

Primary cutaneous nasal-type NK/T-cell lymphoma presenting as purpuric nodules on the lower leg



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INTRODUCTION

Nasal-type extranodal natural killer (NK)/T-cell lymphoma is a rare and aggressive form of peripheral T-cell lymphoma associated with Epstein-Barr Virus and high mortality.^{1,2} It is rare in North America, with a higher prevalence in Asia and Central America.¹ Patients with nasal-type extranodal NK/T-cell lymphoma presenting in an extranasal location represent the minority of such cases, but tend to exhibit a more advanced stage of disease with a worse prognosis.^{2,3} Moreover, skin involvement is significantly more common in nasal-type extranodal NK/T-cell lymphoma in extranasal locations.⁴ Skin lesions usually manifest as a generalized morbilliform exanthem or multiple purpuric subcutaneous nodules with or without ulceration.⁵ Although the presenting clinical signs are difficult to recognize, given that the early cutaneous lesions may mimic an inflammatory process, early diagnosis may improve survival after treatment.

CASE REPORT

A 53-year-old man with a history of paroxysmal atrial fibrillation on warfarin therapy and end-stage renal disease on hemodialysis (complicated by secondary hyperparathyroidism) presented with a 5-day history of rapidly enlarging, mildly tender, purpuric, subcutaneous nodules on his left shin (Fig 1). He was referred to dermatology by his primary care physician, who noticed these lesions at a routine visit and became concerned after failing to elicit any history of trauma to the left shin. In the dermatology clinic, 2 tissue samples were taken by 4-mm punch

Abbreviation used:

NK: natural killer

biopsy, one of which was cultured and negative for bacteria, fungus, or acid-fast bacilli; the other was processed for histology and immunostaining. The latter sample demonstrated a dermal-based malignant lymphoma composed of medium-sized cells with hyperchromatic irregular nuclei, indistinct nucleoli, and moderate amounts of clear cytoplasm. Abundant karyorrhectic debris, hemorrhage, and necrosis were observed, along with epidermotropism, extension into subcutaneous adipose tissue, and evidence of angiodestruction. Tumor cells showed positive immunostaining for CD3 (cytoplasmic staining using a monoclonal antibody targeting the carboxy-terminal region of the CD3 epsilon chain), CD7, CD56, perforin, T-cell intracellular antigen 1, and CD30 and *in situ* hybridization for the Epstein-Barr encoding region (Fig 2); the Ki67 proliferation index was approximately 80% (not shown).

Immunostaining results for CD5, CD4, and CD8 were negative. These findings were consistent with a diagnosis of primary cutaneous nasal-type extranodal NK/T-cell lymphoma.

Three weeks after the patient's diagnosis, the initial positron emission tomography-computed tomography scan revealed that the lymphoma was limited to the left leg, with no extracutaneous spread despite that he developed extensive local tissue necrosis requiring debridement and wound care (Fig 3).

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Fig 1. Nasal-type NK/T-cell lymphoma. The left leg at presentation. *NK*, Natural killer.

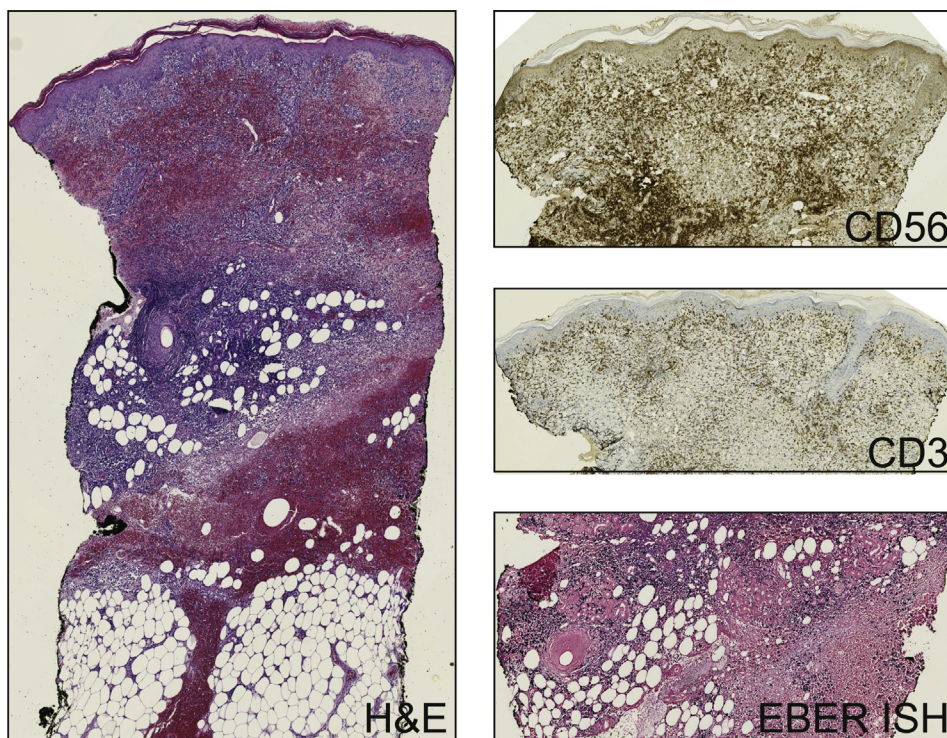


Fig 2. Nasal-type NK/T-cell lymphoma. Histopathology with hematoxylin-eosin, immunohistochemistry for CD56 and CD3 (cytoplasmic staining of the epsilon chain), and *in situ* hybridization for the Epstein-Barr Encoding Region. *EBER*, Epstein-Barr Encoding Region; *H&E*, hematoxylin-eosin; *ISH*, *in situ* hybridization; *NK*, natural killer.



Fig 3. Nasal-type NK/T-cell lymphoma. Developing lesions on left leg. NK, Natural killer.

Five weeks after his diagnosis, the patient began receiving treatment, which consisted of 6 repeating 3-week cycles of gemcitabine and cisplatin (days 1, 3, 5, and 8, with a break on days 9-21) for the first cycle and subsequent cycles substituting pegylated L-asparaginase on day 5. After the first treatment cycle, the patient experienced rapid improvement in his skin lesions. Unfortunately, after just 1 dose of the L-asparaginase on the second treatment cycle, he had to discontinue it for the remaining cycles because of medication-related acute liver failure. Despite this, after resuming treatment without L-asparaginase, his open wounds had closed by 5 and a half months after diagnosis and follow-up positron emission tomography—computed tomography 7 months after diagnosis showed that the disease had not spread beyond the skin and subcutis of the left leg. His treatment was completed 6 months after diagnosis, and 1 year after his diagnosis, all of his lesions had healed with scarring and he felt well (Fig 4).

DISCUSSION

The case discussed here is illustrative in its presentation and course. It highlights important clues to the diagnosis of nasal-type extranodal NK/T-cell lymphoma that may be useful for clinicians who encounter similar cases.

First, this case illustrates important deviations from most cases of nasal-type extranodal NK/T-cell

lymphoma, which is much more common in Asia and Central America, presents on the nose, and follows a rapidly progressive course with high mortality.¹ In a retrospective study of nasal-type extranodal NK/T-cell lymphoma on the nose, patients treated optimally with pegylated asparaginase, gemcitabine, and oxaliplatin combined with radiotherapy demonstrated a 2-year progression-free survival and 2-year overall survival of 77.1% and 82.9%, respectively.⁶ In contrast, our patient is from the United States and presented with lesions on the leg. Non-nasal nasal-type extranodal NK/T-cell lymphoma has been shown to portend a much worse prognosis, with a 5-year progression-free survival of 4.2% (vs 50.9% for nasal) and 5-year overall survival of 16% (vs 55.8% for nasal).² Despite his poor prognosis, the patient presented here has responded very well to treatment after 1 year, but there is a potential for relapse.

Second, this case highlights the critical role of the primary care physician in identifying clues that the patient's lesions warranted immediate referral to dermatology. The seriousness of the diagnosis could have been easily overlooked on examination or mistaken as resulting from minor trauma while on warfarin therapy. Moreover, the differential diagnosis of his purpuric nodules included several other much more common entities, such as erythema nodosum, calciphylaxis, warfarin-induced

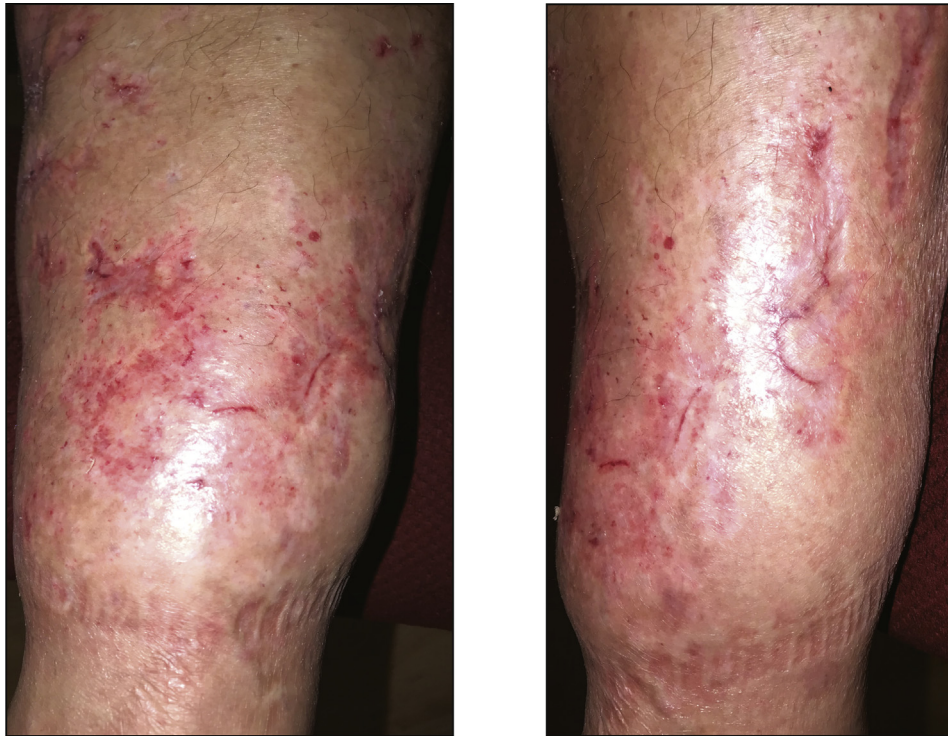


Fig 4. Nasal-type NK/T-cell lymphoma. Healed lesions on the left leg after treatment. *NK*, Natural killer.

skin necrosis, and other vasculitis/vasculopathy. However, the patient lacked a trauma history, risk factors for erythema nodosum, pain out of proportion on examination, or retiform purpura, which hinted at this more insidious diagnosis. In a large multicenter cohort study by Abramson et al,⁷ the dominant positive prognostic factors for peripheral T-cell lymphomas were earlier stage at diagnosis and initial response to treatment. Therefore, it was important that his primary care physician recognized this concerning presentation and referred him to dermatology, resulting in a diagnostic biopsy within just 2 days of the initial encounter.

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