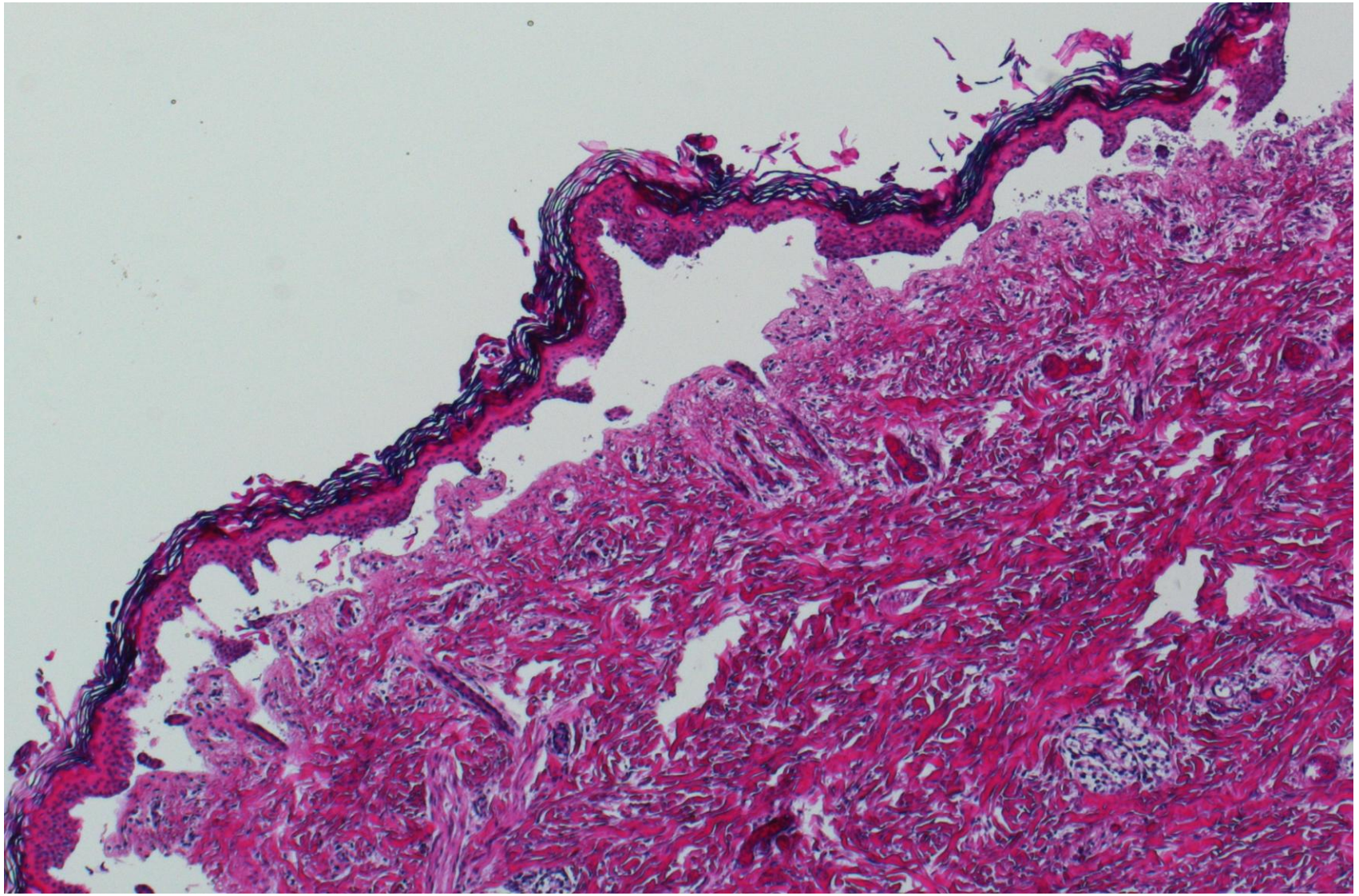
Epidermolysis bullosa herpetiformis, Dowling-Meara type, seen in a 29-year-old female patient. In this special subtype of EB simplex, bulla formation at the basal cell level is observed ultrastructurally. Tonofilaments are poorly developed. EM (a)



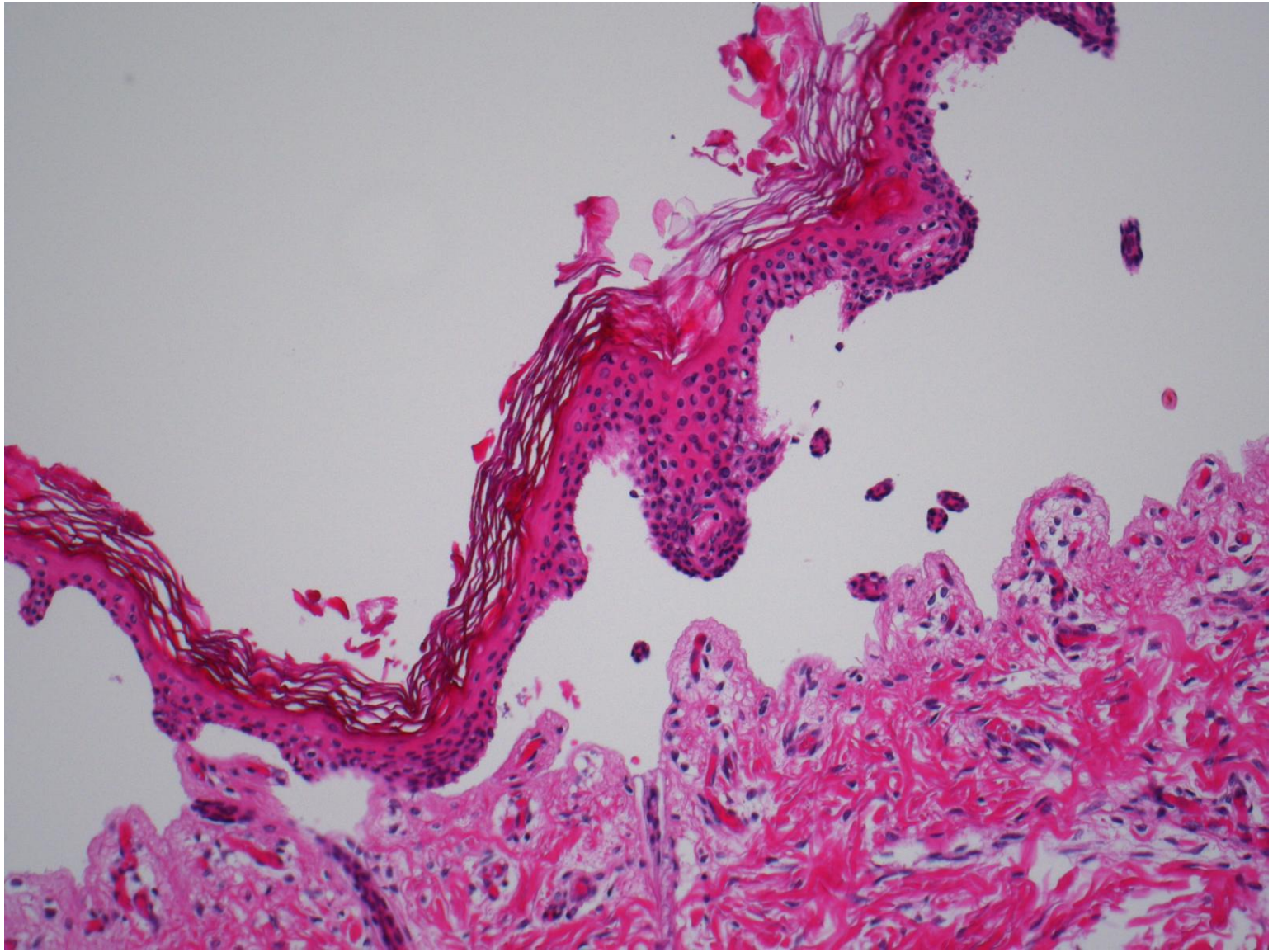
Epidermolysis bullosa herpetiformis, Dowling-Meara type, seen in a 29-year-old female patient. In this special subtype of EB simplex, the detached basal cell show poor formation of tonofilaments and their poor connection with desmosomes ultrastructurally. EM (b)



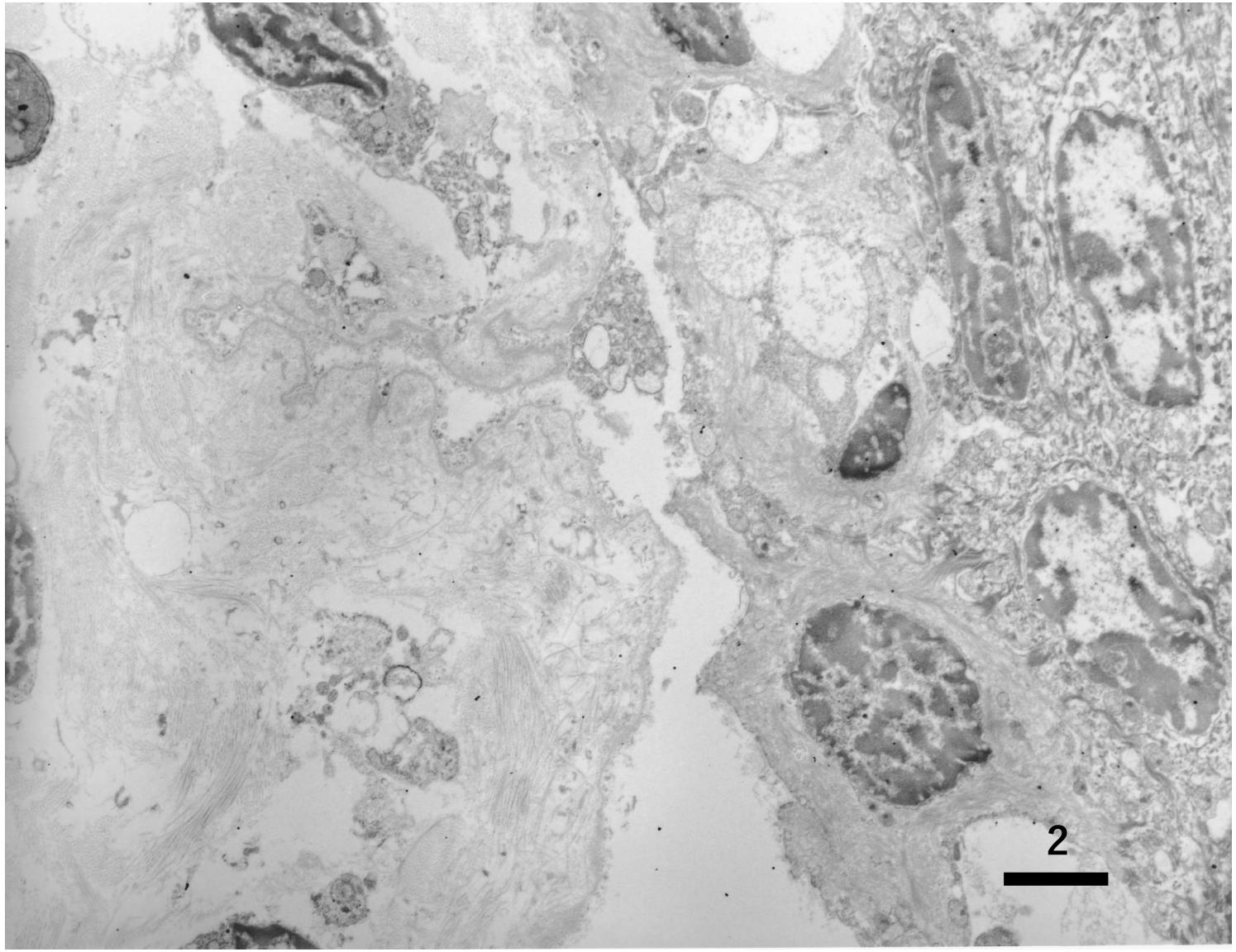
Epidermolysis bullosa herpetiformis, Dowling-Meara type, seen in a 29-year-old female patient. In this special subtype of EB simplex, bulla formation at the basal cell level is observed. At the bottom of the basal bulla, the basal lamina and anchoring fibrils remain intact ultrastructurally. EM (c)



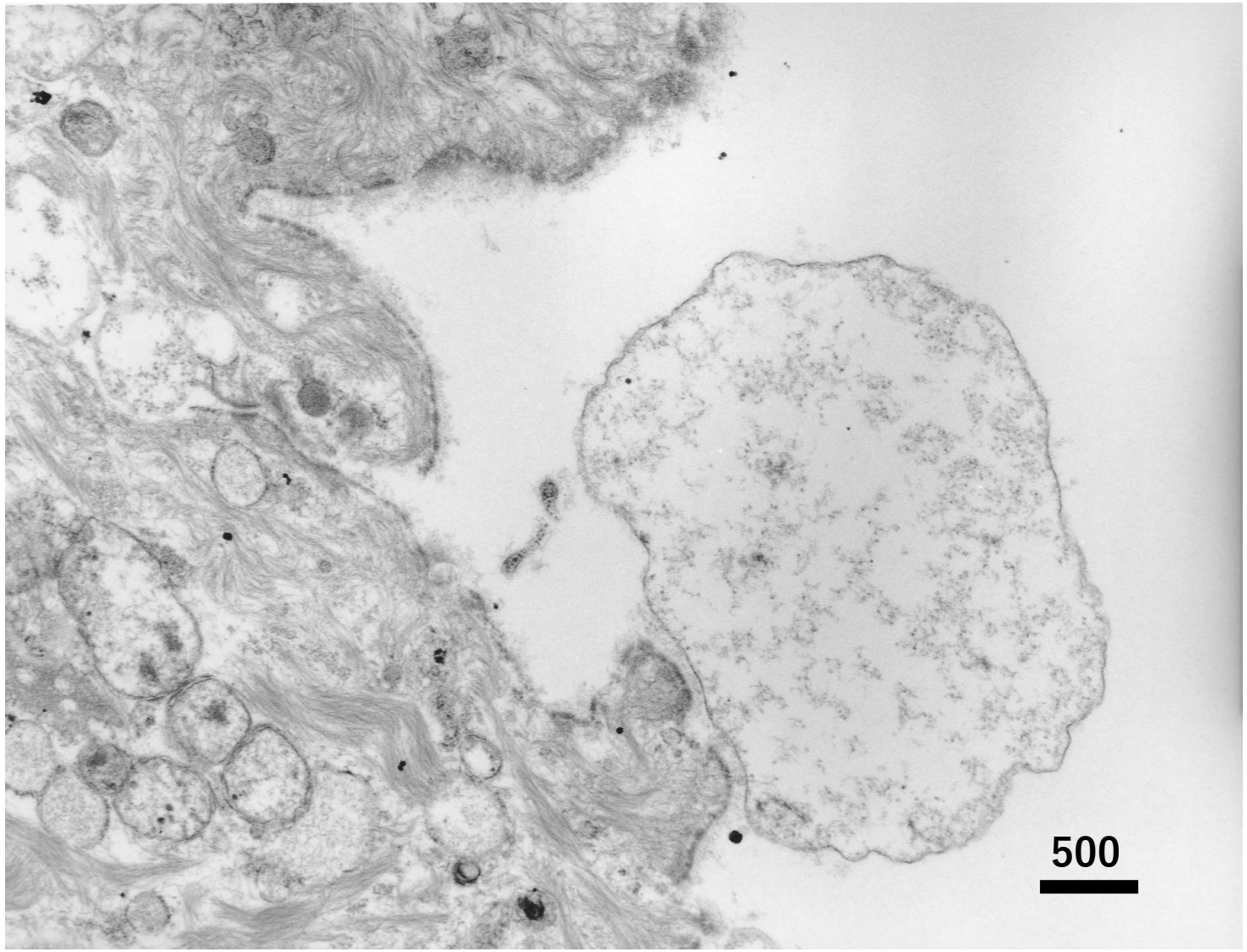
Junctional epidermolysis bullosa gravis (lethal Herlitz type). The forearm skin of the intrauterine dead female fetus at the 37th week of gestation. Diffuse subepidermal bulla formation is evident. H&E-1



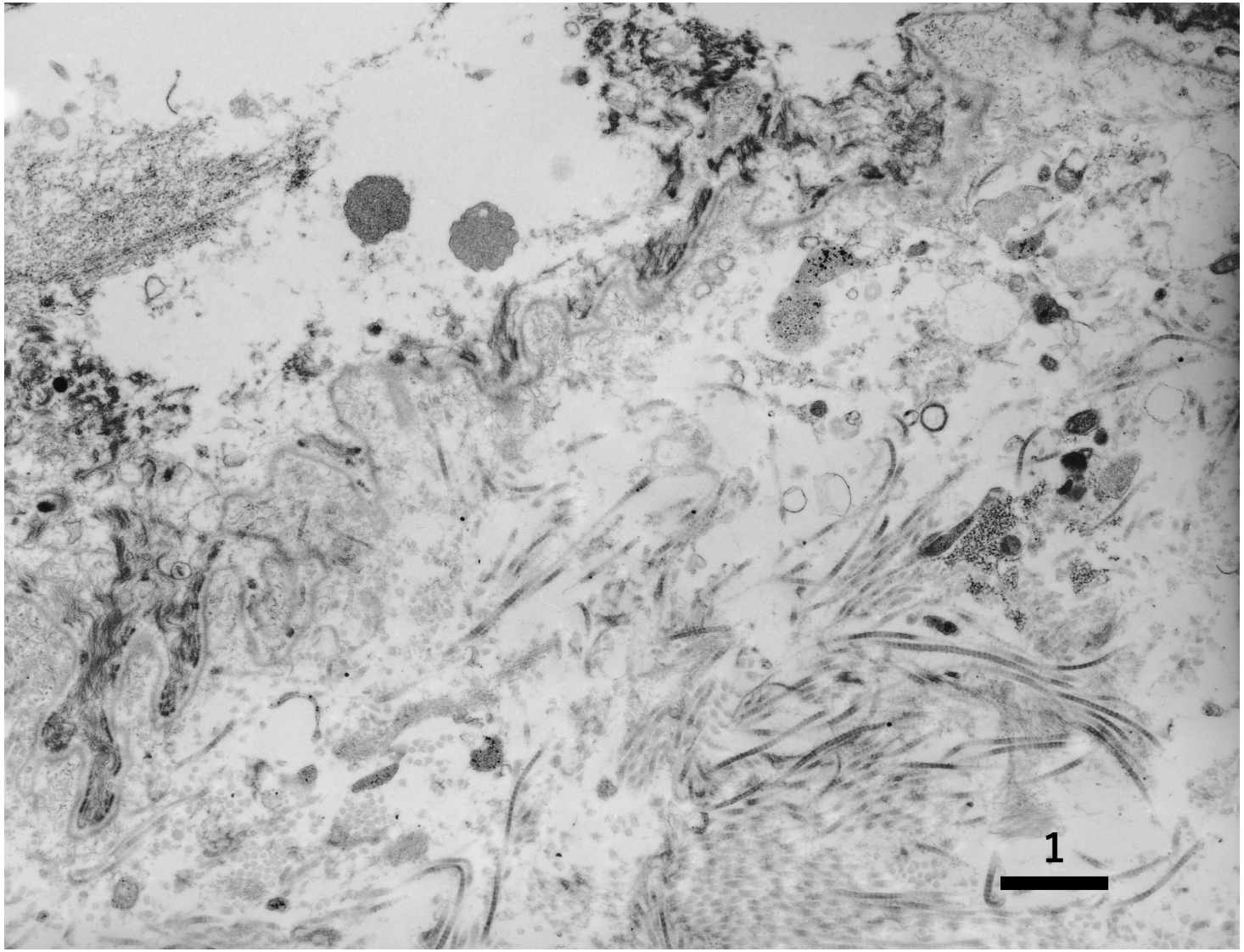
Junctional epidermolysis bullosa gravis (lethal Herlitz type). The forearm skin of the intrauterine dead female fetus at the 37th week of gestation. Diffuse subepidermal bulla formation is evident. H&E-2



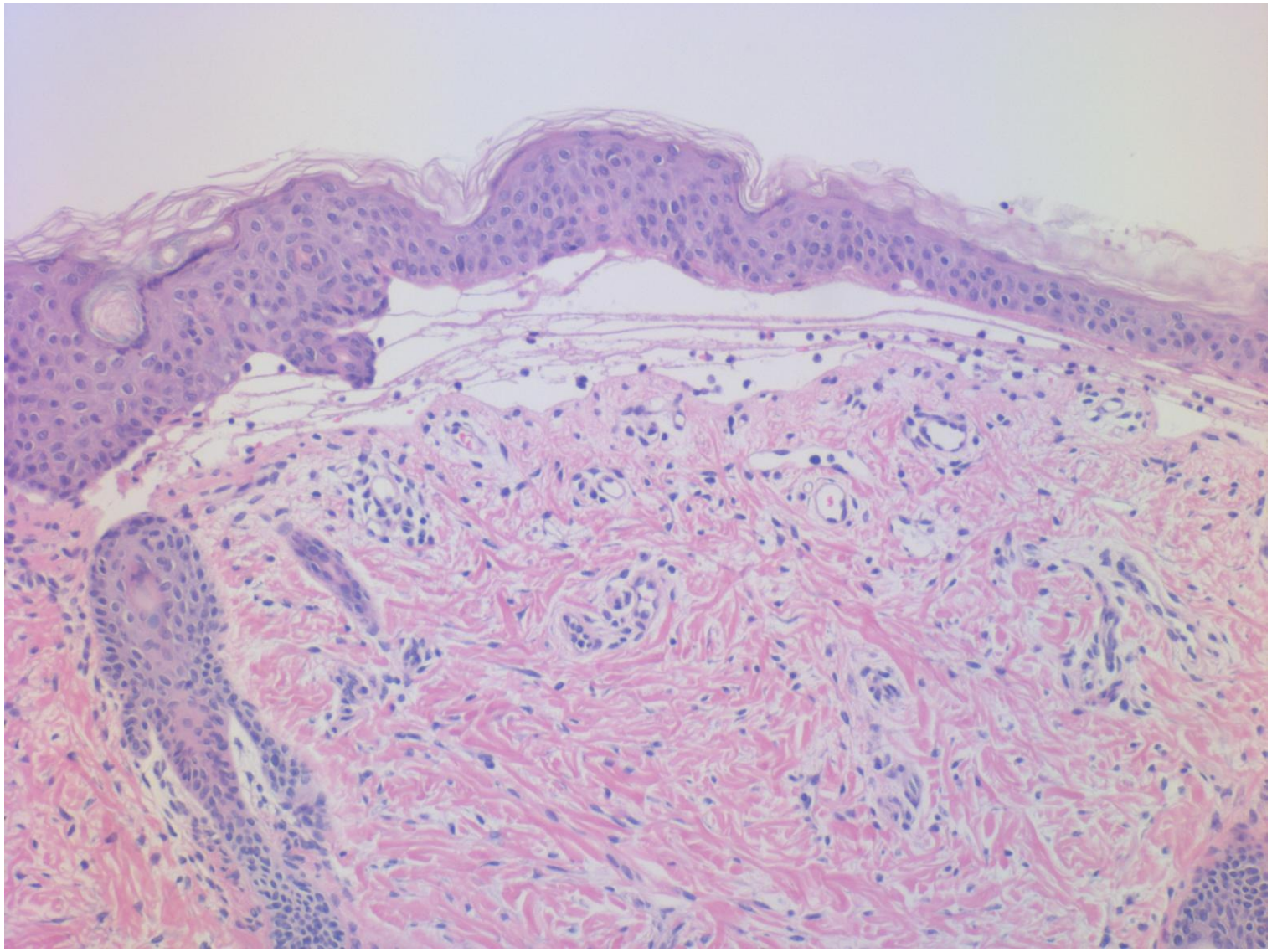
Junctional epidermolysis bullosa gravis (lethal Herlitz type). The forearm skin of the intrauterine dead female fetus at the 37th week of gestation. Ultrastructurally, subepidermal bulla is formed by the split of the lamina lucida of the basement membrane. EM-2



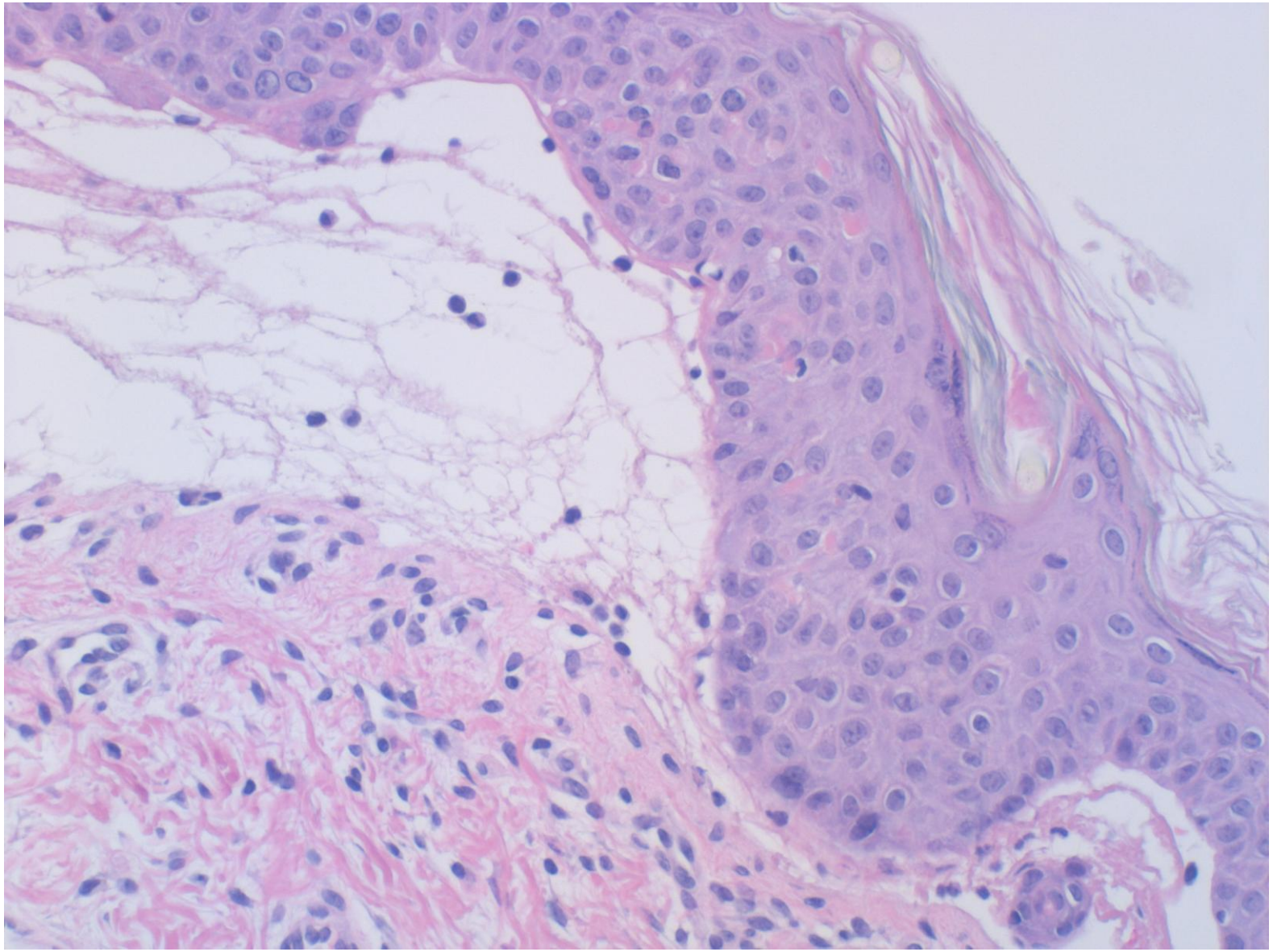
Junctional epidermolysis bullosa gravis (lethal Herlitz type). The forearm skin of the intrauterine dead female fetus at the 37th week of gestation. Ultrastructurally, subepidermal bulla is formed by the split of the lamina lucida of the basement membrane. EM-2



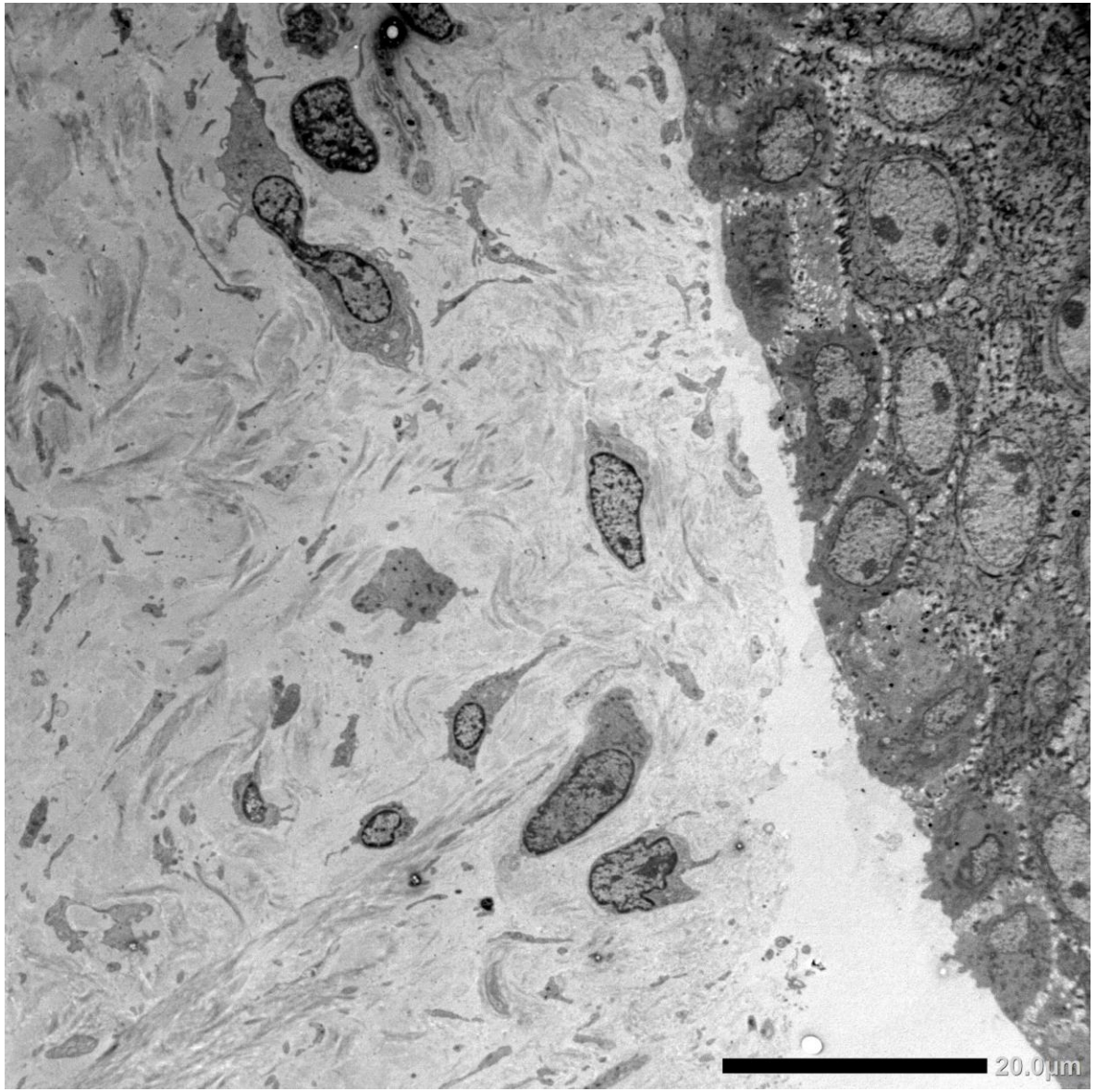
Junctional epidermolysis bullosa gravis (lethal Herlitz type). The forearm skin of the intrauterine dead female fetus at the 37th week of gestation. Ultrastructurally, subepidermal bulla is formed by the split of the lamina lucida of the basement membrane. Anchoring fibrils remain intact. EM-3



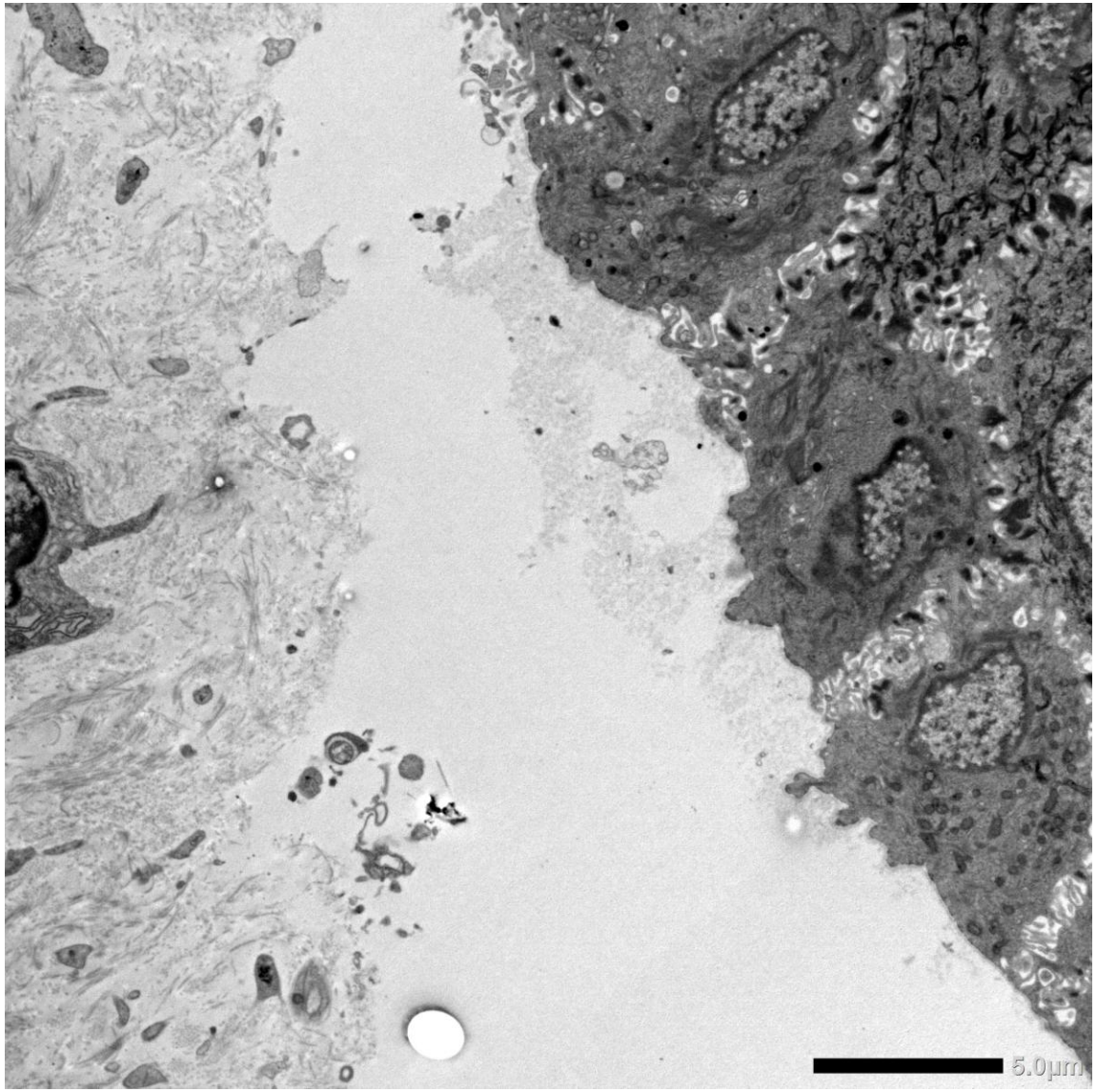
Epidermolysis bullosa, dermolytic type seen in a female neonate. Subepithelial bulla formation is evident. H&E (a)



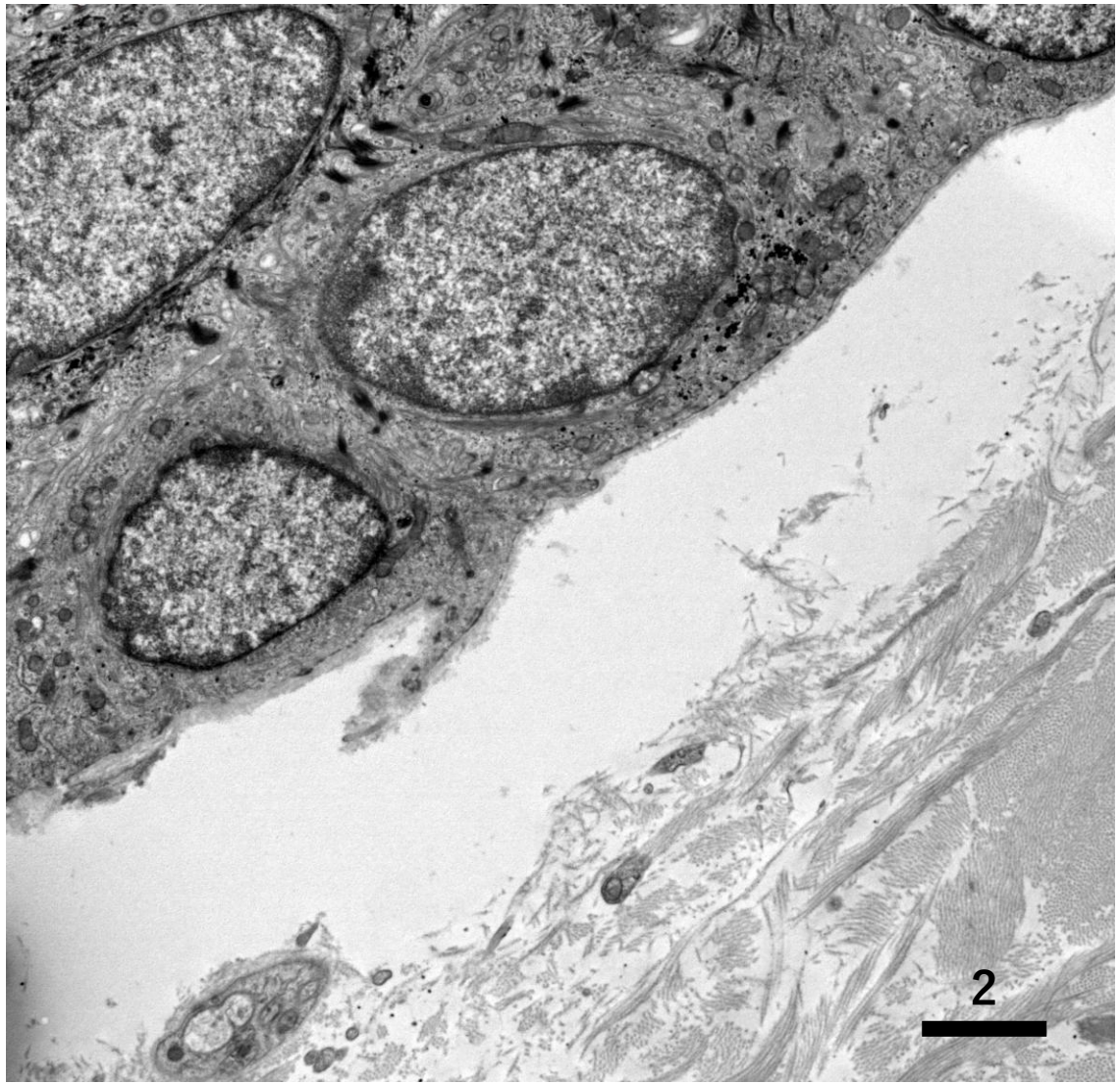
Epidermolysis bullosa, dermolytic type seen in a female neonate. Subepithelial bulla formation is evident. H&E (b)



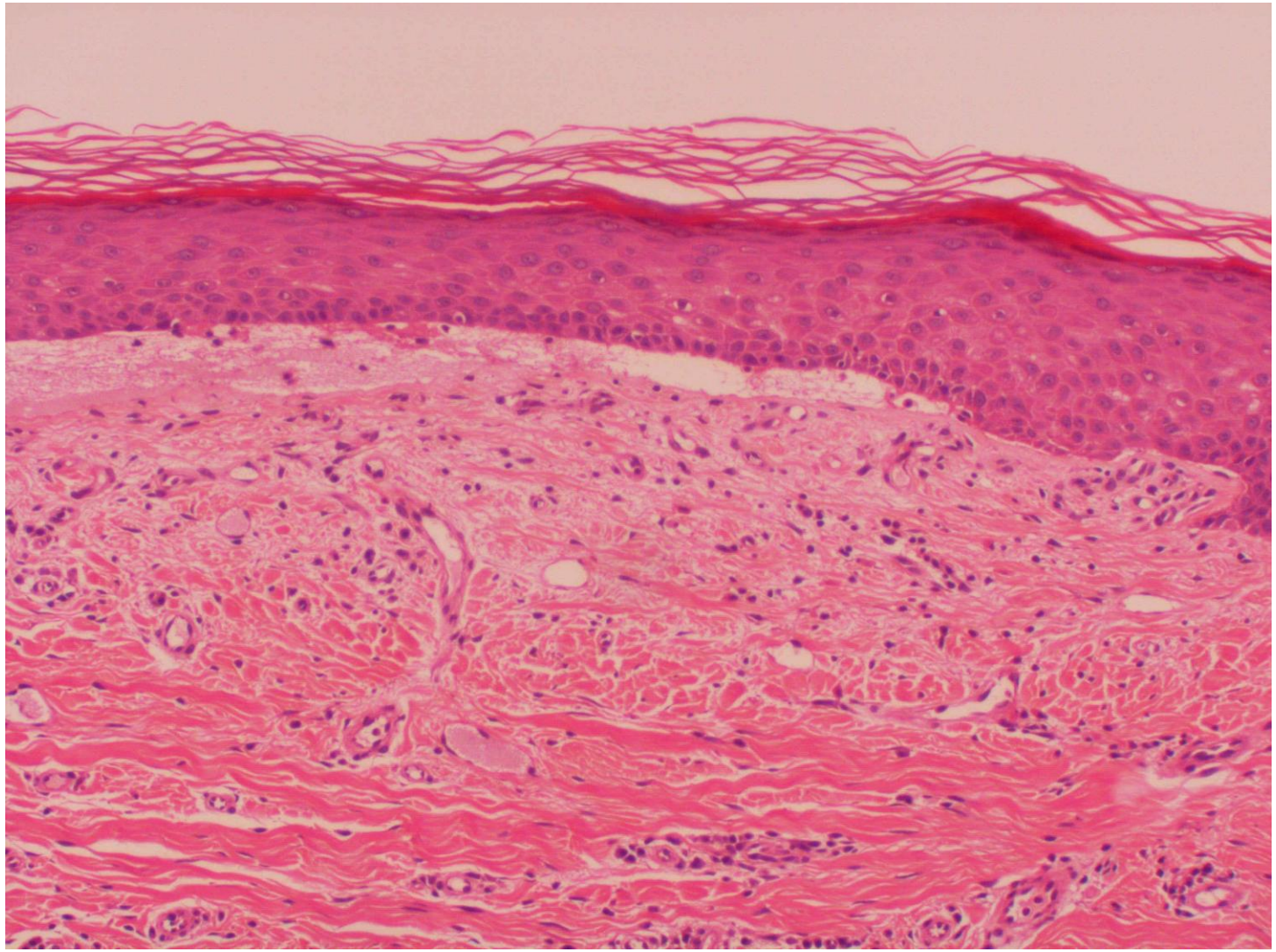
Epidermolysis bullosa, dermolytic type seen in a female neonate.
Ultrastructurally, subepithelial bulla formation is evident.
Anchoring fibrils are scarcely seen. EM (a)



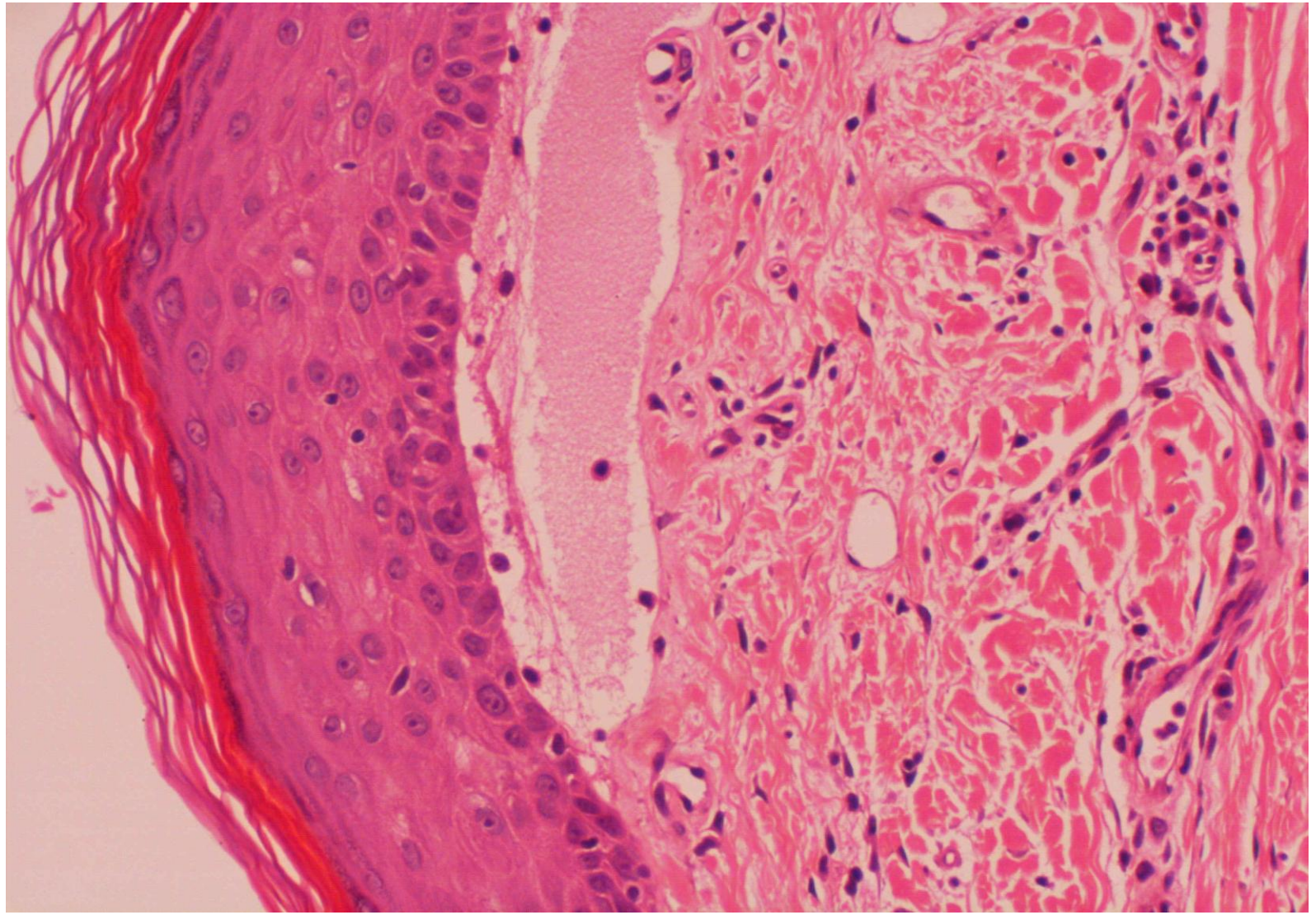
Epidermolysis bullosa, dermolytic type seen in a female neonate.
Ultrastructurally, subepithelial bulla formation is evident.
Anchoring fibrils are scarcely seen. EM (b)



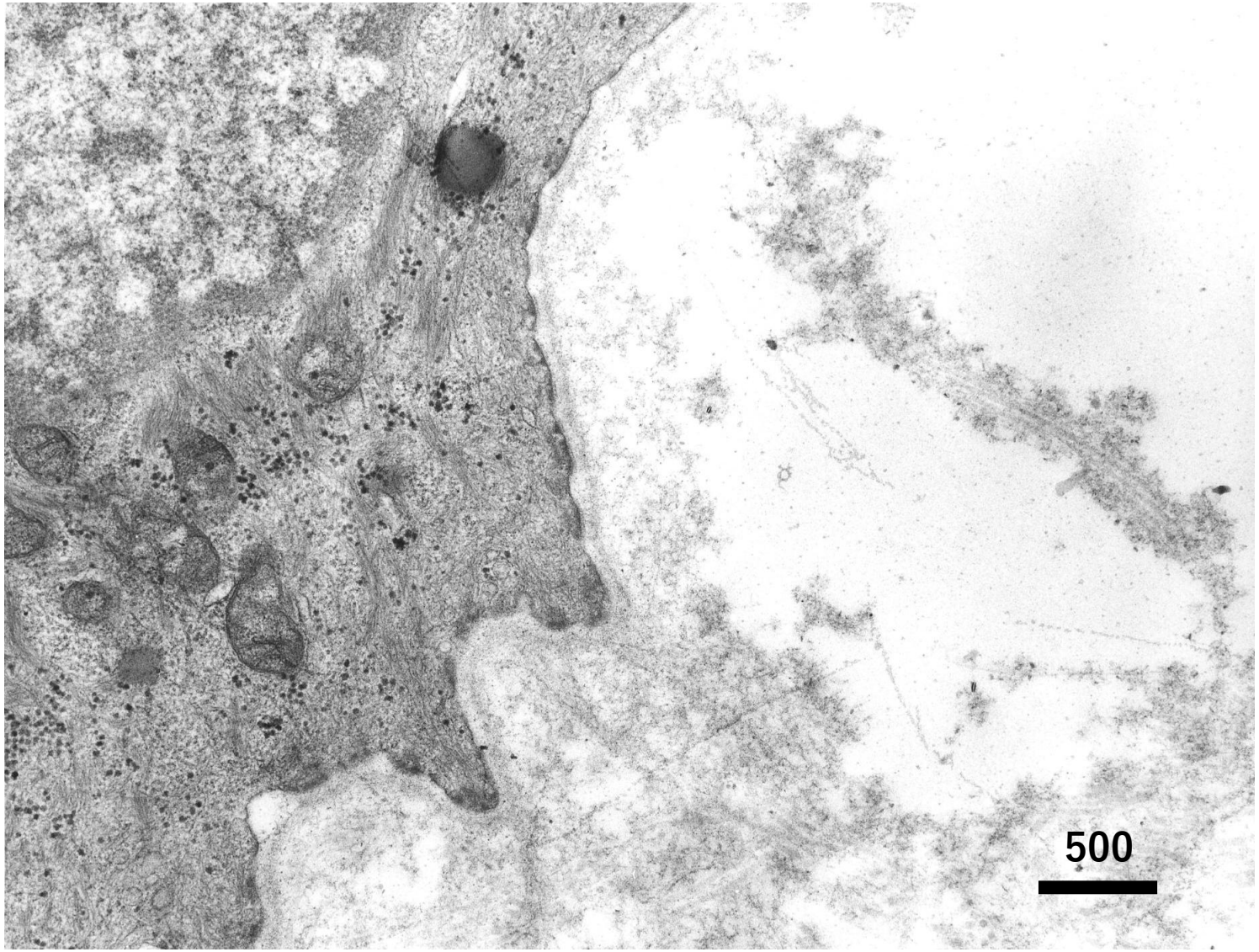
Epidermolysis bullosa, dermolytic type seen in a female neonate. Ultrastructurally, subepithelial bulla formation is evident. The basal lamina is seen on the detached basal cells. Anchoring fibrils are scarcely seen. EM (c)



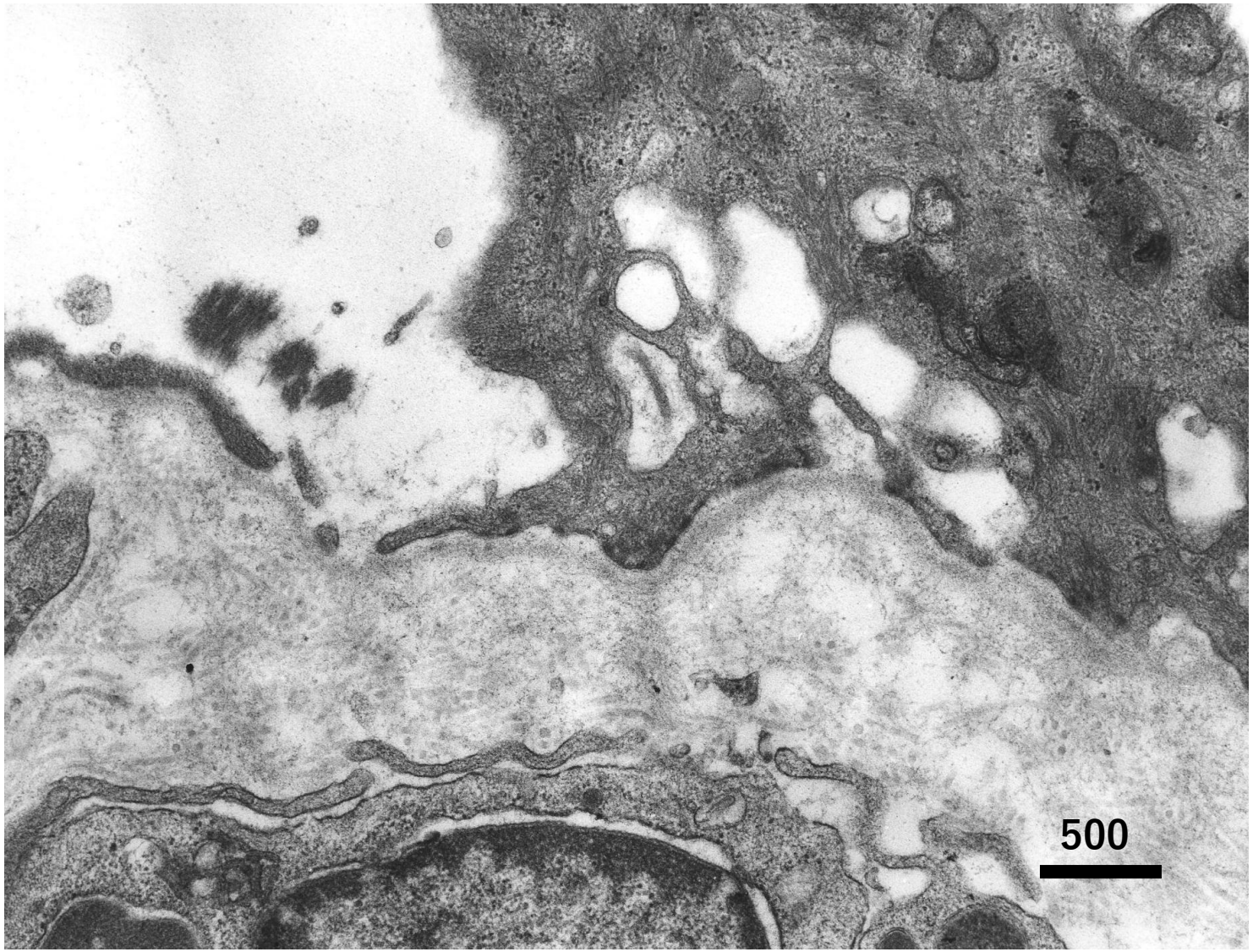
Epidermolysis bullosa dermolytica, seen in the lower leg skin of a 48-year-old female patient. Subepidermal bulla formation is observed. H&E (a)



Epidermolysis bullosa dermolytica, seen in the lower leg skin of a 48-year-old female patient. Subepidermal bulla formation is observed. H&E (b)



Epidermolysis bullosa dermolytica, seen in the lower leg skin of a 48-year-old female patient. Ultrastructurally, subepidermal bulla formation is observed. Hemidesmosomes and the basal lamina are seen along the basal keratinocytes. EM (a)



Epidermolysis bullosa dermolytica, seen in the lower leg skin of a 48-year-old female patient. Ultrastructurally, subepidermal bulla formation is observed. Hemidesmosomes and the basal lamina are seen along the basal keratinocytes. Distortion of the anchoring fibrils is associated. EM (b)