*** no patient handout***

Necrobiosis lipoidica

Synopsis

Necrobiosis lipoidica (NL) is a rare, chronic granulomatous disease characterized by indolent atrophic plaques typically located on the lower extremities.

While the majority of NL cases are found in patients with diabetes (studies range from 11%-65% of cases), the incidence of NL in diabetic patients is low, only 0.3%-1.2%. NL is also associated with sarcoidosis, inflammatory bowel disease, autoimmune thyroiditis, monoclonal gammopathies, and has even been described in otherwise healthy patients. Importantly, NL may be the first sign of diabetes in a patient with no previous diagnosis. NL typically presents in the third decade of life and later in patients without diabetes. There are documented cases of pediatric onset as well. It is 3 times more common in women than in men and has no known racial predilection.

The exact etiology of NL remains unclear, but microangiopathy due to glycoprotein deposition, immunoglobulin deposition, and abnormal collagen production have all been linked.

NL typically presents unilaterally or bilaterally on the pretibial surface of the lower extremities as well-demarcated yellow, red, or brown atrophic plaques with prominent telangiectasias and an elevated violaceous rim. Atypical cases of NL have been reported on the face, trunk, upper extremities, and penis. The lesions predictably enlarge slowly over the course of months to years without intervention. The lesions may begin as asymptomatic papules, but as they progress, patients often report pruritus, dysesthesia, or pain. NL has the ability to Koebnerize, may ulcerate, and can be exacerbated by trauma. Treatment for NL remains largely unsatisfactory, and the disease process is chronic and, for the most part, progressive.

Codes

ICD10CM:
E13.620 – Other specified diabetes mellitus with diabetic dermatitis

SNOMEDCT:
9418005 – Necrobiosis lipoidica

Look For

Beginning as yellowish-brown or reddish-brown papules or nodules, the lesions progress over time into yellow-brown-red colored atrophic plaques with an elevated violaceous border. Plaques are atrophic and shiny in appearance and often have prominent telangiectasias.

Nearly one-third of cases will develop ulcerations, often in the setting of trauma.

Plaques may be unilateral or bilateral. They are most common on the lower extremities,

particularly on the pretibial surface, but can also be seen on the thighs, calves, ankles, and feet. Atypical cases involving the face, scalp, trunk, and genitals have all been reported.

Diagnostic Pearls

NL classically occurs in patients with type 1 diabetes.

Look for well-circumscribed plaques with a central shiny, waxy appearance.

NL that develops in atypical anatomical locations may be more annular or serpiginous in appearance, and may be less atrophic or shiny.

Koebnerization is a common feature in NL, and trauma may lead to ulceration of plaques.

Plaques may have a variable yellow appearance, depending on background skin phototype.

Differential Diagnosis & Pitfalls

- **Majocchi granuloma**
- **Pretibial myxedema**
- **Granuloma annulare**
- **Sarcoidosis**
- Xanthomas (eg, **xanthoma tuberosum**, **plane xanthoma**)
- **Diabetic dermopathy**
- Chronic **stasis dermatitis**
- **Necrobiotic xanthogranuloma**
- **Pyoderma gangrenosum**
- **Calciphylaxis**
- **Vasculitis**
- **Panniculitis**, including **erythema nodosum**
- **Morphea**
- **Lichen sclerosus**
- **Lipodermatosclerosis**

- **Leprosy**

Best Tests

Biopsy is characteristic.

Histopathology Findings:

- Epidermis normal or atrophic
- Rectangular appearance to punch on low power secondary to sclerosis
- Pale, acellular degenerated collagen between layers of palisading granulomas oriented parallel to epidermis forming a "layered cake" pattern
- Plasma cells typically seen in deep dermis
- Dermal interstitial inflammation consists of histiocytes, multinucleated giant cells, and lymphocytes
- Mucin absent

Management Pearls

NL is a chronic disease that is difficult to treat and frustrating for both patients and health care providers. Refer patient to a dermatologist for ongoing management.

Baseline blood work including fasting blood glucose or HgbA1c should be obtained to screen for diabetes. Patients should obtain annual glucose tolerance screenings as NL may be the initial presentation of diabetes.

In patients with diabetes, the severity (or frequency) of the disease does not correlate with the degree of glycemic control. Nevertheless, lifestyle modifications that include optimizing glucose control, smoking cessation, and avoiding trauma are all important for healing and preventing future complications. Venous disease or lymphedema may complicate healing of ulcers and compression therapy should be considered when appropriate.

Minimize trauma as much as possible and encourage fastidious wound care for any ulcerations that may develop. In severe cases, a protective pad may be indicated to prevent trauma and further ulceration. Squamous cell carcinomas are a known but rare sequelae of chronically ulcerated lesions.

Therapy

Numerous therapies have been tried, but to date there is relatively little data comparing the efficacy of these treatments. There is no established standard regimen of care. The below recommendations are for adult patients, although some are appropriate for use in pediatric

patients as well, particularly adolescents.

Corticosteroids:
Topical and intralesional steroids are typical first-line treatments. Intralesional triamcinolone or high-potency topical steroids twice daily under occlusion (plastic wrap) allow for targeted treatment and are particularly useful for solitary lesions. Systemic corticosteroid tapers can be effective in halting rapidly progressing lesions, although hyperglycemia and hypertension are common side effects.

High-potency topical corticosteroids (class 1-2): use for a maximum of 2 consecutive weeks out of the month and limit length of use.

- Clobetasol cream, ointment – Apply every 12 hours (30, 45, 60 g), or
- Halobetasol cream, ointment – Apply every 12 hours (15, 50 g), or
- Betamethasone dipropionate cream, ointment – Apply every 12 hours (15, 45, 60 g), or
- Fluocinonide cream, ointment – Apply every 12 hours (15, 30, 60, 120 g), or
- Desoximetasone cream, ointment – Apply every 12 hours (15, 60, 120 g).

Immunomodulators:
Tacrolimus 0.1% ointment once or twice daily for 8 weeks has been shown in case reports to be effective. Systemic cyclosporine at 2-4 mg/kg/day has been shown in case studies to have improvement over several months, but ulcerations often recurred upon discontinuation.

Mycophenolate mofetil (MMF) showed good effect in healing an ulcerated lesion in one case study, but also had recurrence upon completion.

Ultraviolet Light Therapy:
Psoralen-UV-A (PUVA) twice weekly for a maximum of 4 months or a cumulative dose of 200 J/cm^2 may help reduce active lesions, but has been found to have little benefit for atrophic areas.

Photodynamic therapy (PDT) has been tested with variable response for both nonulcerated and ulcerated cases of NL.

Biologics:
Both infliximab and etanercept have been found to be effective as monotherapy for ulcerating NL in case series.

Antimalarial:
Chloroquine and hydroxychloroquine have case reports showing efficacy, although it may take 3 months before results are seen.

Miscellaneous:

There are single cases studies and small series reporting efficacy of:

- Topical tretinoin reducing plaque atrophy in nonulcerated NL
- Pentoxifylline (400 mg 3 times per day) improving ulcer healing when used in addition to another systemic medication
- High-dose aspirin and dipyridamole, although results are conflicting
- Hyperbaric oxygen and fractionated carbon dioxide lasers