Hailey-Hailey Disease Goes Undiagnosed for Years

BY BETSY BATES
Los Angeles Bureau

SCOTTSDALE, ARIZ. — An accurate diagnosis of Hailey-Hailey disease was delayed an average of 8 years after onset of the painful disorder, while dermatologists and nondermatologists treated what they presumed to be dermatitis, psoriasis, or a rash, according to a 40-year retrospective study.

"In three patients, believe it or not, the disease actually preceded the diagnosis by more than 30 years," Dr. Kenneth J. Tomecki, vice chair of dermatology at the Cleveland Clinic, said at the annual meeting of the Noah Worcester Dermatological Society.

Often remembered for the "dilapidated brick wall" appearance of its histology, Hailey-Hailey disease is a rare but important genetic dermatosis, he said.

Intrigued by the disorder since residency, Dr. Tomecki decided to conduct a review of every histologically confirmed case seen at the Cleveland Clinic from 1965 to 2005.

The 28 cases that emerged showed a female predominance (20:8) and an average age of onset of 35 years, although one patient recalled an onset of disease at 10 years old.

In 20 cases, patients reported a family history of the disease. One patient "recalled, in tree fashion," 10 family members who also had confirmed Hailey-Hailey disease or its signs and symptoms.

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Characteristic moist, macerated plaques were present in the patients.

The disease had caused cutaneous symptoms in 24 patients, who described burning, pain, and tenderness exacerbated by friction, heat and humidity, sunlight, and even massage.

The axillae, groin, and perineum were the most common sites of involvement, followed by the neck, inframammary region, and vulva.

In 25 of the 28 patients, more than one area of the body was involved.

The diagnosis is established by the histology, which Dr. Tomecki described as "suprabasilar bullae with acantholysis against a background clinical appearance of moist, macerated plaques."

All of the patients in Dr. Tomecki's review had received topical therapies: corticosteroids, antifungals, and emollients.

Systemic corticosteroids resulted in improvement in 8 of 12 patients who received them. Tetracycline, likely used for its anti-inflammatory actions, was effective in half of the eight patients to whom it was prescribed. Dapsone, which Dr. Tomecki believed might prove efficacious, only improved 6 of the 10 patients in which it was tried.

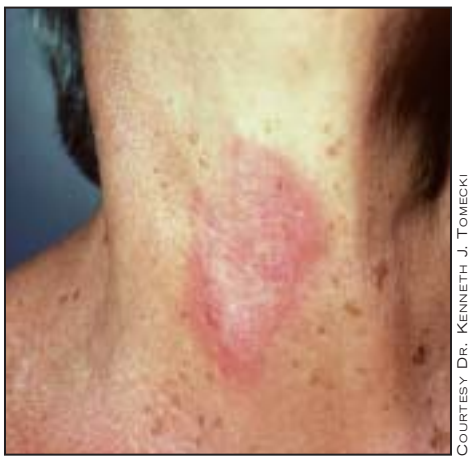
"Interestingly enough, in the hands of the surgeons, CO_2 laser vaporization actually had a good result in all eight of the patients who underwent this therapy," he said.

A literature search revealed a similar potpourri of treatments, with similarly uneven results, reported Dr. Tomecki.

He characterized systemic therapies, including oral antibiotics, dapsone, and systemic corticosteroids as "unpredictable, and really not something to lean on."

First described by dermatologist brothers William Howard Hailey and Hugh Edward Hailey in 1939, Hailey-Hailey disease is a rare autosomal dominant disorder caused by a mutation in chromosome 3q.

"The key abnormality is that the adhesion between epidermal cells is shot," explained Dr. Tomecki. "They no longer have the glue to hold them together."



COURTESY DR. KENNETH J. TOMECKI

Adhesion between epidermal cells is shot, causing moist, macerated plaques.

The adhesion between keratinocytes then deteriorates, affecting the desmosomal/keratin filament complex and triggering acantholysis and clinical vesicular changes, blisters, and plaques.

Beyond the discomfort, most patients also suffer from malodorous secondary effects of the lesions, with social and psychological consequences. Despite these challenges, the long-term outlook for most patients is very good, he said. ■

Four Skin Cancers Warrant Vigilance as Incidence Rates Rise

BY BETSY BATES
Los Angeles Bureau

SCOTTSDALE, ARIZ. — There are four aggressive skin cancers that are increasing in incidence and can be easily overlooked, warned Dr. Marc D. Brown at the annual meeting of the Noah Worcester Dermatological Society.

Lentigo Maligna

The appearance and growth of this tumor, once cavalierly called a "Hutchinson's freckle" because it resembles a dab of shoe polish, might not be noticed by patients. Even dermatologists may overlook the amelanotic variety of this in situ tumor, said Dr. Brown, director of the division of dermatologic surgery, oncology, and Mohs surgery at the University of Rochester (N.Y.).

The lesions are slow to develop and may lie camouflaged in contiguous solar lentigos or pigmented actinic keratoses, but "if you give it a long enough period of time, it will become an invasive tumor." Dr. Brown said that 2 decades ago, he encountered lentigo malignas almost exclusively on elderly patients. Now "it's not at all unusual for me to see patients … in their 40s or 50s with their first lentigo maligna."

Finding a surefire treatment approach to lentigo malignas remains challenging. Increasing evidence suggests the lesions often extend far beyond the 5-mm clinical margins that once were considered adequate for melanoma in situ lesions. Frozen section proponents have reported low recurrence rates, but "you really have to have an excellent lab and be very good at this."

He said he prefers a "modified Mohs" or "slow Mohs" approach that involves sending sequential sections to a histopathologic laboratory over several days after a "very meticulous" collection of tissue around the peripheral margin. In 210 cases performed in such a manner, he reported a recurrence rate of less than 2%.

SCC in Organ Transplant Patients

The growing population of long-term survivors of organ transplantation has a 65-fold increased risk of squamous cell carcinoma. Their cancers may be multiple, fast growing, and atypical in appearance.

In one such case, a liver transplant patient he had seen 3 weeks previously presented with a 3-cm SCC at the base of his thumb. He had a positive lymph node in his axilla and developed metastatic disease in his lung within 3 months.

"We're going to be seeing more and more of these patients," he said. The keys to management are education and vigilance. Many transplant centers fail to warn patients they should be examined frequently. When a lesion appears, have a low threshold for suspicion, he said. "It is very difficult sometimes to determine which is the bad [lesion] and which is not."

High-risk SCCs are those that are large, multiple, deeply invasive, painful or tender, rapidly growing, recurrent, and on high-risk sites such as the scalp, ear, lip, neck, and face. Dr. Brown disclosed that he is a consultant to Graceway Pharmaceuticals LLC and Novartis. His talk, however, was not sponsored by any company.

Atypical Fibroxanthoma

This tumor is believed to be secondary to UV exposure, but unlike lentigo maligna, atypical fibroxanthoma (AFX) seems to be confined to an older population.

"It usually appears relatively nonspecifically," he said. In general, these tumors are small, superficial, and well managed by excision with a 1-cm margin or Mohs surgery, said Dr. Brown, who was a coinvestigator in a study that found a 100% cure rate in 20 such tumors (J. Dermatol. Surg. Oncol. 1989;15:1287-92).

"If it sounds too good to be true, it's too good to be true," he said, noting that he has now had 6 cases of metastatic AFX in his practice, and 25 have been reported in the literature.

In his experience with metastatic cases, the original lesion was small (average, 1.5 cm) and metastasis occurred early (on average, 9 months after diagnosis). The most common metastatic site was the regional lymph nodes.

Fortunately, there is a clue to potential aggressive behavior in such tumors: The immunostain LN-2 (CD74) often "lights up" in more aggressive AFX tumors, including five of the six of his cases. When he sees a worrisome clinical AFX tumor and LN-2 is strongly positive, he refers patients for adjunctive radiation therapy.

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DR. BROWN

Merkel Cell Carcinoma

Merkel cell carcinoma was unknown until 1972 and then considered exceedingly rare. More than 1,000 cases have been reported in patients aged 7-75 years (although most patients are older than 65 years). Up to 15% of cases are seen in immunocompromised patients.

"I'm seeing a lot of these," said Dr. Brown. Sometimes dome shaped and distinctly red or violaceous, they may present more subtly.

In one case, the small scalp lesion was barely pink, ill defined, and bound down to the adjacent skin. "No way I thought this was a Merkel cell," he admitted.

"This is probably one of the worst cutaneous tumors that we, as dermatologists, can see. It's right up there with a bad angiosarcoma," he said.

Local recurrences are seen in 25%-33% of cases, regional spread in 25%, and distant metastasis in 33% of cases—50% by some reports—with a 3-year overall survival of 31%.

Treatment is controversial, noted Dr. Brown.

Wide local excision down to the fascia or Mohs surgery with sentinel lymph node biopsy is recommended, guiding the need for total lymph node dissection, postoperative radiation therapy, and perhaps even adjuvant chemotherapy, he said, adding that a negative sentinel lymph node carries a fairly reassuring prognosis. ■