CLINICAL VIGNETTE

Erythema Nodosum: An Unusual Reaction to Lidocaine

Karen Cheng, MD and Daryl Lum, MD

Case

A 59-year-old female was seen in Dermatology for a routine skin exam. She had an atypical nevus on her left forearm and skin biopsy was performed using 2% lidocaine for anesthesia. One day later, she developed erythematous, tender subcutaneous nodules on her bilateral shins and left thigh. She denied fever, chills, sore throat, mouth lesions, fatigue or joint pain. The patient reported similar lesions 30 years ago after trigger point injections with lidocaine for low back pain. She was evaluated by dermatology and diagnosed as erythema nodosum. Her past medical history also includes hypertension and adult acne. Her medications include diltiazem, hydrochlorothiazide, topical clindamycin, Vitamin D and a multivitamin. None were new or recently restarted.

On physical examination, she was afebrile and well-appearing. She had no ocular nor oral lesions. Her lungs were clear and she had regular heart sounds. There was no joint swelling or redness. She had a subcutaneous, erythematous 15 mm nodule on her anterior left shin just proximal to the ankle and two similar, smaller lesions at the right anterior shin and left thigh just proximal to her knee. There were no enlarged lymph nodes. Her complete blood count with differential, sedimentation rate, and C-reactive protein levels were in normal range. Chest x-ray revealed no hilar lymphadenopathy or infiltrates.

Discussion

Erythema nodosum (EN) is the most common clinical presentation of panniculitis, inflammation of subcutaneous fat tissue. It is characterized by erythematous, tender nodules which present most often on the anterior aspects of the lower extremities/ shins. They can range in size from 1 to 6 cm. and are bilateral and often symmetrical in location. They can also spread to the thighs and arms and less commonly the face and neck. There is no associated ulceration. There is a female predominance, occurring 3 - 5 times more often in women, particularly in the second to fourth decades. On histopathology, there is septal inflammation of subcutaneous fat tissue without vasculitis.[1] Erythema nodosum is a delayed-type hypersensitivity reaction whose pathogenesis is not fully understood. There are many patients, up to 55%, in whom no cause is found.

The most common known precipitant is infection, which may explain the increased incidence of EN in the first half of the calendar year. Streptococcal pharyngitis is the most common etiology. The skin lesions tend to occur about 2 – 3 weeks after resolution of the pharyngitis. Other precipitating infectious agents include Yersinia, Mycoplasma, Chlamydia, Histoplasma, Coccidiodes, and Mycobacterium.[2]

The second most common cause of EN is sarcoidosis with skin involvement observed in 25% of patients. The triad of erythema nodosum, arthritis, and hilar lymphadenopathy is called Lofgren syndrome.

The increased incidence in women suggests a hormonal etiology which is further supported by the increased occurrence of EN in pregnancy and with oral contraceptive pills. Oral contraceptive pills were previously the most common drug to cause EN before the introduction of lower dose estrogen formulations in the 1980s. There is also evidence associating the relative levels of estrogens and progesterones to EN.

Cutaneous lesions are the most common extra-intestinal manifestation of inflammatory bowel disease (IBD) and of these cutaneous lesions, erythema nodosum is the most common. EN tends to increase with IBD activity but may also precede the diagnosis. Erythema nodosum can also be associated with occult malignancy. Paraneoplastic EN occurs most often with Hodgkin's lymphoma, non-Hodgkin's lymphoma, and leukemia, as well as some solid tumors.

Despite these known precipitating factors, a substantial number of patients with erythema nodosum have no known trigger. Drugs as causative agents are not commonly described and if so often as anecdotal reports. As the clinical presentation and histopathology are indistinguishable from other causes, the historical administration of medication prior to the onset of erythema nodosum may be the only clue.

In our case, the patient had a prior exposure to a common local anesthetic, lidocaine, with the subsequent development of erythema nodosum. When subsequently exposed to lidocaine for a skin biopsy many years later, the patient developed an identical reaction. True allergic reactions to local anesthetics are rare,[3] and oral contraceptive pills are amongst the most common causative agents. Other drugs include nonsteroidal anti-inflammatory drugs, antibiotics including sulfonamides and penicillin, halogens, azathioprine, and leukotriene-modifying agents.[4,5]

A 2008 report described a 33-year-old female who presented with erythematous and violaceous macules, papules, and tender subcutaneous nodules as well as arthritis of the small and large joints. Her symptoms began a few hours after upper endoscopy in which lidocaine spray was administered. Subsequently, a skin biopsy was performed using 2% lidocaine as a local anesthetic followed one day later by development of erythematous macules and target lesions on the extremities including palms and soles consistent with erythema multiforme. Histology of a subcutaneous nodule was consistent with erythema nodosum and she was diagnosed with simultaneous erythema nodosum and erythema multiforme secondary to lidocaine.[6]

Diagnostic evaluation for newly diagnosed erythema nodosum should include a complete blood count, tests for inflammation including erythrocyte sedimentation rate and/or C-reactive protein, testing for streptococcal pharyngitis, anti-streptolysin-O titer (repeated in 2 – 4 weeks), chest x-ray and interferon-gamma release assay or tuberculin intradermal skin test. Skin biopsy is only necessary if the presentation is atypical.[1,7]

Erythema nodosum is a self-limited cutaneous pathology which resolves without treatment. If there is a known offending agent such as a medication or treatable cause, should prompt cessation of the precipitant as targeted therapy. Otherwise symptomatic relief is the mainstay of therapy. Aspirin and nonsteroidal anti-inflammatory drugs can be helpful for pain relief. As reported in the literature, this patient had spontaneous resolution within 3 - 4 weeks and the nodules healed with no residual scarring or atrophy.

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