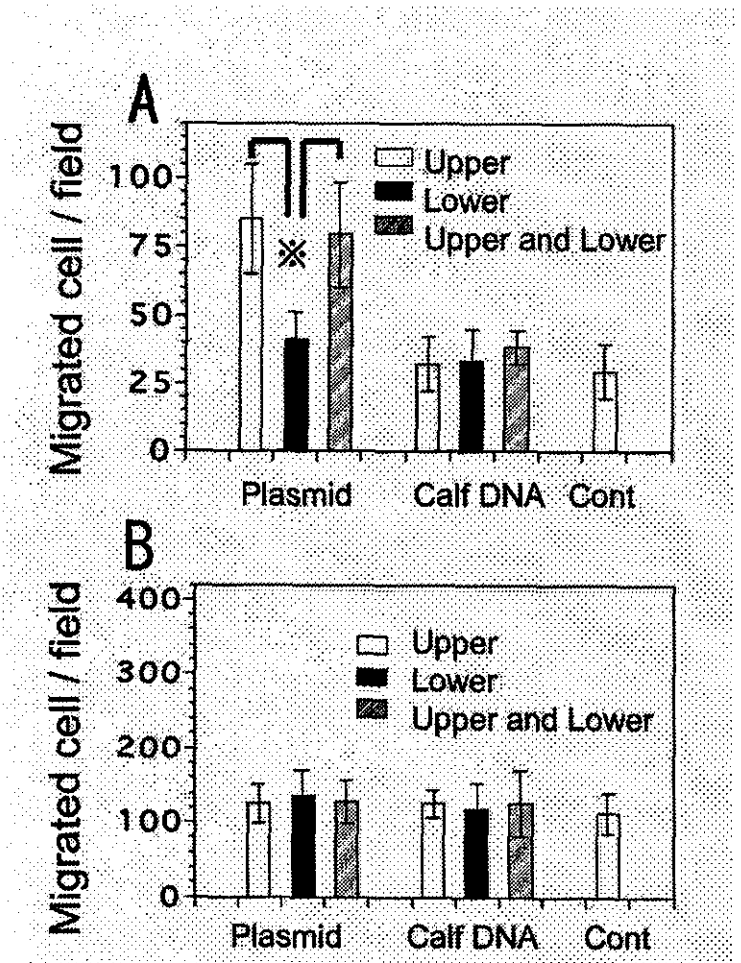

Fig 4 Sawamura et al.

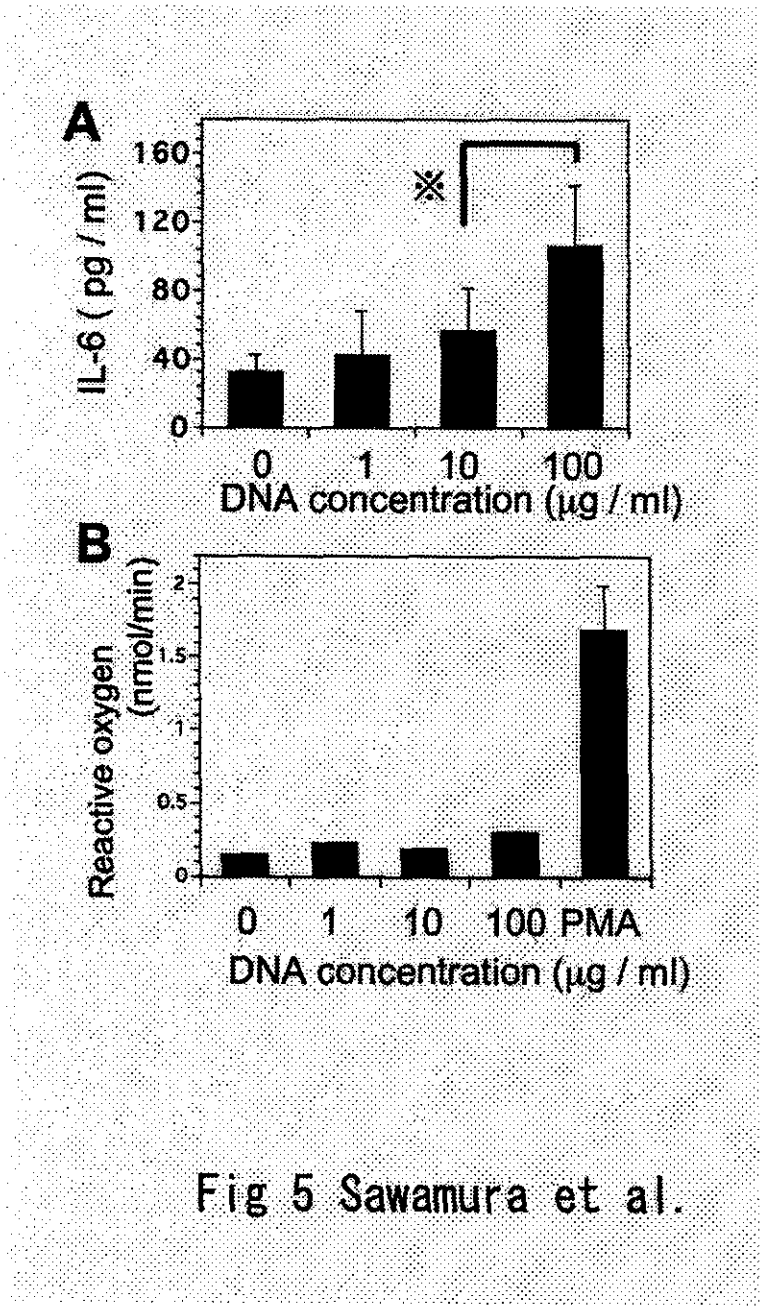

Fig 5 Sawamura et al.

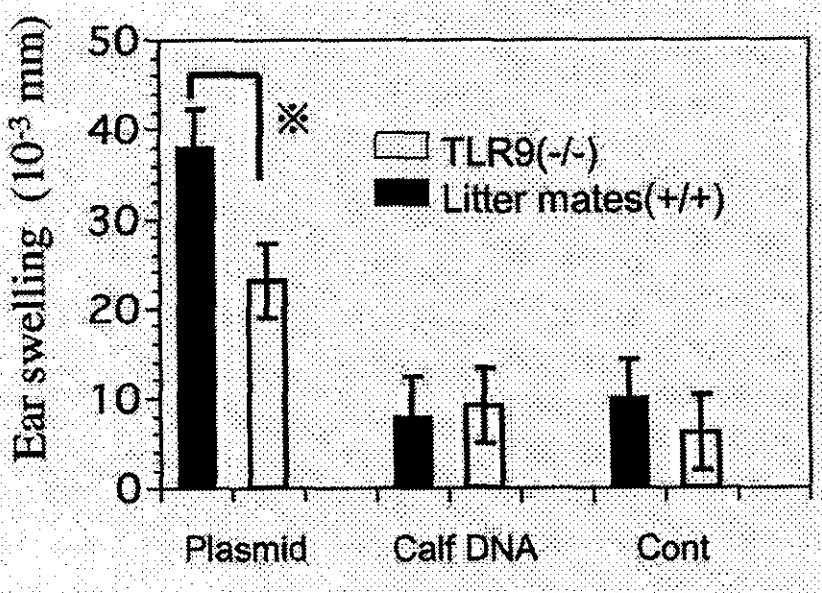

Fig 6 Sawamura et al

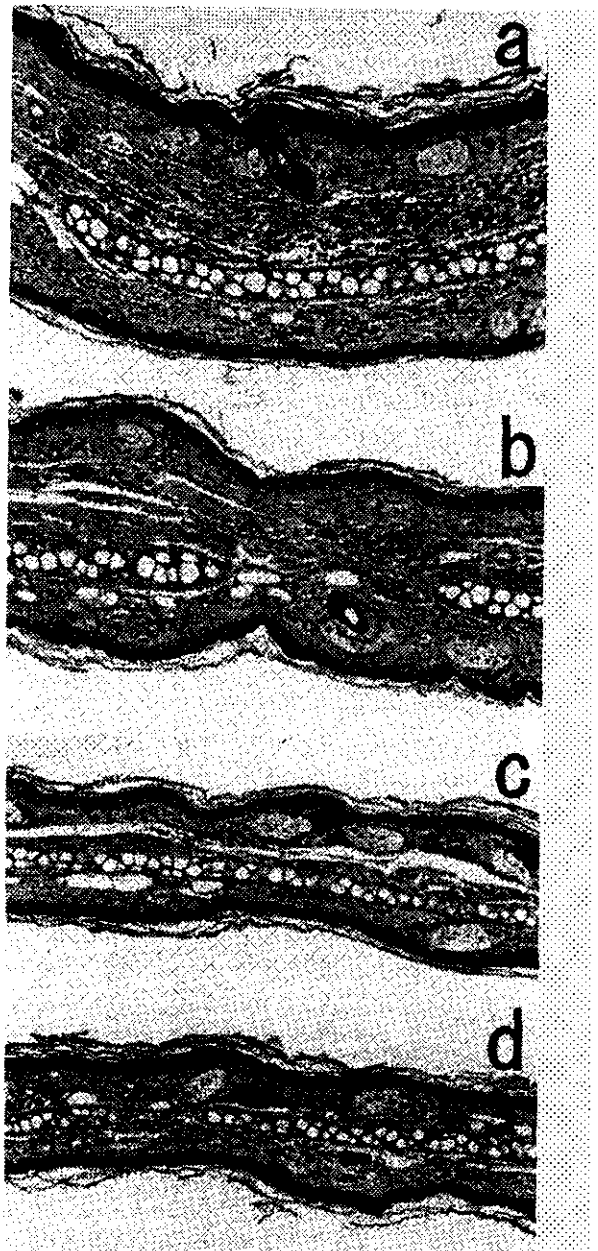

Fig 7 Sawamura et al

episodes (4/4 Assier criteria).[1] Moreover, no further episodes of HSV infection or EM were noted on acyclovir prophylaxis, at 12-month follow-up visit.

Our case highlights the fact that the extent and the severity of the mucosal lesions are not helpful in making etiological assumptions in patients with EM.

Elena Pope, MD, MSc, FRCPC
Bernice R. Krafchik, MB, ChB, FRCPC
Department of Paediatrics, Section of Dermatology
University of Toronto
Hospital for Sick Children
Toronto, Canada

Reprint requests: Elena Pope, MD, MSc, FRCPC
Head, Section of Dermatology
Hospital for Sick Children, 555 University Avenue
Toronto, Ontario, M5G 1X8, Canada

E-mail: elena.pope@sickkids.ca

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Keratotic lesions in epidermolysis bullosa simplex with mottled pigmentation

To the Editor: Epidermolysis bullosa simplex with mottled pigmentation (EBS-MP) is a rare genodermatosis of characteristic mottled pigmentation in addition to typical intraepidermal blister formation occurring after minor trauma. Only the P25L mutation in the keratin 5 has been identified in EBS-MP so far.[1] Keratotic lesions in EBS-MP including wart-like or punctate keratoses seem to be different from keratoses seen in other EBS-subtypes.[2] We have observed keratotic lesions in a Japanese EBS-MP family in precise detail using electron microscopy.

CASE 1

A 2-year-old girl with a history of blistering on the palms and soles since 1 month of age, presented with mottled pigmentation and wart-like hyperkeratotic papules on the axillae, the wrists, and the dorsa of the hand (Fig 1, *a-c*).

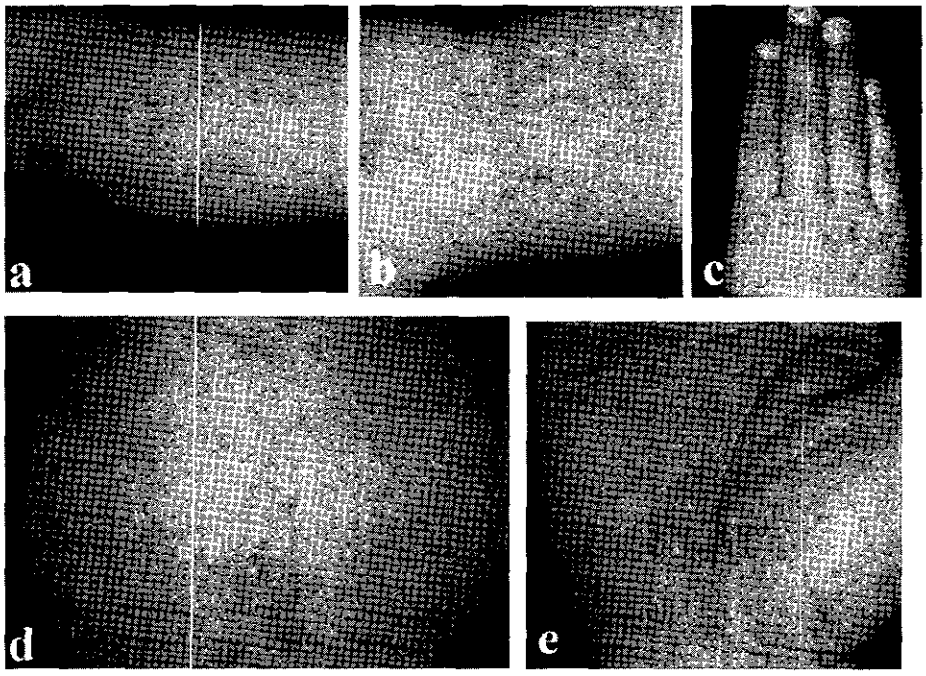

Fig 1. a-c, Mottled pigmentation and wart-like keratotic papules on the dorsum of the hand, wrist, and axillae of case 1. **d-e,** Reticular hyperpigmented macules on the trunk and hyperkeratotic lesion with plane wart-like papule on the palm of case 2.

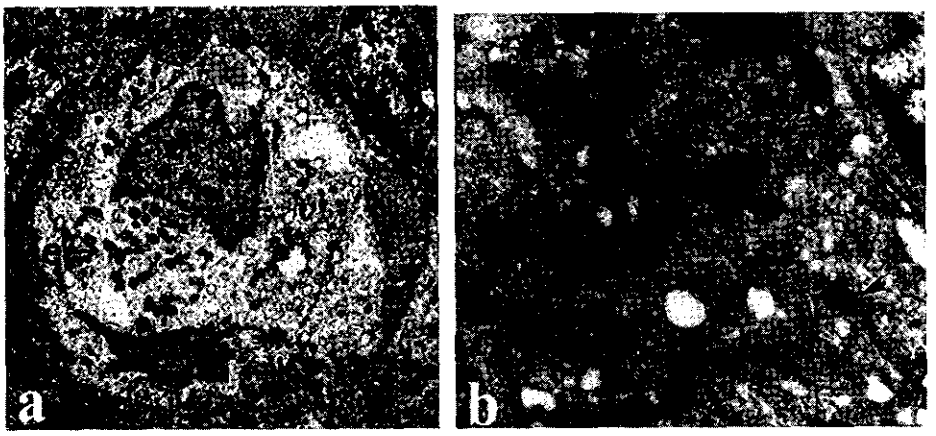

Fig 2. a, Ultrastructure of case 2 shows disorganized keratin filaments (Kf) and aggregation of multiple, densely packed-compound melanosomes (Me) in the basal cells. **b,** The keratotic lesion of case 2 demonstrates desmosomes failing to connect with keratin filaments in the basal keratinocytes (*arrowheads*). They appear to be smaller than normal desmosomes.

CASE 2

The 30-year-old father of case 1 also suffered blistering on the palms and soles during his infancy. Physical examination revealed reticular hyperpigmented macules involving most of his body (Fig 1, *d*) and wart-like papules with focal hyperkeratoses on his palms and soles (Fig 1, *e*). Electron microscopy on pigmented skin of case 2 showed the disorganized keratin filaments (KF) and aggregation of multiple densely packed compound melanosomes in the basal cells (Fig 2, *a*), which are the same findings reported previously.[1-2] The skin biopsy taken from a keratotic papule on the palm of case 2 demonstrated the number of desmosomes was with normal limits but some desmosomes failed to connect with the KF in the basal keratinocyte (Fig 2, *b*). Some desmosomes in the basal keratinocytes layers seemed to be smaller than normal controls.

The P25L mutation in the keratin 5 gene was detected in both cases, which now brings the total number of EBS-MP families with this mutation to 9. This result suggested that the P25L mutation was not derived from a common founder effect but does appear to be specific for EBS-MP. The P25L mutation is located in the amino-terminal head domain of keratin 5, which contain the keratin-desmoplakin I binding sites.[3] Recently, abnormalities of desmosome–associated molecules such as desmoplakin and desmoglein 1 have been shown to cause palmoplantar keratoderma,[4] which suggests that the disruption of binding between KF and desmosomal proteins causes abnormal keratinization resulting in hyperkeratotic lesions. Histologic findings of the wart-like keratotic papules characteristic of EBS-MP showed that some desmosomes had poor KF association or without KF binding in the basal keratinocytes. In bullous congenital ichthyosiform erythroderma, a genetic disorder affecting keratinization which is caused by mutations in keratin 1, KF were abnormally aggregated, but were still attached to the desmosomes.[5] Therefore, these findings of KF–desmosome disruption have significant implications for keratotic lesions in EBS-MP. The P25L mutation may cause peculiar keratotic lesions in EBS-MP.

Kana Yasukawa, MD, PhD
Daisuke Sawamura, MD, PhD
Masashi Akiyama, MD, PhD
Natsuki Motoda, MD
Hiroshi Shimizu, MD, PhD
Department of Dermatology
Hokkaido University Graduate School of Medicine

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