

Imiquimod Useful Before, After Cancer Surgery

Pretreatment can shrink a BCC lesion, and use after surgery may improve scarring and prevent recurrence.

BY DAMIAN McNAMARA
Miami Bureau

MIAMI BEACH — Think imiquimod before basal cell carcinoma surgery to shrink a tumor or afterward to minimize cancer recurrence, experts advised at a symposium sponsored by the Florida Society of Dermatology and Dermatologic Surgery.

Evidence now suggests that imiquimod cream 5% (Aldara) has efficacy against nodular forms of basal cell carcinoma (BCC) beyond the superficial BCC indication approved by the Food and Drug Administration in July 2004. Multiple studies support this combination approach to BCC management.

It is common practice for oncologists to combine treatments for cancer therapy, “but interestingly enough, we as dermatologists tend to do one thing at a time,” said Dr. James Spencer, director of dermatologic surgery at Mount Sinai School of Medicine, New York. “Surgery and radiation therapy are well described as effective for skin cancer. Use of medical therapies, such as imiquimod, is emerging,” he said.

“Advances in nonsurgical approaches to nonmelanoma skin cancer treatment will significantly impact our practices in the next 5-10 years,” predicted Dr. Darrell S. Rigel, clinical professor of dermatology at New York University, New York.

“The most important thing to me is to

look at ... ways to treat skin cancers other than surgery. Combination modalities seem to make sense,” he said.

Electrodesiccation and curettage is the traditional, and probably still the most widely used, therapy for nonmelanoma skin cancer. Adjunctive topical imiquimod looks promising. “This modality has changed my practice—it is rare that I will only [do electrodesiccation and curettage on] my patients at this point,” said Dr. Rigel, who is a consultant and investigator for 3M Pharmaceuticals, the manufacturer of imiquimod.

Pretreatment with imiquimod can shrink a BCC lesion, which should yield a smaller and more effective surgery, said Dr. Spencer, who has received research funding from 3M and is a former member of its speakers’ bureau.

There also is evidence that topical treatment immediately following surgery improves scarring, perhaps by releasing interferon. In one study of 15 patients who had breast surgery, clinicians rated the side treated with imiquimod better in appearance at 6 months (*Plast. Reconstr. Surg.* 2005;115:966-72).

In contrast, another study found a worse aesthetic outcome with imiquimod (*Der-*



matol. Surg. 2005;31:1399-403). A total of 20 patients who each had two nevi excised were instructed to apply topical imiquimod to one and a control substance to the other. “The cosmetic outcome was rated worse with imiquimod, but the rating scale included a pink appearance as a bad outcome,” Dr. Spencer said.

Imiquimod also may have a role in the prevention of recurrence. In a double-blind study, 10 patients who had undergone BCC surgery applied imiquimod cream nightly for 1 month. Another 10 patients applied a placebo cream. There was a significant drop in the residual tumor rate at 1 month, Dr. Spencer reported—one patient in the imiquimod group and four in the placebo group.

DR. SPENCER

The catch with imiquimod is longer healing time. By the end of the month, 100% of the placebo patients had healed, compared with 40% in the imiquimod group. “So Aldara delays healing, but by 2 months, everyone healed,” he said. The study was funded by 3M Pharmaceuticals.

Delayed wound healing and a diminished short-term cosmetic appearance both were demonstrated in two studies that assessed a combination of curettage and imiquimod on either 90 patients with BCC or 86 patients with squamous cell carcinoma (SCC), said Dr. Donald K. Tillman, a dermatologist practicing in Hays, Kan.

Patients applied imiquimod once daily

5 days/wk for 6 weeks. The overall cure rates were 96% in the BCC study and 95% in the SCC study, he reported at the meeting. Publication of the studies is pending, and 3M Pharmaceuticals provided a grant to support publication. Dr. Tillman is on the speakers’ bureau for 3M.

“I use Aldara primarily out of necessity,” said Dr. Tillman. His practice covers large rural areas of western Kansas, and imiquimod can facilitate management of a nursing home patient treated several times with surgery or a farmer who lives more than 200 miles from the nearest Mohs surgery center. Dr. Tillman gets asked if imiquimod’s clinical effect is age dependent. “The answer in my practice is no. A 105-year-old patient got a nice result, just like younger patients.”

No cancer recurrence was reported in another study that evaluated imiquimod following curettage without electrodesiccation for basal cell carcinoma. Dr. Rigel and his associates enrolled 57 patients with either nodular or superficial BCC lesions. One week after curettage, patients applied imiquimod once daily 5 days/wk for 6 weeks.

“Six weeks seems to work well,” Dr. Rigel said in response to a meeting attendee question about duration of imiquimod therapy. “We need more studies to optimize treatment protocols, but we know they work.”

At 1 year, there were zero recurrences. There were excellent cosmetic results, superior to electrodesiccation and curettage, and some mild hypopigmentation, but “we are now out to 2 years with no recurrences,” said Dr. Rigel. ■

Military Experts Say Newer Hemostatic Dressings Beat Gauze

BY JOHN R. BELL
Associate Editor

WASHINGTON — Gauze deserves to be permanently retired in favor of more effective wound fillers and hemostatic agents, according to several presenters at a meeting cosponsored by the American Academy of Orthopaedic Surgeons and the Orthopaedic Trauma Association.

Col. John Holcomb, MC, USA, of the U.S. Army Institute of Surgical Research at Fort Sam Houston, Tex., discussed his experience with HemCon dressing (HemCon Medical Technologies Inc.). HemCon contains the hemostatic agent chitosan and was approved by the Food and Drug Administration in 2003. Dr. Holcomb noted that although chitosan is derived from purified shrimp shells, it is a filler in many cosmetics and food products and thus is unlikely to cause an allergic reaction, even in people with seafood allergies.

He presented preliminary data derived from a survey he and his colleagues sent to military medics,

physician assistants, and nurses regarding their use of this dressing in combat injuries. There were 48 uses of HemCon, 4 of them duplicative. Of the 44 included cases, 29 followed gauze failure. Of those, the HemCon succeeded in controlling the bleeding 100% of the time. In 42 of all 44 included cases (95%), HemCon either improved hemostasis or stopped the bleeding entirely.

These data are similar to those he and his colleagues published last year for an uncontrolled case series of 68 patients, in which use of HemCon achieved hemostasis in 97% of cases (*J. Trauma* 2006;60:655-8). The responding medical personnel “thought this was useful in places where tourniquets didn’t work and useful after gauze had failed.”

Preventing exsanguination for large wounds is especially important in the current war in Iraq, where Dr. Holcomb said the increasing use of roadside bombs has led to more wounds that are hemorrhagic. “I think injuries are worse now than they were 3 years ago,” he said. He noted that

HemCon is now included in all Army first-aid kits, as well as in Army ICUs. Another brand of chitosan-based hemostatic bandage is ChitoFlex (North American Rescue Products Inc.).

In addition to stopping bleeding in extremity wounds, Dr. Holcomb said that HemCon also does so in wounds to internal organs, notably the bowel and the kidney, though this use is off label. One caveat he offered is that when the dressing is removed, the wound may present the appearance of infection despite being sterile. “It doesn’t look very good when you take it out,” he said.

Also commonly used in combat injuries is the hemostatic dressing QuikClot (Z-Medica Corp.), a granular wound filler that eventually is washed out of the wound. Capt. Peter Rhee, MC, USA, director of the Navy Trauma Training Center, Los Angeles, discussed off-label uses of the product.

He presented prepublication data from a group of civilian and military medical personnel regarding their use of QuikClot. Of

103 cases, 95 (92%) showed efficacy in stopping the bleeding. There were 34 cases treated by civilian personnel, and 69 cases were treated in a military setting. Dr. Rhee disclosed no potential conflicts of interest.

Maj. Martin Schreiber, MC, USA, in a presentation discussed the merits of fibrin dressings, which contain fibrin and/or thrombin.

Tisseel VH (Baxter International Inc.), the first such product to be approved by the FDA, requires 20 minutes of warming and stirring before it can be applied. FloSeal (also from Baxter) is a gelatin matrix derived from bovine collagen; unlike Tisseel, it does not require heating before mixing. Evicel (Omrix Biopharmaceuticals) is made from human fibrinogen and thrombin and requires no mixing. This product can be stored up to 2 years if frozen. Evicel can be used in liver resection surgery when standard hemostatic techniques have failed, said Dr. Schreiber, director of surgical critical care at Oregon Health

and Science University, Portland.

Not yet approved by the FDA is dry fibrin-sealant dressing, developed by Dr. Holcomb and the Red Cross. This product is made from lyophilized human thrombin and fibrinogen from blood donors, as well as calcium chloride, contained in a synthetic mesh. The dry fibrin-sealant dressing has been used in one combat victim (for whom clinical data were not presented), but several animal studies by Dr. Holcomb and colleagues have shown a reduction in blood loss and better overall survival, compared with gauze—including in animals with grade V liver injury (*J. Trauma* 1999;46:49-57).

“The emphasis has really turned from resuscitating patients to stopping hemorrhage. What we’re seeing really is an explosion in the field of the technology, of the various hemostatic [agents],” Dr. Schreiber said.

On that point, Dr. Holcomb noted that whichever hemostatic dressing is chosen for use in the emergency department, “they are all better than gauze.” ■