

# Squamous cell carcinoma arising in long-standing necrobiosis lipoidica treated with radical resection and split-thickness skin graft



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## INTRODUCTION

Malignant transformation within lesions of necrobiosis lipoidica (NL) is rare and challenging to diagnose and manage.<sup>1</sup> We present a patient in whom squamous cell carcinoma (SCC) developed within a long-standing, ulcerated plaque of NL that was successfully treated with limb-sparing resection and split-thickness skin graft.

## CASE REPORT

A 78-year-old nondiabetic woman with a past medical history of remote pulmonary mycobacterium avium complex infection, *Staphylococcus aureus* osteomyelitis of the right clavicle, and SCC in situ on the right thigh presented with progressive ulceration of a long-standing plaque of NL that had been present on the right shin for 40 years.

On initial examination, her right shin had a 9.0 × 25.0-cm atrophic telangiectatic yellow-pink plaque with a central 4.5 × 4.0-cm ulcer (Fig 1). The differential diagnosis included infection with exuberant reactive epithelial hyperplasia, vegetative pyoderma gangrenosum with or without underlying active NL, and SCC. Biopsies of the ulcer over time showed pseudoepitheliomatous hyperplasia with limited keratinocyte atypia, fibrosis, and mixed inflammation (Fig 2, A). Occult infection was ruled out by tissue cultures, microbial stains,

### Abbreviations used:

NL: necrobiosis lipoidica  
 SCC: squamous cell carcinoma

polymerase chain reaction, and gamma-interferon release assay. To avoid perpetuating possible pathology and following the patient's preference, anti-inflammatory and conservative treatments were then attempted, including oral and intralesional steroids, pentoxifylline, oral tofacitinib, and intralesional 5-fluorouracil. The ulcer initially waxed and waned over the course of several years in response to various treatments until it developed a verrucous appearance and became painful. Given the heightened concern for SCC, the patient was discussed at the interdisciplinary tumor board with Surgical Oncology, which then performed multifocal incisional biopsies revealing atypical squamous proliferation with foci of well-differentiated but definitive SCC (Fig 2, B and C). Subsequent magnetic resonance imaging showed extension of the tumor to abut muscle and the anterior tibial shaft.

Because the tumor was well defined clinically with islands of well-differentiated SCC histologically, Surgical Oncology pursued resection of the mass

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Progression of recalcitrant ulcer within longstanding necrobiosis lipoidica



**Fig 1.** Clinical images of the development of squamous cell carcinoma within ulcerated necrobiosis lipoidica treated with radical resection and split-thickness skin grafting. Progression of the ulcerated lesion within the waxy plaque of necrobiosis lipoidica on the right anterior shin with telangiectasias, central atrophy, and elevated erythematous borders.

with 1- to 2-cm margins and partial resection of the anterior tibia, followed by vacuum-assisted closure to promote granulation tissue formation over the large wound bed (Fig 3, A). Negative margins were achieved, and final pathologic findings confirmed well-differentiated SCC, without perineural or lymphovascular invasion. Preoperative imaging had shown no locoregional or distant disease, and the patient deferred sentinel node biopsy or further treatment. After 1.5 months, a scouting biopsy showed granulation tissue without recurrence (Fig 2, D), and a split-thickness skin graft was placed (Fig 3, B). The graft healed well, and the patient has remained disease free for 8 months with no evidence of nodal disease on ultrasound of the right inguinal nodal basin and clinical examination.

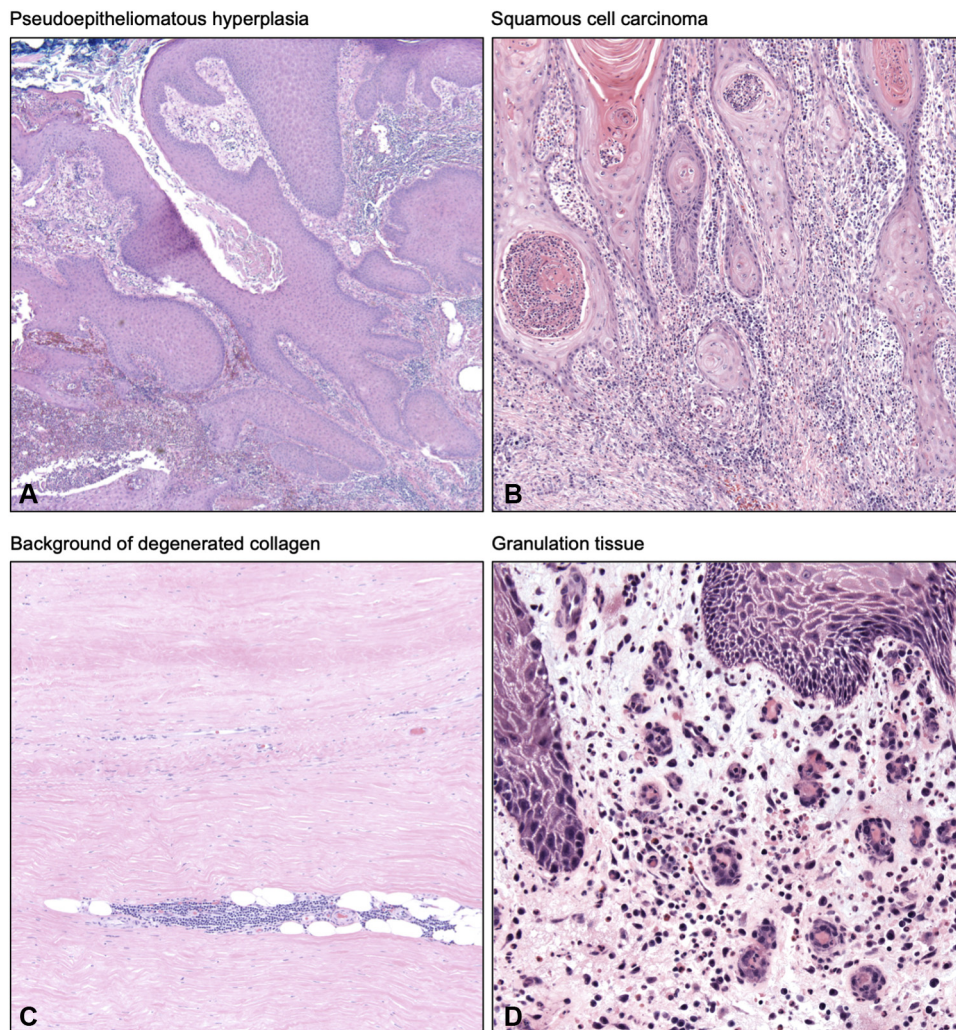
## DISCUSSION

Malignant transformation within chronic ulcerated NL is a rare complication that can be challenging, and we present a case that was successfully diagnosed and managed through a multidisciplinary approach.<sup>1,2</sup> Distinguishing pseudoepitheliomatous hyperplasia from true SCC within extensive areas of inflammation is difficult and requires careful clinicopathologic correlation.<sup>3,4</sup> Furthermore, most reports of SCCs associated with NL describe them as low-grade lesions, such

as “well-differentiated squamous cell carcinoma” and “verrucous carcinoma.”<sup>3,4</sup> In our case, multiple biopsies were required to definitively distinguish invasive SCC from reactive atypia. Once SCC was confirmed, more aggressive surgical treatment of the entire clinical lesion was clearly warranted. Whether NL-associated pathology predisposed this patient to development of SCC remains speculative. We hypothesize that a proinflammatory tissue microenvironment, along with potential immune dysfunction, as indicated by our patient’s history of unusual infections, may have played a role in the initiation of cancer.<sup>5</sup>

There are no established guidelines for the management and follow-up of SCCs associated with NL. Case reports have demonstrated clearance of such SCCs by aggressive surgeries, often leading to amputations, and historically, excision down to the fascia to avoid recurrence was sometimes recommended for treatment-resistant NL, even without malignant transformation.<sup>6</sup> Our patient was successfully treated by limb-sparing resection, which minimized morbidity and allowed her to remain active and continue her prior activities, including tennis.

A recent prospective study examining risk factors for metastasis or local recurrence of cutaneous SCCs recommended evaluating high-risk cutaneous SCCs (>6.0-mm thickness in this case) every 3 to



**Fig 2.** Pathologic images of progression from pseudoepitheliomatous hyperplasia to squamous cell carcinoma. **A**, Florid pseudoepitheliomatous hyperplasia, inflammation, and fibrosis. **B**, Focus of well-differentiated squamous cell carcinoma. **C**, Margin of squamous cell carcinoma with layers of degenerated collagen, consistent with end-stage necrobiosis lipoidica. **D**, Reactive squamous epithelium overlying exuberant granulation tissue.

4 months for 4 years with clinical examination plus ultrasonography of the regional nodal basin.<sup>7</sup> In addition to being safe and cost effective, ultrasonography was found to be more reliable for early detection of lymph node metastases than palpation or computed

tomography scans.<sup>7</sup> Given the size of our patient's tumor and rare instances of metastasis reported in cases associated with NL, this patient will continue to be monitored regularly with clinical examination and ultrasonography of the regional lymph nodes.<sup>2</sup>



**Fig 3. A,** Radical resection of the squamous cell carcinoma, followed by granulation tissue formation. **B,** Split-thickness skin grafting performed following excision.

**Conflicts of interest**

None disclosed.

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