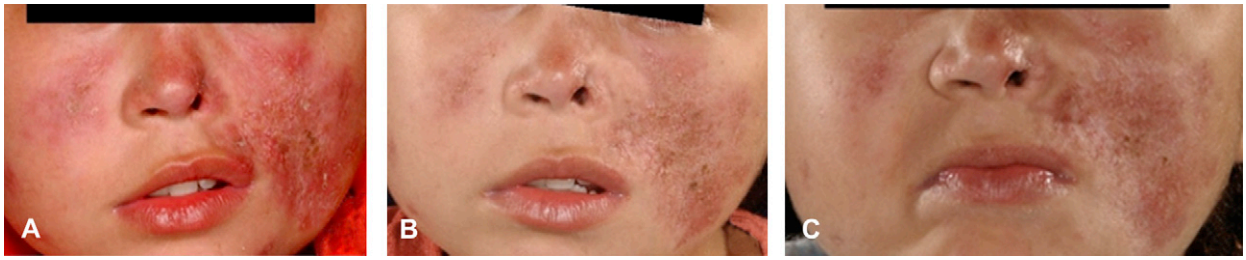

Fig 2. **A**, Before treatment with infliximab; **B**, 4 weeks after treatment with infliximab; **C**, 12 weeks after treatment with infliximab.

infliximab despite a history of lymphoma. We had concerns as to whether infliximab may increase the already elevated risk of lymphoma in AT patients, but the balance of risks was thought to support its use in this child. Our experience supports use of TNF antagonists to treat severe progressive granulomas associated with primary immunodeficiency disorders after excluding an infective cause and failure of standard therapy. Infliximab was well tolerated and was not thought to have contributed to the death of this child.

Angana Mitra, MBChB,[a] Jimmy Gooi, MBChB,[b] Jonathan Darling, MBChB,[c] and Julia A. Newton-Bishop, MBChB[a]

Departments of Dermatology,[a] Immunology,[b] and Paediatrics,[c] St James's University Hospital, Leeds, United Kingdom

Funding sources: None.

Conflicts of interest: None declared.

Correspondence to: Angana Mitra, MBChB, Department of Dermatology, St James's Hospital, Beckett Street, Leeds, LS9 7TF

E-mail: a.mitra@leedsac.uk

REFERENCES

1. Aukrust P, Lien E, Kristoffersen AK, Muller F, Haug CJ, Espevik T, et al. Persistent activation of the tumor necrosis factor system in a subgroup of patients with common variable immunodeficiency—possible immunologic and clinical consequences. Blood 1996;87:674-81.
2. Mitra A, Pollock B, Gooi J, Darling JC, Boon A, Newton-Bishop JA. Cutaneous granulomas associated with primary immunodeficiency disorders. Br J Dermatol 2005;153:194-9.
3. Schroeder S, Swift M, Sandoval C, Langston C. Interstitial lung disease in patients with ataxia-telangiectasia. Pediatr Pulmonol 2005;39:537-43.
4. Hatab AZ, Ballas ZK. Caseating granulomatous disease in common variable immunodeficiency treated with infliximab. J Allergy Clin Immunol 2005;116:1161-2.
5. Lin JH, Liebhaber M, Roberts RL, Dyer Z, Stiehm ER. Etanercept treatment of cutaneous granulomas in common variable immunodeficiency. J Allergy Clin Immunol 2006;117:878-82.
6. Askling J, Baecklund E, Granath F, Geborek P, Fored M, Backlin C, et al. Anti-TNF therapy in RA and risk of malignant lymphomas. Relative risks and time-trends in the Swedish Biologics Register. Ann Rheum Dis 2008;68:648-53.

doi:10.1016/j.jaad.2010.06.060

Linear IgA disease limited to the oral mucosa

To the Editor: A 38-year-old Chinese woman was referred to our clinic by her dentist. She had been suffering from gingival erythema and pain, as well as difficulty in eating for 2 years. There was no history of medication before the occurrence of the oral lesions. The woman was otherwise healthy and had no history of allergy. Examination revealed localized erythema of the gingiva. White striae and patches were found on the labial and buccal side of the maxillary gingiva and the vestibular groove of the molars of the right mandible (Fig 1). Nikolsky's sign was negative. There were no other oral or extraoral lesions. A provisional diagnosis of oral lichen planus (OLP) was made. An incisional biopsy specimen was taken from the attached gingiva immediately adjacent to the erythema. The routine histopathological examination did not show the typical pathological changes of OLP, such as parakeratosis and lymphocytic infiltration in the lamina propria. However, focal separation of the epithelium from lamina propria (Fig 2, *A* and *B*) was observed. Direct immunofluorescence (DIF) showed linear deposition of immunoglobulin (Ig) A and IgM along the basement

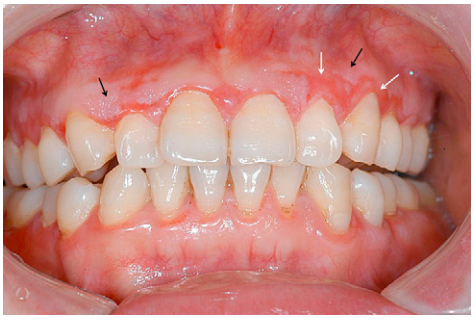

Fig 1. Regional erythema (*white arrow*) and white patches on the gingiva (*black arrow*).

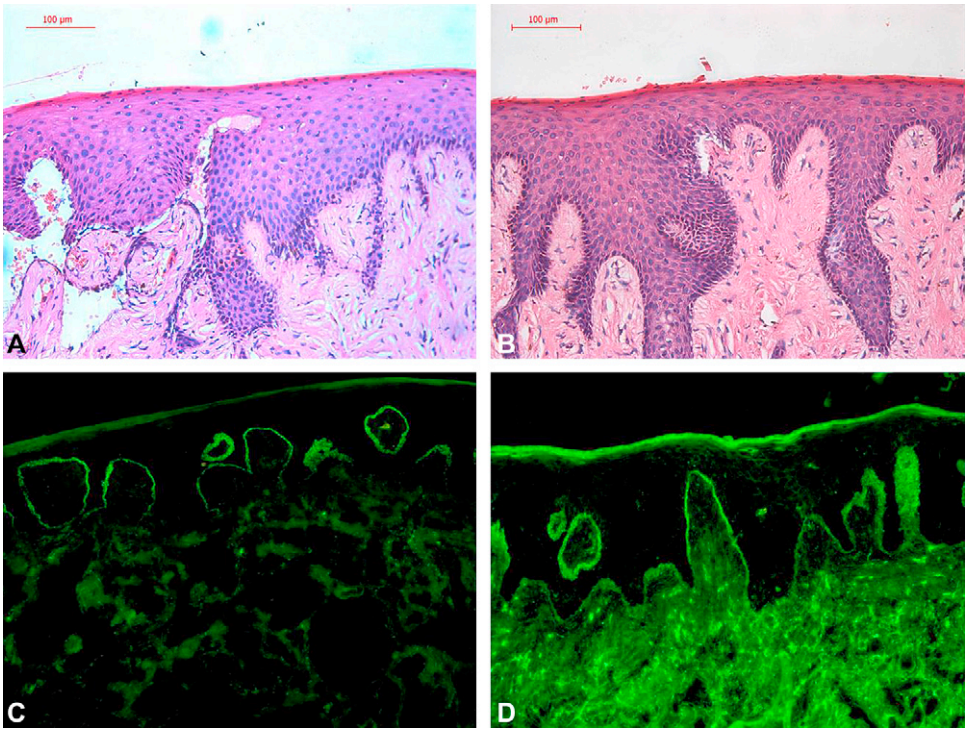

Fig 2. **A** and **B**, Focal separation of epithelium from lamina propria (hematoxylin-eosin stain, original magnification: ×200); **C** and **D**, Direct immunofluorescence demonstrates linear deposition of IgA and IgM along basement membrane zone, respectively.

membrane (Fig 2, *C* and *D*). IgG and complement C3 were undetectable. A diagnosis of linear IgA disease (LAD) was made according to these findings.

Intralesional injection of triamcinolone was performed. At review after 2 weeks, the erythema had diminished and pain had been greatly relieved. Topical dexamethasone paste was used to control the remaining lesion. During subsequent visits, no new lesion was seen. The patient has been symptom free for approximately 3 months.

The etiology of LAD is still unclear. Gluten-sensitive enteropathy has been reported in some patients with adult LAD.[1] However, the patient in this case has no history or symptoms of this disease.

DIF on fresh tissue is the gold standard for diagnosis of LAD. The typical manifestation is a continuous linear IgA deposition along the basement membrane. Occasionally, other immunoreactants such as IgG, IgM, and complement C3 may also be detected.[2] When both IgA and other immunoreactants are present, it is difficult to differentiate LAD from other subepidermal blistering diseases, such as pemphigoid and epidermolysis bullosa acquisita.[3,4] However, IgG is the major type of autoantibody in those diseases. Therefore LAD can be distinguished from those diseases by comparing the fluorescence intensity of IgA and IgG against the clinical and immunopathological features.[2] In the current case, IgA and IgM deposits were detected; however, IgG was undetectable. Therefore we made the diagnosis of LAD by the exclusion of pemphigoid and epidermolysis bullosa acquisita. Interestingly, in this case, discontinuity of IgA deposition was found in some regions (see Fig 2, *C*). We speculated that the discontinuity of IgA deposition might be a sign of mild immune damage at the basement membrane zone, which was consistent with the relatively mild oral lesions and focal separation of epithelium from lamina propria. Further investigation is needed to confirm our suspicion.

LAD limited to the oral mucosa is rare; it has not been reported in Chinese people before. However, we inferred from this case that localized oral LAD might be more prevalent than we thought it was and was easy to be misdiagnosed as other diseases. So we suggest that DIF should be performed as a routine examination on patients with chronic erythematous, erosive, and vesicular lesions of the oral mucosa.

Hongxia Dan, PhD, DDS,[a] Rui Lu, PhD, DDS,[a] Wei Li, MD,[b] Qianming Chen, PhD, DDS,[a] and Xin Zeng, PhD, DDS[a]

State Key Laboratory of Oral Diseases and Department of Oral Medicine, West China College of

Stomatology, Sichuan University,[a] and the Department of Dermatology, West China Hospital, Sichuan University,[b] Chengdu, China

Funding sources: The National Natural Science Foundation of China (No. 30930100 and 30772424) and the Science Funds for Talented Professionals of Sichuan Province in China (No. 09ZQ026-037).

Conflicts of interest: None declared.

Correspondence to: Xin Zeng, PhD, DDS, State Key Laboratory of Oral Diseases, West China College of Stomatology, Sichuan University, No. 14, Sec 3, Renminnan Road, Chengdu, Sichuan 610041, China

E-mail: zengxin22@163.com

REFERENCES

1. Lewis MAO, Yaqoob NA, Emanuel C, Potts AJC. Successful treatment of oral linear IgA disease using mycophenolate. Oral Surg Oral Med Oral Pathol Oral Radiol Endodontol 2007;103:483-6.
2. Guide SV, Marinkovich MP. Linear IgA bullous dermatosis. Clin Dermatol 2001;19:719-27.
3. Peters MS, Rogers MS. Clinical correlations of linear IgA deposition at the cutaneous basement membrane zone. J Am Acad Dermatol 1989;20:761-70.
4. Cozzani E, Drosera M, Parodi A, Carrozzo M, Gandolfo S, Rebora A. Frequency of IgA antibodies in pemphigus, bullous pemphigoid and mucous membrane pemphigoid. Acta Derm Venereol 2004;84:381-4.

doi:10.1016/j.jaad.2010.07.007

Hydroxyurea-associated squamous dysplasia in a monozygotic twin

To the Editor: The sudden onset of actinic keratoses (AKs), cutaneous squamous cell carcinomas (SCC), and squamous dysplasia in a photodistribution has been reported in mostly elderly patients taking hydroxyurea for hematologic conditions. Although there have also been case series reported, case-control studies are lacking, raising concerns as to the validity of the observed association.

An 80-year-old woman presented with a 2-year history of multiple red scaly lesions on the face. On general skin examination her skin was noted to be hyperpigmented in a photodistribution. There were multiple large hyperkeratoses on sun-exposed sites—cheeks, forehead, lower lip, and temple—and on the backs of her hands (Fig 1). She was accompanied by her monozygotic twin who had no hyperkeratotic lesions, was not hyperpigmented, and looked 20 years younger. Both twins had lived in the same region, worked in comparable professions (housekeeper and sales clerk), and shared daily hikes together. Their sun exposure was similar on history and they had the same skin phototype (Fitzpatrick II). The patient had essential thrombocytosis, treated with hydroxyurea for the previous 13 years (dose 750 mg/d, cumulative dose approximately 3500 g). This was her only medication and her twin sister took no medications. There was no history of skin cancer and neither twin had ever smoked.

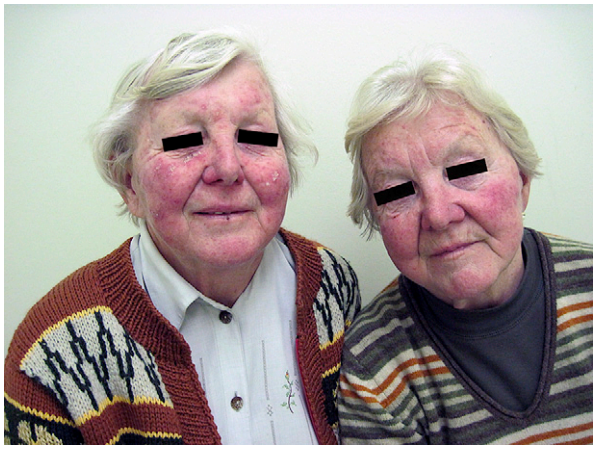

Fig 1. Eighty-year-old monozygotic twins, only one of whom shows extensive squamous dysplasia on the face.

Excised lesions were reported as Bowenoid AK and Bowen disease.

Since the first report in 1992, there have been an increasing number of case reports of SCC and AK developing in association with hydroxyurea use.[1] Some of these cases have died from metastatic SCC.[1] The majority of patients had Fitzpatrick type I or II skin, had been taking hydroxyurea for many years for myeloproliferative diseases or sickle cell anemia, and had other well-recognized skin side effects of hydroxyurea such as xerosis and hyperpigmentation. The AKs or SCCs were limited to sun-exposed skin, yet there had been no history of treatment required for AK or SCC before hydroxyurea use. The patient presented shares these same features and is therefore consistent with the diagnosis of hydroxyurea-associated squamous dysplasia.

Two large case series of patients with hydroxyurea have been reported. A prospective study during a 2-year period observed 26 patients on hydroxyurea for more than 6 months: 8 patients developed AKs and two developed SCC.[2] A retrospective study of 158 patients treated with hydroxyurea for chronic myeloid leukemia found 21 patients had severe cutaneous side effects including 5 with cutaneous SCC or keratoacanthomas on sun-exposed skin.[3]

A large twin study of skin pattern deterioration found the genetic influence on skin pattern decreases with age, from 86% at age 12 years, to 62% in adults