Underlying Disease May Drive Neuropathic Itch

BY BETSY BATES
Los Angeles Bureau

SANTA BARBARA, CALIF. — When a patient comes to you with neuropathic pruritus, the most important thing to do is listen, not just look.

If you see anything on the skin at all, it will be a vague, after-the-fact sign such as erythema or lichenification.

It may be hard for a busy physician to do, but the key to making the diagnosis of neuropathic itch is to "sit there and listen to the patient," said Timothy G. Berger, M.D., professor of clinical dermatology at the University of California, San Francisco, during the annual meeting of the California Society of Dermatology and Dermatologic Surgery.

The patient's history and description of the sensation contain the clue as to whether the itch is central (multiple sclerosis, polymorphous light eruption); peripheral (brachioradial pruritus, notalgia paresthetica, postherpetic neuralgia, and possibly anogenital pruritus); or cutaneous (lichen simplex, and, in Dr. Berger's opinion, prurigo nodularis).

Although neuropathic pruritus is notoriously difficult to treat, Dr. Berger offered suggestions for specific conditions:

▶ **Notalgia paresthetica.** This itch occurs lateral to the central spine, often just below the scapula. Research has established an anatomical correlation between the location of the itch and abnormalities on spinal x-rays of many patients. Among the potential treatments are topical capsaicin 0.025% up to 4 times/day, acupuncture, and occlusion, as well as spinal manipulation and treatment of spinal disease.

▶ **Brachioradial pruritus.** Patients may enter your office with what Dr. Berger calls "the ice pack sign," carrying ice to apply to their arms or upper torso in desperation, since "nothing else works."

The itch associated with this condition can be severe and potentially debilitating and primarily impacts fair-skinned, affluent, middle-aged people, especially women, he said.

This severe itch develops in patients with chronic sun damage. The specific trigger is sun exposure late in the summer. The timing of itch onset (late versus early summer) distinguishes brachioradial pruritus from polymorphous light eruption (PMLE).

The differential diagnosis should include PMLE, cervical spine disease with nerve entrapment, and even a spinal cord tumor.

Once those conditions are ruled out, ice packs provide relief, but there are other effective treatments as well, including avoiding the sun and wearing protective clothing; using topical steroids or capsaicin, and lidocaine patches (for localized disease); applying an Unna's boot medicated gauze bandage to interrupt central sensitization; and prescribing drugs such as gabapentin, doxepin (Sinequan), mirtazapine (Remeron), or paroxetine (Paxil), and in severe cases, thalidomide.

Best of all, though, is physical therapy, according to Dr. Berger.

"These patients will get better with physical therapy, acupuncture, spinal manipulation, and TENS [transcutaneous electrical nerve stimulation]," he said.

▶ **Anogenital pruritus.** Chronic pruritus of the scrotum, labia majora, and perianal skin that is unrelieved by anti-inflammatories may respond to hygiene measures, Pramosone (hydrocortisone-based) cream, or imidazole.

Another option is a novel therapy pioneered by gastroenterologists in Israel (Gut 2003;52:1323-6). These researchers identified the dose at which topical capsaicin could be applied to the anogenital region without inducing burning—0.006%—and found that two-thirds of their patients were able to tolerate it, with an 80% response rate and 50% reduction in pruritus.

Although the formulation the Israeli physicians used is not available in the United States, Reliable Rexall Compounding Pharmacy in San Francisco can mix 0.006% capsaicin in a hydrophilic ointment base www.reliablerexall.com; 415-664-8800. (Dr. Berger has no financial interest in this product.)

▶ **Prurigo nodularis.** Dr. Berger noted that sensory neural receptors for touch, temperature, pain, and itch are more numerous and the nerves are enlarged in lesions of prurigo nodularis, that mast cells and eosinophils are prolific in these areas of neural hyperplasia, and that these cytokines may be stimulating nerve growth.

"My hypothesis is that prurigo nodularis is a keloid of the nerve," he said, induced in predisposed patients by rubbing and scratching.

Superpotent topical steroids with occlusion, intralesional triamcinolone acetonide (Kenalog), capsaicin 0.076%-0.3% every 4 hours, and thalidomide 100-200 mg daily are all potential therapies.

"Thalidomide has moved up on my list," Dr. Berger said. "In this situation, thalidomide has the potential to make patients who have been miserable forever and ever much better."

Unfortunately, patients with prurigo nodularis are more susceptible than others to neurotoxicity associated with thalidomide, so he prescribes it according to an aggressive protocol that involves a neurologic evaluation at baseline and frequent nerve conduction studies, he said.

"Usually you buy them a few years, but sometimes the patient ends up with neuropathy [and you have to] back down," he said. ■

Is Itch Neuropathic? Distinguishing Signs and Symptoms

▶ Itch presents with hypesthesia, a known neurologic disease or a previous injury (such as back injury).
▶ Itch is "too deep to scratch."
▶ Itch sometimes feels more like burning or pain.
▶ Itch feels as if it is formicating (crawling).
▶ Itch strikes in sharp spasms.
▶ There is no primary cutaneous lesion or is only erythema.

Source: Dr. Berger

Itch May Portend Cancer or Could Present Later in Disease Course

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SANTA BARBARA, CALIF. — Severe pruritus may be the first presenting sign of cancer, which most typically turns out to be Hodgkin's disease, Timothy G. Berger, M.D., said at the annual meeting of the California Society of Dermatology and Dermatologic Surgery.

But the question that always arises is when to suspect cancer and not one of the many neuropathic causes of itch on normal-appearing skin.

When do you work up a patient when there's nothing to see? "The reason all of us are totally paranoid is that you can't do a CT scan on every patient with itch," said Dr. Berger, professor of clinical dermatology at the University of California, San Francisco.

His advice is to treat the patient conservatively, but to schedule repeat visits if traditional therapies fail to relieve long-standing idiopathic itch.

He is most concerned, he said, when the itching is "disproportionately severe."

In such a case, he orders tests of liver function, iron and lactic hydrogenase levels, and endocrine function.

Dr. Berger described a patient with a history of years of severe itch whose sedimentation rate and lactic hydrogenase levels were normal, but who had a CD4 count of 180 cells/μL despite a negative HIV test.

He referred the patient to an oncologist to evaluate a bulge in the groin that the patient thought was a hernia, but proved to be a low-grade T-cell lymphoma.

When patients are undergoing radiation and chemotherapy treatments for Hodgkin's disease but continue to suffer from severe pruritus, Dr. Berger recommends systemic corticosteroids; cimetidine (200 mg, four times daily); or mirtazapine (7.5-15 mg each night) possibly in combination with paroxetine (20-40 mg each night). Patients with solid tumors can also experience severe pruritus, and his advice is to "pick from the bag" of effective therapies, including paroxetine (5-20 mg nightly), mirtazapine (7.5-15 mg nightly), a combination of paroxetine and mirtazapine, or thalidomide (100 mg nightly).

Pruritus is a problem for a third to half of patients with the myeloproliferative disorder polycythemia vera as well, Dr. Berger said. For the vast majority of patients, the itch associated with this disease is aquagenic, occurring for 5-120 minutes after bathing.

The standard treatment has been aspirin (81-300 mg/day); however, a recent survey of patients suggests that a good second choice is paroxetine (20 mg up to 40 mg/day). Other SSRIs do not have the same antipruritic effect in polycythemia vera patients, he said. ■

Skin Complications Commonly Are Seen With Varicose Veins

ORLANDO — Approximately half of limbs with varicose veins will have a skin complication, according to a retrospective study.

Venous disease affects an estimated 20% of women and 7% of men in the United States. Patients often present with one or more of these symptoms: aching, tiredness, heaviness in the legs, pain, cramping, swelling, itching, restless legs, and numbness, Ricardo Mejia, M.D., said at the annual meeting of the Florida Society of Dermatologic Surgeons.

Dr. Mejia and his colleague, Lawrence Tretbar, M.D., conducted a 10-month study of skin complications associated with venous disease. They assessed 113 limbs on 105 patients. Participants had surgery for incompetence of the great saphenous vein (102 limbs) or small saphenous vein (11 limbs). The age range was 23-83 years, and 78 of the participants were women. Approximately 50% of limbs (57 total) had skin findings, according to Dr. Mejia of Jupiter, Fla.

Men were 1.5 times more likely to present with dermatologic complications, although varicose veins are three times more common in women. Others at higher risk for skin manifestations include patients with advanced disease or of advanced age, and younger patients if they have a large saphenofemoral junction diameter (greater than 12 mm).

Clinical findings in the study included edema (32% of limbs), hyperpigmentation (24%), lipodermatosclerosis (13%), dermatitis (7%), atrophie blanche (4%), and lymphedema (1%).

In addition, 12% of participants developed ulcers. Venous ulcers are significantly more common than arterial ulcers, Dr. Mejia said. Venous ulcers tend to have a less necrotic base and are in general less painful than arterial ulcers.

In the study, "intractable" ulcers healed after vein stripping surgery, Dr. Mejia said. The treatment also softened lipodermatosclerosis and reduced edema. However, he added, half of the participants required continued compression.

—Damian McNamara