See Ash Leaf Macules, Think Tuberous Sclerosis

BY DOUG BRUNK

PORTLAND, ORE. — If an infant presents with at least three hypopigmented macules, think tuberous sclerosis.

Tuberous sclerosis is described as a triad of neurologic impairment, multisystem hamartomas, and skin findings (such as ash leaf macules and facial angiofibromas). The disease is of autosomal dominant inheritance, with an incidence of 1:6,000 to 1:10,000. Spontaneous mutation occurs in 50%-75% of cases.

Ash leaf spots or hypopigmented macules occur in 90% of patients with the disease, Dr. Dawn Siegel said at the annual meeting of the Pacific Dermatologic Association. They can range in size from 1 to 12 cm in diameter and "are rounded at one end and tapered at the other, resembling the leaf of an ash tree. They can vary quite a bit in their presentation. In some cases, they present as confetti macules, which are only 1-2 mm in diameter," she said.

If an infant presents with more than three hypopigmented macules, she recommends screening evaluations, which could include a renal ultrasound, an eye exam, and a cardiac echocardiogram. "I usually reserve head MRI or CT for babies who are developing seizures, or who have a positive finding on one of the other screening tests, or if I have a high clinical suspicion," said Dr. Siegel, assistant professor of dermatology and pediatrics at Oregon Health and Science University, Portland.

Infantile spasms, the most common presenting neurologic sign, tend to develop by 4-5 months of age in about 70% of patients.

Establishing a definitive diagnosis of tuberous sclerosis requires the presence of two major clinical diagnostic criteria or one major and two minor criteria.

Major criteria include facial angiofibromas or forehead plaque, nontraumatic ungual fibroma, three or more hypomelanotic macules, shagreen patch (most commonly on the torso and chest), multiple retinal nodular hamartomas, cortical tuber, subependymal nodule, subependymal giant cell astrocytoma, single or multiple cardiac rhabdomyoma, renal angiomyolipoma, and pulmonary lymphangiomyomatosis, said Dr. Siegel.

Minor clinical criteria include multiple randomly distributed pits in dental enamel, hamartomatous rectal polyps, bone cysts, cerebral white matter radial migration lines, gingival fibromas, nonrenal hamartoma, retinal achromic patch, "confetti" skin lesions, and multiple renal cysts.

Current treatments for the facial angiofibromas include pulsed dye laser and pulsed KTP (532 nm) laser. "Some people use a CO_2 laser or the erbium:YAG laser to try and flatten down the lesions," Dr. Siegel said.

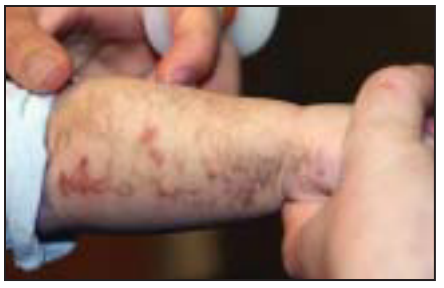
Studies of oral and topical rapamycin are underway after a published case report demonstrated that the agent significantly improved angiofibroma lesions in a patient with tuberous sclerosis complex who took rapamycin after undergoing renal transplantation (Br. J. Dermatol. 2008;159:473-5).

"This would be exciting, because angiofibromas are so disfiguring and treatment has been frustrating," she said.

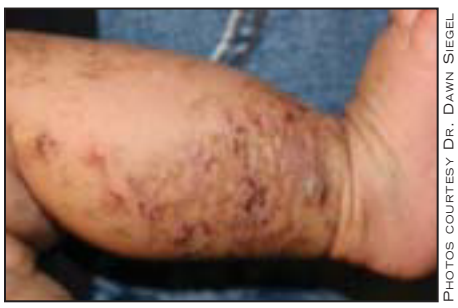
Incontinentia Pigmenti

Dr. Siegel went on to discuss incontinentia pigmenti, which is caused by a genomic rearrangement of the gene for nuclear factor kappa B essential modulator and has an incidence of 1:40,000. The skin disorder is marked by four stages that occur in most patients.

In stage I, vesicles in linear streaks follow the lines of Blaschko. These lesions are present at birth in 50% of cases and wax and wane for up to 1 year. In stage II, verrucous-hyperkeratotic streaks usually appear at 2-6 months of age. Stage III is marked by hyperpigmentation in streaks along the lines of Blaschko in a so-called "marble-cake pattern," she said.



Viral illness can precede recurrence of the vesicular phase of incontinentia pigmenti (shown on an infant's arm).



PHOTOS COURTESY DR. DAWN SIEGEL

Recurrence of the vesicular phase of incontinentia pigmenti (shown on an infant's leg) typically lasts 1-2 weeks.

Cutaneous findings in stage IV typically involve atrophy and hypopigmentation that may be subtle. Affected infants may have a lack of hair along the lines of Blaschko.

Recurrence of the vesicular phase may occur, but this typically lasts only 1-2 weeks and is often preceded by a viral illness. "Sometimes these lesions are mistaken for herpes zoster," Dr. Siegel noted.

Additional findings of incontinentia pigmenti may include scarring alopecia, most commonly on the vertex; conical or peg-shaped teeth; absence of teeth; nail dystrophy; and abnormal sweating.

"The management of incontinentia pigmenti in the newborn period should focus on skin care with emollients and monitoring for skin infection," she said.

"Topical steroids can sometimes be beneficial for symptomatic relief in the verrucous phase. Referral to an ophthalmologist for a retinal exam is important. If neurologic symptoms are present, then evaluation includes an EEG and an MRI," she added.

Neurofibromatosis Type 1

Dr. Siegel concluded her presentation by discussing neurofibromatosis type 1 (NF1), a multisystem disorder caused by a mutation of a gene on the long arm of chromosome 17 that occurs in about 1 in 4,000 births.

According to the 1988 National Institutes of Health Consensus Development Conference, a diagnosis of NF1 requires two or more of the following clinical features: six or more café-au-lait macules, two or more neurofibromas or one or more plexiform neurofibromas, freckling in the axilla and inguinal region (Crowe's sign), tumor of the optic nerve pathway, two or more Lisch nodules (iris hamartomas), and distinctive osseous lesions.

Café-au-lait macules, the hallmark clinical feature, are present in nearly all cases. The size is age dependent, with macules typically exceeding 5 mm in prepubertal children and 15 mm in postpubertal children.

"They often appear in the first few months of life and increase in number over the first couple of years of life," Dr. Siegel said.

Axillary or inguinal freckling tends to present later in childhood, while neurofibromas begin to appear in childhood or later. "They are not usually present in infancy," she said. "They increase in number in puberty and during pregnancy."

Plexiform neurofibromas present in about 25% of cases in infancy. They can have associated hypertrichosis and hyperpigmentation, and can run along the lines of nerves. "It's difficult to excise them for that reason," she said.

Plexiform neurofibromas also can be painful and, although rare, there is a risk that they will develop a malignant peripheral nerve sheath tumor.

"Because they're difficult to completely excise, it's always hard to know when they develop to cancer in the plexiform neurofibroma, or if the lesion is just growing," she noted.

"There are a lot of clinical trials going on right now looking at various medical, nonsurgical treatments for plexiform neurofibromas," Dr. Siegel added.

Dermatologic exams for children with NF1 should include evaluation for the presence of café-au-lait spots, neurofibromas, plexiform neurofibromas, and skinfold freckling. "Enlarging or disfiguring plexiform neurofibromas may require referral to a surgical specialist to discuss debulking or to a specialty center for enrollment in a clinical trial," she said.

Dr. Siegel disclosed having no relevant conflicts of interest. ■

New Wound Dressing Reduces Pain During Changes

BY KERRI WACHTER

PHILADELPHIA — A new dressing using a lipido-colloid contact layer reduced pain during dressing changes and improved quality of life for patients with epidermolysis bullosa.

The 20 patients involved in the trial reported most of the dressing changes to be pain-free (91%). The remaining 9% of dressing changes were reported as mild to moderately painful, according to the results presented in a poster at the annual meeting of the Society for Pediatric Dermatology.

The contact layer consists of petrolatum and carboxymethylcellulose on a mesh. When exudate comes in contact with the dressing, the carboxymethylcellulose swells and retains moisture, which keeps the environment moist, said coauthor Dr. Mary Regan, who is the director of clinical affairs for Hollister Wound Care (a joint venture between Hollister Incorporated and Laboratoires URGO), which markets and sells the dressing as the Restore family in the United States. The study was funded by Laboratoires URGO, which markets and sells the dressing (UrgoCell, Urgotul) in Europe.

This open-label, single-center study involved 11 adults and 9 children with simplex or dystrophic epidermolysis bullosa. Skin lesions were managed with the lipido-colloid contact layer dressing for a maximum of 4 weeks. At dressing changes, the researchers assessed pain and quality of life.

All 20 patients completed the trial, with a total of 152 dressing changes. Dressing application was considered by the patients to be "easy" or "very easy" for most of the dressing changes (95%). Likewise, dressing removal was considered to "easy" or "very easy" for almost all of the dressing changes (98%). Dry dressing removal was recorded for 87% of dressing changes; in 13% of dressing changes saline soaking was used for removal.

Roughly half of patients (55%) reported that using the experimental dressing had improved their quality of life, due to easier dressing removal.

"Most adults and children felt less apprehensive about the procedure than they had with their usual dressing," the researchers wrote. All but one patient said that they would use the experimental dressing to manage their lesions in the future. ■