stimulating factor, which is stimulated by *P. acnes*.[3] It also inhibits the antigen-presenting activity of Langerhans cells and keratinocytes,[4] and suppresses the transcriptional activity of the androgen receptor.[5] These non-antibiotic effects are known as novel or anti-inflammatory effects.

Due to its topical application, it acts directly on epidermal keratinocytes at high local concentrations. The skin concentration of nadifloxacin 4 h after application was 82.3 ± 21.1 μg/g, and that at 12 h after application was 6.7 ± 5.8 μg/g,[2] which is similar to the concentration used in our experiment.

Matrix metalloproteinases are produced as inactive pro-MMP, which are then activated by proteolysis to become active MMP. In inflammatory tissues, pro-MMP are activated by the proteolytic enzymes which exist abundantly in inflammatory skin. In acne lesions, MMP-1, -13 and -9 are abundant,[1] and are thought to be induced by the inflammatory cytokines such as TNF-α produced by inflammatory infiltration or by *P. acnes* and involved in the scar formation of acne lesions. The inhibitory effect of nadifloxacin on these MMP could partly explain its clinical effectiveness in acne treatment. We also speculate that nadifloxacin has a preventive effect on scar formation. The induction of and the inhibitory effect on MMP-9 and -13 were controlled at the RNA level, while those of MMP-1 were not. The mechanism of the suppression of MMP-1 production is not clear and needs to be elucidated.

Acne vulgaris could be considered as a kind of chronic inflammatory condition, rather than as a bacterial infection. Topical application of nadifloxacin could be considered as one such anti-inflammatory treatment for acne vulgaris in addition to antimicrobial treatment.

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REFERENCES

1 Trivedi NR, Gilliland KL, Zhao W *et al.* Gene array expression profiling in acne lesions reveals marked upregulation of genes involved in inflammation and matrix remodeling. *J Invest Dermatol* 2006; **126**: 1071–1079.
2 Kuwahara K, Kitazawa T, Kitagaki H *et al.* Nadifloxacin, an antiacne quinolone antimicrobial, inhibits the production of proinflammatory cytokines by human peripheral blood mononuclear cells and normal human keratinocytes. *J Dermatol Sci* 2005; **38**: 47–55.
3 Jenny Kim, Ochoa MT, Krutzik SR *et al.* Activation of toll-like receptor 2 in acne triggers inflammatory cytokine responses. *J Immnol* 2002; **169**: 1535–1541.
4 Murata K, Sugita K, Kobayashi M *et al.* Nadifloxacin downmodulates antigen-presenting functions of epidermal Langerhans cells and keratinocytes. *J Dermatol Sci* 2006; **42**: 91–99.
5 Inui S, Nakao T, Itami S. Modulation of androgen receptor transcriptional activity by anti-acne reagents. *J Dermatol Sci* 2004; **36**: 97–101.

Dyschromatosis symmetrica hereditaria: A case report from Turkey, a new association and a novel gene mutation

Dear Editor,

A 5-year-old boy was referred to our clinic because of pigmentation involving the hands and feet, which had been present since he was 7–8 months old. There was no history of sun sensitivity. He had undergone dilatation operation three times because of achalasia. His parents and relatives were found to be free of similar symptoms. Dermatological examination revealed areas of mottled hyperpigmentation and hypopigmentation involving the dorsa of the hands and feet (Fig. 1a). Mild symptoms of the disease were also found on the knees and there were hyperpigmented freckle-like (1–2 mm) macules on the cheeks (Fig. 1b). Routine laboratory tests were unremarkable. Histopathological examination of skin biopsy specimen taken from a pigmented macule revealed melanin incontinence in the basal layer and a hypopigmented macule was non-specific. The *ADAR1* gene was sequenced for our patient and his family members. It detected a pathological mutation, c.1110-1111delCAp.N370fsX373 in exon 2, in our patient and his father (Fig. 2). However, the same mutation was not detected in his mother or sister. Based on these findings, our patient was diagnosed as having dyschromatosis symmetrica hereditaria (DSH).

Dyschromatosis symmetrica hereditaria is an autosomal dominant pigmentary disorder characterized by a combination of hyperpigmented and hypopigmented macules distributed on the dorsal aspects of the extremities and freckle-like macules on the face.[1] Although DSH is a rare autosomal dominant genodermatosis predominantly occurring among Japanese and Korean individ-

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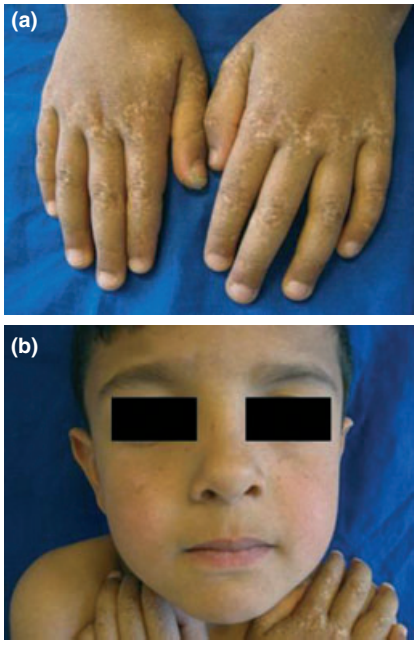

Figure 1. (a) Reticulated hyperpigmented and hypopigmented macules on the dorsa of hands and feet. (b) Hyperpigmented freckle-like (1–2 mm) macules on the cheeks.

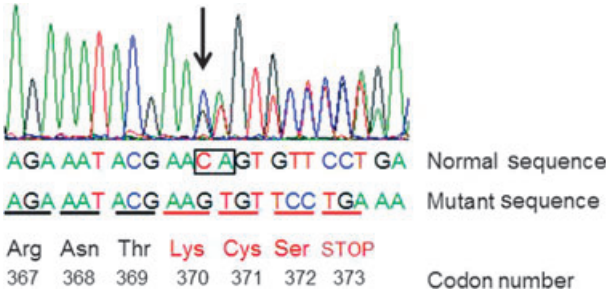

Figure 2. DNA sequence of the patient's *ADAR1* gene, from c.1099 to c.1121. The boxed c.1110_1111CA was deleted in the mutant sequence of the case, which leaded to a frame-shift and resulted in a stop at codon 373. Deletion of the two nucleotides occurred at the point marked with an arrow.

uals, it occurs in families of every ethnic origin all over the world.[1,2] The widest series on this topic was reported by Oyama *et al.*[2] in 1999. In that paper, 185 cases of DSH are reviewed and clinical, histological and genetic features of this condition are delineated. Of the 185 cases, 170 (92%) were reported from Japan.[2] To our knowledge, Aliağaoğlu *et al.*[3] reported the first Turkish patient that presented hyperpigmented and hypopigmented macules in a generalized distribution with dyschromatosis universalis hereditaria in 2008.[3]

The cause and pathogenesis of the disease have not been clarified. The pattern inheritance was basically autosomal dominant. On the other hand, there was no family history of DSH in the great majority of cases (114/185) and the autosomal dominant form of DSH is due to a mutation in the DSRAD gene (*ADAR1*) which encodes a dsRNA-specific adenosine deaminase on an RNA editing enzyme.[1,2] Our patient's parents and relatives were found to be free of symptoms except his father. The novel pathological mutation named c.1110-1111delCAp.N370fsX373 in exon 2 was detected in our case as well as his father. So, we examined his father in detail but there was no finding except a few slightly hyperpigmented macules on the extensor surfaces of his feet, although he described to us that he had had the same hyperpigmented macules on the hands and feet during his childhood but that they had disappeared over time. However, none of the previous studies reported seasonal changes or spontaneous regression with age.[3]

In the great majority of cases, DSH is present as an isolated entity.[4] Our patient was associated with achalasia and this is the first reported case of DSH and achalasia in the same patient. Achalasia is a rare esophageal motility disorder characterized by absent peristalsis and failure of the lower esophageal sphincter to relax. There is increasing evidence that genetic alterations might play an important but underestimated role.[5] This association is probably coincidental but if the two entities are clarified, a significant association may be described between the two facts. We believe that more genetic studies on DSH and achalasia are needed to clarify this association.

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REFERENCES

1 Suzuki N, Suzuki T, Inagaki K *et al.* Mutation analysis of the *ADAR1* gene in dyschromatosis symmetrica hereditaria and genetic differentiation from both dyschromatosis universalis hereditaria and acropigmentatio reticularis. *J Invest Dermatol* 2005; **124**: 1186–1192.

2 Oyama M, Shimizu H, Ohata Y *et al.* Dyschromatosis symmetrica hereditaria (reticulate acropigmentation of Dohi): report of a Japanese family with the condition and a literature review of 185 cases. *Br J Dermatol* 1999; **140**: 491–496.

3 Aliagaoglu C, Atasoy M, Yıldırım U *et al.* Generalized dyspigmentation on the body. *Clin Exp Dermatol* 2009; **34**: 737–738.

4 Darouti M, Marzouk SA, Fawzi M *et al.* Reticulate acropigmentation of Dohi: a report of two new associations. *Int J Dermatol* 2004; **43**: 595–596.

5 Gockel HR, Schumacher J, Gockel I, Lang H, Haaf T, Nöthen MM. Achalasia: will genetic studies provide insights? *Hum Genet* 2010; **128**: 353–364.