the same velvet antler preparation were all negative, implying that the pustular reaction in our patient was not an irritant reaction.

Herbal medications, which are major components of complementary and alternative medicines, are easily accessible and have become increasingly popular worldwide, and healthy people as well as patients with chronic illness take herbal medicines as part of health-seeking behaviours. Consequently, they have emerged as significant causes of adverse drug reactions such as toxic hepatitis or drug eruption in recent years. A major concern is that it is not always possible to know what exactly is contained in herbal remedies; even though we can identify the contents in some cases, it is still often not clear whether the causative agent of the drug eruption is some constituent of the herbs or a synthetic chemical, heavy metal or possible contaminant contained in the herbal medication.

Velvet antler is known to have anti-inflammatory, antineoplastic, immune-stimulatory and growth-promoting effects and to contain several amino acids, alkaline earth metals and other minerals.[5] Although we also could not establish which substance was responsible for the generalized pustular eruption in our patient, velvet antler must be the culprit of the AGEP because the skin eruption developed after taking it without any underlying medical conditions and the patch test revealed a positive reaction; our case might necessitate a more specific approach to the research into the safety of herbal remedies.

In conclusion, we present a unique case of AGEP induced by taking velvet antler. Herbal medicines such as velvet antler should always be considered as a cause of drug eruption including AGEP. Dermatologists should be familiar with the cutaneous adverse effects of herbal medicines as well as conventional medicines and a thorough history taking is mandatory when considering a patient with suspected drug eruption.

Departments of Dermatology and T.Y. Yoon
**Internal Medicine, School of Medicine and* D.Y. Lee
Medical Research Institute, Y.J. Kim
Chungbuk National University, J.Y. Lee
Cheongju, Chungbuk 361-763, M.K. Kim*
Korea
E-mail: tyyoon@chungbuk.ac.kr

References

1 Manzur A, Kiyani KA. Acute generalized exanthematous pustulosis triggered by intake of herbal medications. *Int J Dermatol* 2006; **45**:1247–8.
2 Choi MJ, Kim HS, Park HJ *et al.* Clinicopathologic manifestations of 36 Korean patients with acute generalized exanthematous pustulosis: a case series and review of the literature. *Ann Dermatol* 2010; **22**:163–9.
3 Park YM, Park JG, Kang H *et al.* Acute generalized exanthematous pustulosis induced by ingestion of lacquer chicken. *Br J Dermatol* 2000; **143**:230–2.
4 Min JA, Park HJ, Cho BK *et al.* Acute generalized exanthematous pustulosis induced by *Rhus* (lacquer). *J Am Acad Dermatol* 2010; **63**:166–8.
5 Zhao L, Li JH, Zhu DZ *et al.* Principal component analysis of nutrients in five varieties of velvet antler (Cornu Cervi Pantotrichum) [in Chinese]. *Guang Pu Xue Yu Guang Pu Fen Xi* 2010; **30**:2571–5.

Mutational analysis in familial and sporadic patients with white sponge naevus

DOI: 10.1111/j.1365-2133.2011.10404.x

Madam, We describe eight unrelated Chinese subjects with asymptomatic, white, soft, corrugated or shaggy plaques in the oral mucosa (Fig. 1a,b). After informed consent, biopsies were performed in all cases. Histologically, the affected lesions showed different degrees of epithelial oedema or vacuolization extending from the parabasal region to the near surface, especially in both the shallow spinous and the keratinized layers, dispersed keratohyalin granules in the shallow spinous layer (Fig. 1c,d), and, most importantly, conspicuous perinuclear eosinophilic condensation of the cytoplasm of prickle cells (Fig. 1e,f). Based on the clinical and histological features, all cases were identified as white sponge naevus (WSN; OMIM 193900). Three of the eight probands, whose families were affected, were classified into group A (subjects A1–3); the remaining five were sporadic cases and were classified into group B (subjects B1–5). The extraoral mucosa, including nasal, laryngeal, oesophageal, anal and vaginal mucosa, was inspected and no abnormality was found in any of the patients.

Genomic DNA was isolated from venous blood samples of the subjects. By DNA sequencing of the entire coding regions of both the *KRT4* and *KRT13* genes, a novel heterozygous missense mutation in the *KRT13* gene (c.340 C>T) was revealed in subject A1 (Fig. 2a) and confirmed to be a pathogenic mutation; results were negative in 60 normal controls. The mutation predicted a substitution of arginine 114 by cysteine (p.R114C) in keratin 13. Two causal mutations previously reported[1,2] were identified in subjects A2 (c.344 T>C in the *KRT13* gene, p.L115P) (Fig. 2b) and A3 (c.478–480delCAA in the *KRT4* gene, p.160delN) (Fig. 2c). In one patient (subject B1) from the sporadic group, the p.160delN mutation was detected. Similar clinical appearances were displayed by the probands with the different *KRT* mutational genotypes. No clinical phenotypic distinction was shown between the hereditary group (group A) and the sporadic group (group B) (Table 1).

WSN is a rare autosomal-dominant disorder. It predominantly affects the noncornified stratified squamous epithelium.[3] It is characterized by bilateral, white, soft, 'spongy' plaques in the mucosa. The surface of the plaque is thick and folded, and can be peeled away from the underlying tissues. The buccal mucosa is most commonly affected, followed by the mucosa of the lip, lingual margin, ventral tongue and floor of the mouth. Extraoral involvement in nasal, esophageal, rectal or anogenital mucosa is occasionally reported.[4]

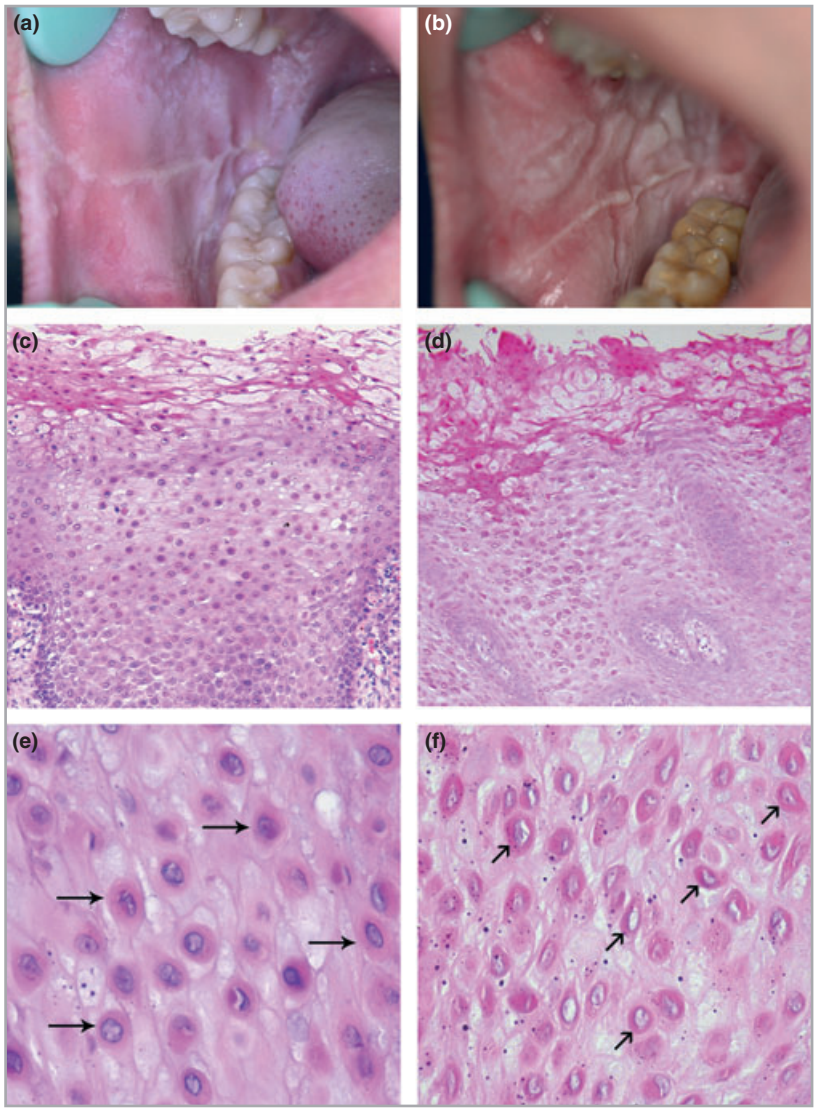

Fig 1. Clinical and histological features of the subjects. Diffuse white lesions in the buccal mucosa of subject A1 (group A, familial) (a) and subject B1 (group B, sporadic) (b). Thickened epithelium, vacuolization in the shallow spinous layer and within the keratinized layer (haematoxylin–eosin stain; original magnification: × 40) in subject A1 (c) and subject B1 (d). Perinuclear eosinophilic condensation seen under a light microscope in subject A1 (e) and subject B1 (f) (haematoxylin–eosin stain; original magnification: × 100). Lesions are indicated by arrows.

Similar oral white 'spongy' plaques can occur in pachyonychia congenita (OMIM 167200) or hereditary benign intraepithelial dyskeratosis (OMIM 127600), two other autosomal-dominant epithelial disorders, which additionally present with hypertrophic nail dystrophy and palmoplantar keratoderma[5] or bulbar conjunctival abnormalities,[6] respectively. Because there was no extraoral involvement in our cases, these disorders could be excluded.

WSN is putatively attributed to mutations of keratin 4 and/or keratin 13, which are specifically composed of keratin intermediate filaments in pairs in the spinous layer of non-keratinizing stratified epithelium affected by the disorder. In human keratin 13, missense mutations of p.L119P, p.N112S, p.L115P, p.M108T, p.L111P and p.R114H have been shown to be associated with WSN.[2,6–9] In keratin 4, the causal mutations are p.160delN,[6] p.153–154insQ[3] and p.E449K.[10] In mutant mouse models, a missense mutation of p.N154S in keratin 4 was also shown to induce the clinical WSN phenotype.[11] Recently, in exon 2B of *KRT4*, a new candidate missense mutation of c.1829 G>A (p.E520K) was reported to be responsible for a Chinese WSN pedigree.[12] In the present study, this mutation was not detected, but the mutations p.L115P and p.160delN were confirmed to be pathogenic for WSN by sequencing the coding regions of *KRT4* and *KRT13*. Furthermore, a novel heterozygous missense mutation of p.R114C (c.340 C>T) in keratin 13 was revealed. The arginine at codon 114 is highly conserved and its biological importance has also been demonstrated by Nishizawa *et al.*[9] who found the missense mutation p.R114H (c.341 G>A) in a WSN proband.

Fulfilling the characteristics of autosomal-dominant disorders, the majority of causal mutations addressed so far come from different WSN pedigrees. However, a 48-year-old Japanese woman was recently reported by Nishizawa *et al.*[9] to be a sporadic case with a pathogenic gene change. Similarly, we identified a *KRT4* gene mutation of p.160delN in a sporadic proband.

Paradoxically, in our study, four other sporadic probands with the clinical and histological manifestations of WSN exhibited no hereditary and mutational evidence. It has

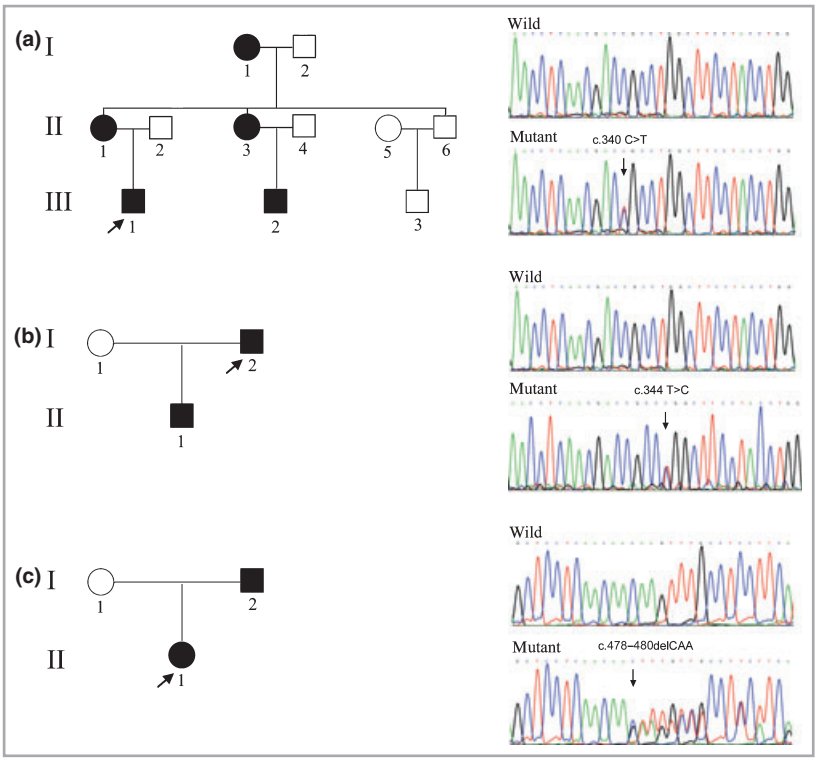

Fig 2. Family pedigrees (left panels) and sequencing results (right panels). Left panels, affected patients are represented by black symbols; the numbers under the symbols are the identification numbers of subjects in the pedigree; the initial proband is indicated by an arrow. Right panels, (a) a C>T transition at the 340 nucleotide of KRT13 in subject A1; (b) a T>C substitution at nucleotide 344 of KRT13 in subject A2; (c) a 3-bp (CAA) deletion of nucleotide 477–479 of KRT4 in subject A3. The mutated nucleotides are indicated by arrows.

Table 1 Data for the probands with white sponge naevus

Case	Sex	Age at onset (years)	Sites affected	Keratin mutation
Group A (familial)				
A1	M	13	Bilateral B, bilateral V	p.R114C in K13[a]
A2	M	7	Bilateral L, bilateral B, bilateral V	p.L115P in K13
A3	F	12	Bilateral B	p.160delN in K4
Group B (sporadic)				
B1	M	16	Bilateral L, bilateral B, bilateral V	p.160delN in K4
B2	M	12	Bilateral B	No gene mutation
B3	F	10	Bilateral B, bilateral V	No gene mutation
B4	M	11	Bilateral L, bilateral C	No gene mutation
B5	M	25	Lower L, bilateral B, bilateral V	No gene mutation

B, buccal mucosa; C, oral commissure mucosa; L, inner labial mucosa; V, ventral tongue.
[a]Novel mutation.

been suggested that mutational analysis is warranted to reach an accurate diagnosis of WSN. In contrast to the typical WSN cases, the sporadic patients were heterogeneous and various causes might be responsible for their clinical and histological features other than keratin 4 or 13 mutations.

Acknowledgments

We are grateful to Ms Xuejie Chen (School and Hospital of Stomatology, Peking University, Beijing, China), Dr Jia Ning (Daqing Oilfield General Hospital Group, Daqing, China) and Dr Xiangqun Xia (Handanshi Stomatological Hospital, Hebei, China) for their assistance in collecting cases.

Department of Oral Medicine, School and Hospital of Stomatology, Peking University, Beijing 100081, China X. Liu
Q. Li*
**Department of Medical Genetics, Peking University Health Science Center, Beijing 100083, China* Y. Gao†
S. Song*
H. Hua
†Oral Pathology, School and Hospital of Stomatology, Peking University, Beijing 100081, China
Correspondence: Shujuan Song or Hong Hua.
E-mail: shujuansong@gmail.com; honghua1968@yahoo.com.cn

References

1 Rugg EL, McLean WH, Allison WE *et al.* A mutation in the mucosal keratin K4 is associated with oral white sponge nevus. *Nat Genet* 1995; **11**:450–2.
2 Rugg EL, Magee G, Wilson N *et al.* Identification of two novel mutations in keratin 13 as the cause of white sponge nevus. *Oral Dis* 1999; **5**:321–4.
3 Terrinoni A, Candi E, Oddi S *et al.* A glutamine insertion in the 1A alpha helical domain of the keratin 4 gene in a familial case of white sponge nevus. *J Invest Dermatol* 2000; **114**:388–91.
4 Jorgenson RJ, Levin LS. White sponge nevus. *Arch Dermatol* 1981; **117**:73–6.
5 Bowden PE, Haley JL, Kansky A *et al.* Mutation of a type II keratin gene (K6a) in pachyonychia congenital. *Nat Genet* 1995; **10**:363–5.
6 Terrinoni A, Rugg EL, Lane EB *et al.* A novel mutation in the keratin 13 gene causing oral white sponge nevus. *J Dent Res* 2001; **80**:919–23.
7 Richard G, De Laurenzi V, Didona B *et al.* Keratin 13 point mutation underlies the hereditary mucosal epithelia disorder white sponge nevus. *Nat Genet* 1995; **11**:453–5.
8 Shibuya Y, Zhang J, Yokoo S *et al.* Constitutional mutation of keratin 13 gene in familial white sponge nevus. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2003; **96**:561–5.
9 Nishizawa A, Nakajima R, Nakano H *et al.* A *de novo* missense mutation in the keratin 13 gene in oral white sponge naevus. *Br J Dermatol* 2008; **159**:974–5.
10 Chao SC, Tsai YM, Yang MH *et al.* A novel mutation in the keratin 4 gene causing white sponge naevus. *Br J Dermatol* 2003; **148**:1125–8.
11 McGowan KA, Fuchs H, Angelis MH *et al.* Identification of a keratin 4 mutation in a chemically induced mouse mutant that models white sponge nevus. *J Invest Dermatol* 2007; **127**:60–4.
12 Zhang JM, Yang ZW, Chen RY *et al.* Two new mutations in the keratin 4 gene causing oral white sponge nevus in Chinese family. *Oral Dis* 2009; **15**:100–5.

Funding sources: This work was supported by the National Key Health Research Project Foundation of China during the 11th Five-Year Plan Period (2006BAI05A07).

Conflicts of interest: none declared.

News and Notices

DOI: 10.1111/j.1365-2133.2011.10504.x

20th EADV Congress 20–24 October, 2011, Lisbon

The Annual Congress of the European Academy of Dermatology and Venereology will be held for the second time in Lisbon, from the 20th to the 24th of October 2011.

For more details please contact the Local Secretariat: MUNDICONVENIUS, Av. 5 de Outubro, 53 -2.°/1050–048 Lisbon/Portugal/T: +351 213155135/F: +351 213558002/ e-mail: info@eadvlisbon2011.org

Online registration at http://www.eadvlisbon2011.org

The World Academy of Cosmetic Surgery, 2nd Annual Meeting, Marriott Hotel, Vienna, Austria. 1–4 September 2011

Main topics:

Video Sessions:

Face Lift Surgery	Ingection Therapy: Botox and Fillers
Oculoplastic Surgery	Facial Surgery
Liposuction	Luposuction
Body Contouring-Body Lifts	Lipotransfer-Stem cells
Rhinoplasty	New technologies
Lectures:	**Live Workshops (in the hotel):**
Laser Therapy	Minimal invasice therapies

International Congress Secretary:
Dr. Peter Lisborg
Information: Ärztezentrale Med.Info, Helferstorferstraße 4, A-1014 Wien
Pho.: (+43/1) 531 16-48
Fax: (+43/1) 531 16-61
e-mail: azmedinfo@media.co.at

Fondation René Touraine Scientific Meeting of the Fondation Renè touraine 2011:
Musée des Moulages, Hôpital Saint-Louis, 1 avenue Claude Vellefaux, 75010 Paris.
Subject: ''Keratinocytes and cutaneous innate immunity''
Invited speakers: T. LUGER, M.C. LEITE, J.-M. SCHRÖDER, M. MEMPEL, K. WOLK, J. SCHAUBER, M. SCHMUTH, M. GILLIET, P. MUSETTE
Registration: Fondation René Touraine, Hôpital St Louis, Pavillon Bazin, 1, avenue Claude Vellefaux–F-75475- PARIS cedex 10-(France)
Tel. 33-1-53- 72 20 60
Fax: 33-1- 53 72 20 61
e-mail: christina.pitton@fondation-r-touraine.org
Or in the site of the Fondation René Touraine:
http://www.fondation-r-touraine.rog/Scientific-meetings#sommaire

Applied Photodermatology course 21st–22nd May 2012, BAD House, London

The 2012 Applied Photodermatology course will be held at the Headquarters of the British Association of Dermatologists in Central London, 21st–22nd May 2012, organised by Professor Alex Anstey, Royal Gwent Hospital, Newport. The 2 day course meets a number of educational objectives teaching delegates: how to evaluate patients with photosensitivity; how to identify the pros and cons of prephototherapy phototesting in PUVA and UVB; and how to