Clinical reflections®

WHAT LIES BENEATH:
Diagnostic Challenges of Prurigo Nodularis

Provided by RMEI Medical Education, LLC

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This activity is supported by an educational grant from Sanofi and Regeneron Pharmaceuticals.

Olive

Olive is a 72-year-old woman who has been suffering from a chronic itch. She has been to multiple doctors over the past 10 years for her ongoing itchy skin. Her constant itching led to the development of a mystery rash with hundreds of diffuse nodular lesions, papules, and excoriations on her arms, legs, and abdomen. It keeps her up itching all night, which makes her drowsy and irritable all day.

Olive

Olive's PCP diagnosed and treated her for scabies, but it did not resolve her condition.

She was given multiple topical and oral steroids to manage the itch, but the itching and lesions would return whenever the course was completed.

She was diagnosed with dermatillomania and referred to psychiatric evaluation and behavioral counseling, but despite numerous techniques she could not stop itching.

One dermatologist performed a biopsy and reported that the hyperkeratinization, nodular presentation, and histology suggest cutaneous field cancerization and was referred to an oncologist. This further spiraled her anxiety, depression, and isolation.

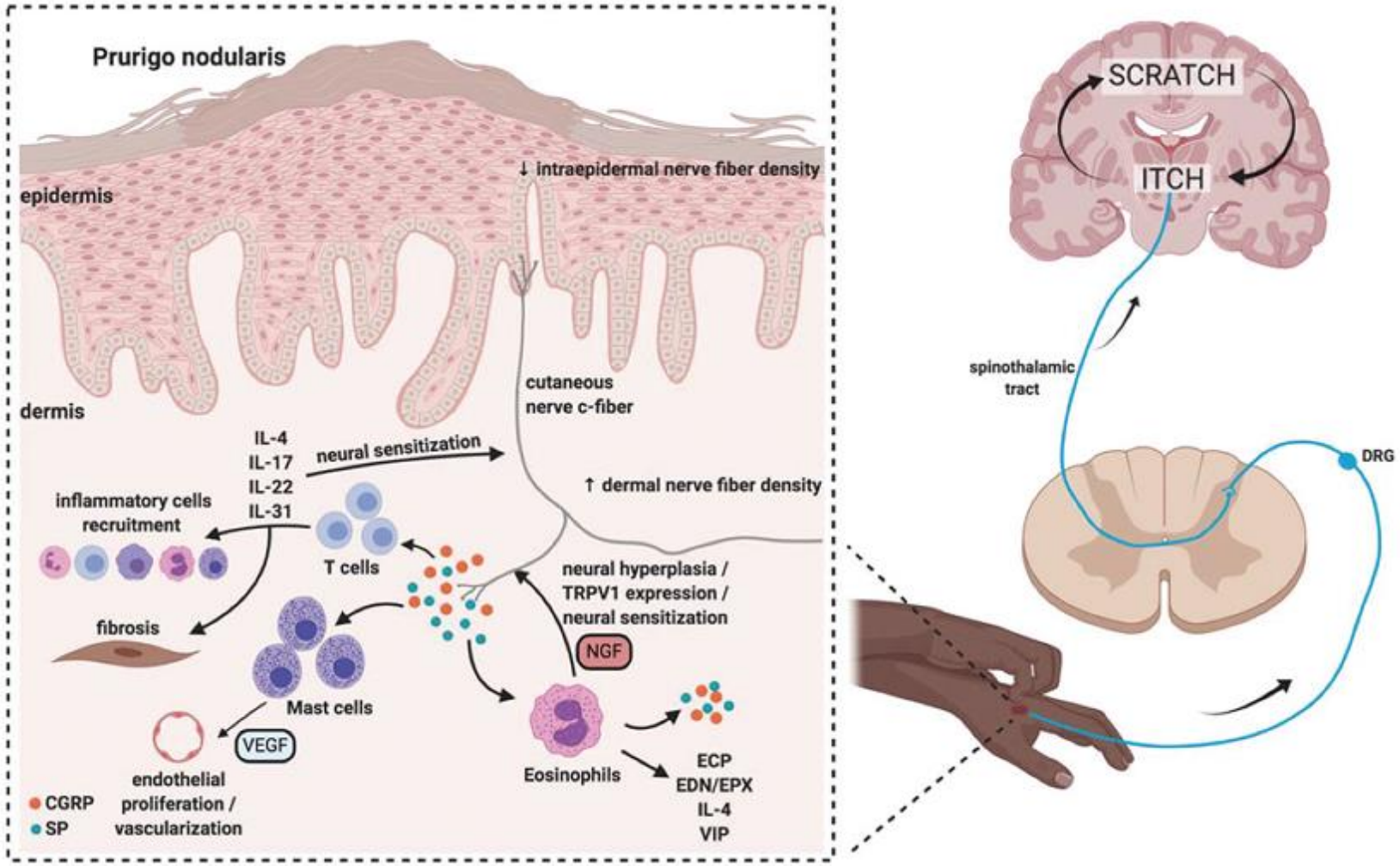
She has multiple chronic conditions, including hypertension and hyperlipidemia, all of which are well controlled on medication.

Reflection Point

In thinking about Olive's history, what could her clinicians have done better?

A. The PCP should have prescribed hydroxyzine to help with sleep and pruritis
B. The PCP should have wrapped her extremities in an unna boot
C. The dermatologist should have administered intralesional steroid injections into all her nodules instead of prescribing orals and topicals
D. The psychiatrist should have advised her to stop itching in order to break the compulsively driven itch-scratch cycle
E. The PCP should have assessed baseline functioning to rule out end stage renal disease, hepatic disease, and type 2 diabetes

Prurigo Nodularis Pathophysiology: Neuroimmune Dysregulation



Williams KA, et al. *Exp Rev Clin Pharmacol.* 2021;14(1):67-77.

Prurigo Nodularis Clinical Presentation

- Primarily affects people in middle age, between 50 to 65
- Disproportionally affects African Americans
- Chronic health conditions associated with PN:
  - Atopic dermatitis
  - Diabetes
  - End-stage kidney disease
  - Hepatitis C
  - HIV
  - Lymphoma
  - Mental health conditions, including depression and anxiety

Boozalis E, et al. *J Am Acad Dermatol*. 2018;79(4):714-719.
Elmariah S, et al. *J Am Acad Dermatol*. 2021;84(3):747-760.
Huang AH, et al. *J Am Acad Dermatol*. 2020;83(6):1559-1565.

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Symptoms of Prurigo Nodularis

- Presence of pruritis >6 weeks
- Nodules ranging from 0.5 to 2.0 cm on at least 2 different body surface areas
  - Nodules can range from a few lesions to several hundred
- Intense, unrelenting itching
- Palm, soles, and face are often spared
- Symmetrical distribution of lesions on the extensor surfaces of extremities
  - Distributed symmetrically on the trunk and extremities
  - May be accompanied by additional burning, stinging, pain, and other sensations
- Patients with back involvement often display the “butterfly sign”
  - Central back is spared as patients cannot reach it

Elmariah S, et al. *J Am Acad Dermatol*. 2021;84(3):747-760.
Williams KA, et al. *Exp Rev Clin Pharmacol*. 2020;14(1):67-77.

Associated Comorbidities

- Impaired liver, renal, or thyroid function
- Diabetes
- HIV
- Hepatitis B, C
- Malignancy
- Atopic dermatitis or other inflammatory dermatoses
  - Psoriasis, cutaneous T-cell lymphoma, lichen planus, dermatitis herpetiformis
- Increase depression and anxiety

Elmariah S, et al. *J Am Acad Dermatol*. 2021;84(3):747-760.

Burden of Prurigo Nodularis (PN)

Poor QoL[1]

- Sleep Disturbance
- Depression
- Anxiety
- Psychosocial Disturbance

Patient Impact[2]

N=36 Patients with PN

Compared to controls, patients with PN had:

- Worse overall health performance
- Pain subdomain was most prominently impacted
- Patients lost an average of 6.5 QALYs
  - Lifetime economic burden per patient: $323,292
  - Societal burden: $38.8 billion

Racial Disparities

- African Americans with PN have higher all-cause mortality than controls[3]
- African Americans are 3 to 4 times more likely to have PN than Whites[4]

QALY, quality-adjusted life year; QoL, quality of life

1. Williams KA, et al. *Exp Rev Clin Pharmacol*. 2020;14(1):67-77.
2. Whang KA, et al. *J Am Acad Dermatol*. 2022;86(3):573-580.
3. Sutaria N, et al. *J Am Acad Dermatol*. 2022;86(2):487-490.
4. Boozalis E, et al. *J Am Acad Dermatol*. 2018;79(4):714-719.

Reflection Point

Olive brought her most recent labs to your office. This included her HbA1c, eGFR, SCr, ALT, AST, and TSH. Considering her age, history, and risk factors, what other lab testing would have been appropriate to include when evaluating her for a PN diagnosis?

A. CBC with differential

B. Stool O & P

C. Creatine kinase level

D. Aldolase

Diagnostic Workup

Clinical Examination	Laboratory Tests	Additional Tests to Consider
• Complete review of systems • Extent of PN (number and firmness of lesions) • Pruritis intensity – Mild, moderate, severe, or very severe • Disease burden – QoL – Sleep disturbance – Anxiety/depression – Associated comorbidities	• Complete blood cell count with differential • Liver function tests • Renal function tests • If risk factors exist, or as indicated by review of symptoms: – Thyroid function tests – Diabetes assessment – HIV and hepatitis B/C virus serologies	• If malignancy is suspected and patient has had pruritus for <1 year, refer for age-appropriate malignancy screening • Biopsy, if suspicion of an alternative or other contributing condition

Elmariah S, et al. *J Am Acad Dermatol*. 2021;84(3):747-760.

Histology

Characteristic Features

Epidermis

- Thick, compact orthohyperkeratosis
- Pseudoepitheliomatous hyperplasia
- Focal parakeratosis
- Hypergranulosis

Dermis

- Papillary dermal fibrosis with vertically arranged collagen fibers
- Increased numbers of capillaries
- Increased fibroblasts
- Mixed, superficial, perivascular or interstitial infiltrate may be observed

Differential Diagnosis

- Kyrles's disease
- Hypertrophic lichen planus
- Atopic dermatitis with lichen simples chronicus
- Autoimmune blistering diseases
  - Bullous pemphigoid
  - Dermatitis herpetiformis
- Neurotic excoriations
- Skin picking syndromes / body-focused repetitive behaviors
- Lichen amyloidosis
- Multiple keratoacanthomas
- Arthropod bites
- Scabies

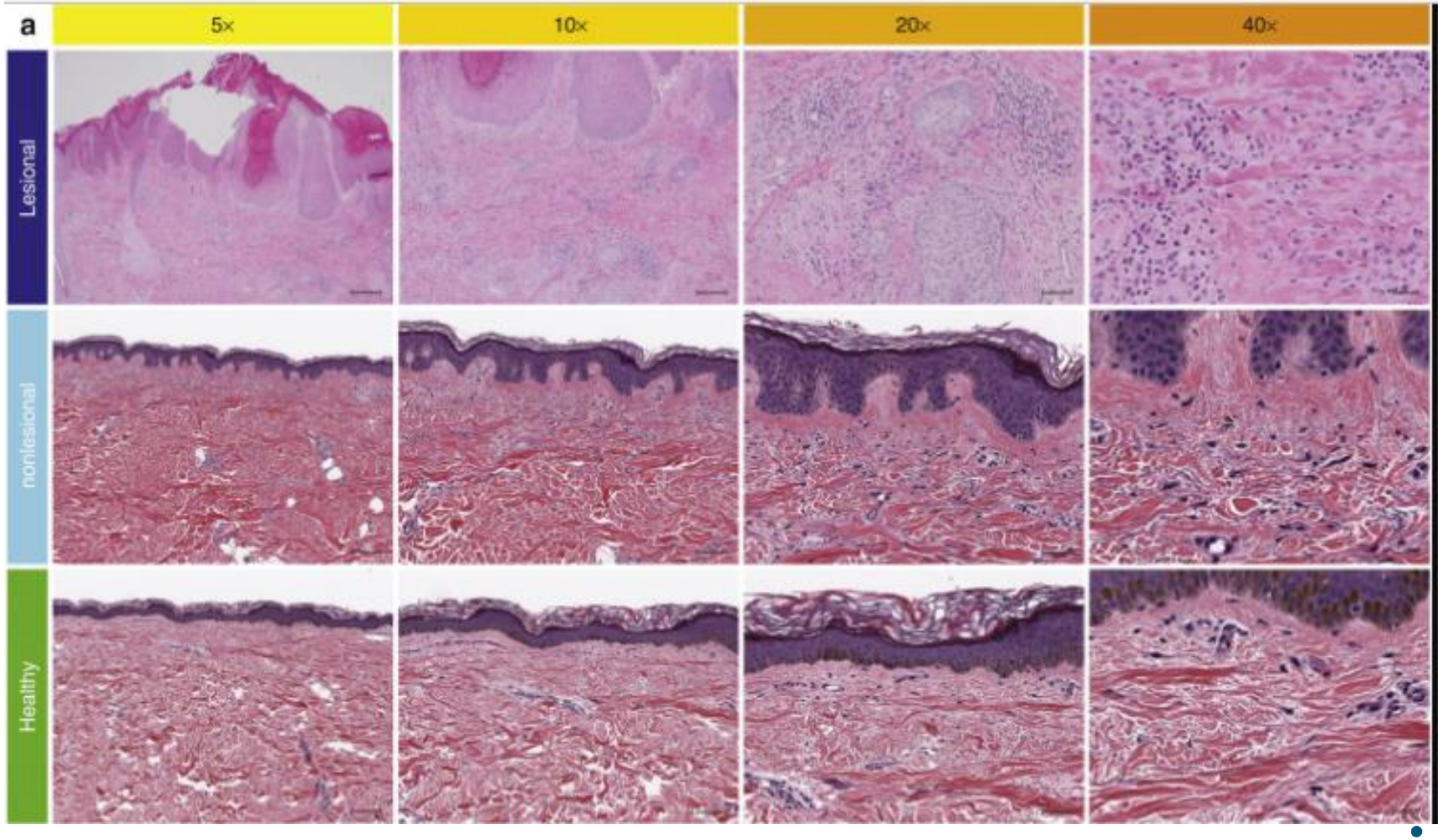
Elmariah S, et al. *J Am Acad Dermatol*. 2021;84(3):747-760.

Histology

Lesional

Non-lesional

Healthy



Belzberg M, et al. *J Invest Dermatol.* 2021;141(9):2208-2218.

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Thank You!

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