toxic substances have been detected in the seeds, root, and bark of the plant.[3]

One case of urticaria was described in an article published in the journal of the Spanish Society of Allergology and Immunology. The authors described a 54-year-old man who presented with urticaria after taking a food supplement consisting of powdered moringa leaves.[5] An article recently published by the Sri Lankan medical association described Stevens–Johnson syndrome in a 53-year-old man who had consumed moringa leaves.[6] Rash and urticaria are the most frequently reported immediate adverse reactions associated with herbal medicines.[2]

The few published studies of moringa have demonstrated that it contains the potentially toxic agents moringin and moringinin, plant alkaloids that are structurally very similar to ephedrine.[7] Both ephedrine and pseudoephedrine exert adverse cutaneous effects, which include eruption, fixed drug eruption, acute generalized exanthematous pustulosis, and erythroderma.[8,9]

Descriptions of lesion histology are absent from most of these reports and, if included, tend to consist of variable, nonspecific changes. Reported findings include hydropic changes in the basement membrane and perivascular infiltrate, but not necrosis as intense as that observed in our patient's biopsy, the results of which were compatible with Stevens–Johnson syndrome.[10]

These types of plants are classified as dietary foods or supplements, and therefore do not require evidence of quality, efficacy, or safety prior to commercialization. Due to the large number of components that a single plant can contain, evaluation of efficacy and safety is much more complex than for conventional drugs.

We wish to highlight the importance of monitoring the consumption and adverse effects of *M oleifera*, given the growing market for this plant in Europe.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Hereditary Epidermolysis Bullosa: A Case Series☆

Epidermólisis ampollosa hereditaria: serie de casos

To the Editor,

Hereditary epidermolysis bullosa (EB) comprises a heterogeneous group of genodermatoses characterized by mechanical skin fragility.[1,2]

We conducted a descriptive, retrospective study of all patients genetically diagnosed with EB at Hospital Clínico Universitario de Valencia between 1968 and 2018. There were no cases on record that had been assessed without a molecular diagnosis. In 2018, the corresponding health district, La Malvarrosa, offered coverage to a population of 344 019 people.[3]

The following variables were analyzed: age at diagnosis, current age, family history of EB, clinical manifestations, location of lesions, dermoepidermal cleavage plane, histologic features, mutated gene, mutation, mode of inheritance, zygosity, type of EB, treatment, and complications (Table 1). Presence of the following complications was assessed: oral cavities, oral erosions and ulcers, gastroesophageal reflux, constipation, growth retardation, anemia,

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Table 1 Clinical and epidemiological characteristics of patients with EB.

Sex	Patient 1 Male	Patient 2 Male	Patient 3 Female	Patient 4 Female	Patient 5 Female	Patient 6 Female	Patient 7 Female	Patient 8 Female
Age at clinical diagnosis/current age, y	Newborn/11	Newborn/6	Newborn/14	School-going age/13	Infant/9	Newborn/2	Preschool age/51	New born/died at 37 y
Family history	Yes	Yes	No	Yes	No[a]	No	Yes	Yes
Clinical Manifestations	Blisters	Blisters	Blisters	Prurigo nodularis–type papules and nodules	Blisters	Blisters	Blisters	Blisters
	Milium cysts Nail dystrophy	Milium cysts Nail dystrophy	PPK Sparse hair	Milium cysts Pruritus	Milium cysts Sparse hair	Milium cysts	Milium cysts Anonychia	Tooth loss No nails
	Pruritus	Pruritus	Hair casts		Nail dystrophy		Pruritus	Flexion contractures
			Nail dystrophy Pruritus		Pruritus			Pruritus
Lesion site	Face Extremities Acral	Extremities Acral location	Trunk Buttocks Extremities Acral Oral mucosa	Trunk Extremities Acral location	Face Trunk Buttocks Extremities Acral location	Face Trunk Buttock Extremities Acral location Oral mucosa	Trunk Extremities Acral location	Trunk Extremities Acral location
Histology[b]	Intraepidermal /EM	Intraepidermal / EM	Intraepidermal /EM	Sublamina densa/antigen mapping	Sublamina densa/antigen mapping	Sublamina densa/antigen mapping	Not performed[c]	Not performed[c]
Mutated gene/ mutation/ age at molecular diagnosis, y	*KRT5*/ p.Gly12rg/1	*KRT5*/ p.Gly12rg/1	*KRT5*/ p.Glu477Lys/1	*COL7A1*/ p.Arg1814_Gly1815delinsLeuHis/7	*COL7A1*/ p.Gly1377Aspfs*22/5	*COL7A1*/ Gly2177Trpfs*113/1	*COL7A1*/ Gly2177Trpfs*113/48	*COL7A1*/ Gly2177Trpfs*113/34
Inheritance/ zygosity	AD Heterozygosity	AD Heterozygosity	AD Heterozygosity	AD Heterozygosity	AR Homozygosity	AD Heterozygosity	AD Heterozygosity	AD Heterozygosity
EB subtype	Localized EBS	Localized EBS	Severe generalized EBS	Pruritic DEB	Severe generalized DEB	Generalized DEB	Generalized DEB	Generalized DEB

Table 1 (*Continued*)

Sex	Patient 1 Male	Patient 2 Male	Patient 3 Female	Patient 4 Female	Patient 5 Female	Patient 6 Female	Patient 7 Female	Patient 8 Female
Treatment	Topical antiseptic Antihistamines Proper wound care and hygiene	Topical antiseptic Antihistamines Proper wound care and hygiene	Topical antibiotic Antihistamines Silicone dressings Tubular netting Proper wound care and hygiene	Topical antiseptic Topical antibiotic Antihistamines Proper wound care and hygiene	Topical antibiotic Systemic antibiotic Antihistamines Silicone dressings Tubular netting Nutrition Oral iron supplements Proper wound care and hygiene	Topical antibiotic Proper hygiene	Topical antibiotic Antihistamines Proper wound care and hygiene	Topical antibiotic Silicone dressings Tubular netting Oral iron supplements Amputation Lymph node dissection Radiotherapy Proper wound care and hygiene
Complications	Anemia	None	Oral erosions	None	Anemia Superinfection Constipation Malnutrition	Oral erosions	Anemia SCC	Anemia Depression SCC Metastasis Death

Abbreviations: AD, autosomal dominant; AR, autosomal recessive; *COL7A1*, collagen 7 gene; DEB, Dystrophic epydermolysis bullosa; EB, epidermolysis bullosa; EBS, epidermolysis bullosa simplex; EM, electron microscopy; *KRT5*, keratin 5 gene; PPK, palmoplantar keratoderma; SSC, squamous cell carcinoma.

[a] Parents: asymptomatic carriers of the mutation.

[b] Dermoepidermal junction cleavage plane and histologic study (EM or antigen mapping).

[c] Genetic study ordered directly.

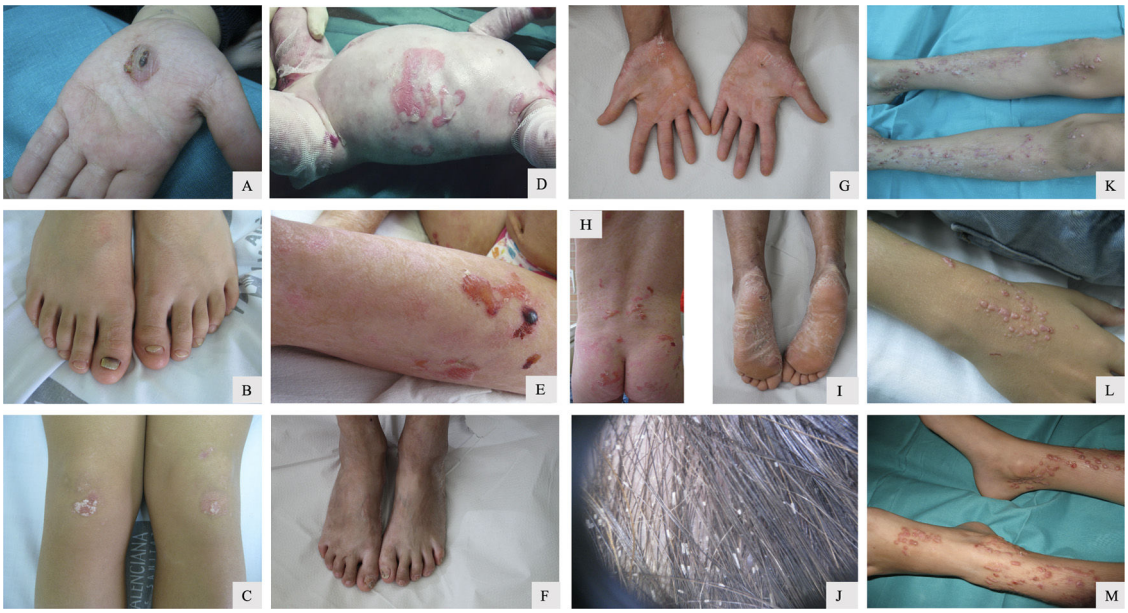

Figure 1 Patient 1: 10-year-old boy with localized epidermolysis bullosa simplex. A, Blister on his palm. B, Nail dystrophy. C, Scarring with milium cysts at sites of trauma. Patient 3: Newborn with severe generalized epidermolysis bullosa simplex. D, Generalized skin blisters and erosions; controlled in childhood. E, H, Herpetiform blistering in lumbar, buttock, and thigh areas together with signs of atrophic scarring; controlled in adolescence. F, Nail dystrophy. G,I, Palmoplantar keratoderma; J, Hair casts (pseudonits). Patient 4: 7-year-old girl with pruritic dystrophic epidermolysis bullosa. K,L,M, Pruritic papules and nodules on the surface of the extremities.

kidney disease, syndactyly, cutaneous squamous cell carcinoma (SCC), and depression.

Eight patients diagnosed with EB during the study period were identified: 3 had EB simplex (EBS) and 5 had dystrophic EB (DEB). The most common subtypes were localized EBS and generalized DEB; 6 of the patients (75%) were women and 5 (62.5%) had been diagnosed at birth and had a family history of EB. Patients 1 and 2 and 7 and 8 were siblings. Blisters were the most common clinical manifestation (87.5%) and were mainly located on the extremities. All patients received topical treatments and 6 required symptomatic treatment with hydroxyzine for pruritus. Topical treatments consisted of antibiotics, local therapy with antiseptics and primary dressings (silicone), and/or secondary dressings (cotton dressings with or without tubular netting). All the patients were instructed on proper wound care and hygiene and were advised to wear cotton fabrics, shower without soap, apply moisturizing creams, pat their body dry, drain their blisters with a sterile needle without breaking the skin, and apply antiseptic chlorhexidine 0.5%. The patient with severe generalized DEB required gabapentin for refractory pruritus and nutritional support for malnutrition. One patient with generalized DEB developed metastatic SCC on her right leg. She was treated with amputation, inguinal lymph node dissection, and palliative radiotherapy. Anemia was the most common complication (50%) and 2 patients with a hemoglobin level of less than 10 g/dL required oral iron supplementation. The clinical course was variable and ranged from improvement of lesions to death due to metastatic SCC (Fig. 1).

EB is caused by mutations in genes encoding the structural proteins in the dermoepidermal junction. EB type and subtype are defined by the mutation involved and the level of skin cleavage on histology. There are 4 types of EB: EBS, junctional EB (JEB), DEB, and Kindler syndrome.[1,2,4] Blisters form in the epidermis in EBS, the lamina lucida in JEB, and the sublamina densa in DEB. JEB and DEB are usually more severe as they can affect other organs with an epithelial lining.[4–6]

EBS usually manifests in the neonatal period. Scars, milium cysts, and nail dystrophy are less common than in JEB or DEB. The most common subtype of EB is localized EBS, which is characterized by palmoplantar blisters. Severe generalized EBS is characterized by generalized blistering in the neonatal period, herpetiform blistering in childhood, and palmoplantar keratoderma.[1,2,4]

Enamel hypoplasia is the most consistent form of JEB and patients with severe disease can develop exuberant granulation tissue in the periorificial regions and skin folds.[1,2,4] Autosomal recessive DEB is the most severe subtype of EB and causes bullous, erosive, mutilating disease with involvement of the skin, mucous membranes, and internal organs. SSC is the main cause of death in EB and is more common—and aggressive—in patients with dystrophic forms.[1,2,4–7] Contrasting with findings by Feinstein et al.,[8] autosomal dominant DEB was more common than recessive DEB in our series. Also of note in our series was the presence of SCC in the 2 women with generalized DEB.

The diagnostic work-up in EB should include skin biopsy of a friction-induced lesion to enable immunofluorescence antigen mapping, which will show the level of cleavage in the dermoepidermal junction, helping to classify the type of EB and guide molecular testing.[1,2] Molecular diag-

nosis is essential, as it provides key prognostic information and guides management. It also enables clinicians to offer genetic counseling to patients and parents of affected individuals.[2,4]

Treatment is symptomatic and multidisciplinary, and several protein-, cell-, and gene-based therapies are currently under development for DEB.[1,2,4,9]

In conclusion, the prevalence of AD in our health care setting is similar to that described in previous studies.[10] Most of the patients were female and had been diagnosed at birth. The clinical manifestations were variable, but the most common findings were blisters, nail dystrophy, and pruritus. The main complication was anemia, possibly because of the higher prevalence of DEB. Treatment was largely symptomatic.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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Diagnostic Value of Cutaneous Ultrasound in Verrucous Venous Malformation☆

Utilidad de la ecografía cutánea para el diagnóstico de la malformación venosa verrucosa

To the Editor,

Verrucous venous malformation (VVM) is a rare vascular lesion currently classified as a vascular malformation by the International Society for the Study of Vascular Anomalies (ISSVA). Diagnosis is based on the integration of clinical and pathologic findings. In this article, we describe the ultrasound features of 3 VVMs and propose ultrasound as a useful, noninvasive diagnostic and follow-up tool that can also be used to guide and optimize treatment.

We selected 3 patients with histologically confirmed VVM from the database in our department. Their lesions were assessed and compared using 22-MHz cutaneous ultrasound.

Patient 1 was a 10-year-old boy with a VVM on his left ankle that had been present since birth (Fig. 1A). Ultrasound showed a thickened, hyperechoic epidermis with hypoechoic vascular channels in the dermis and subcutaneous tissue and no color Doppler signal (Fig. 2A).

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