Extranodal natural killer/T-cell lymphoma, nasal type: A rare but critical diagnosis

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INTRODUCTION

Natural killer (NK)/T-cell lymphoma is a rare subtype of non-Hodgkin lymphoma (NHL) associated with Epstein-Barr virus (EBV).[1-4] While NK/T-cell lymphoma comprises only 5%-10% of NHL in the United States, it is more common in Asia and Central and South America, accounting for 15%-20% of NHL, and less common in Europe, only accounting for 1% of the population with NHL.[1,5-7] NK/T-cell lymphoma most commonly involves the nasopharynx and nasal cavity; however, it might also affect perinasal skin.[1,4,8] This type of NK/T-cell lymphoma, known as extranodal NK/T-cell lymphoma, nasal type (ENKTCL), involves the formation of a tumor on the midface, with symptoms of nasal obstruction, epistaxis, rhinitis, sinusitis, and ulceration of the nasal septum and surrounding areas.[2,4,9] While the prognosis for early-stage ENKTCL has improved recently, the prognosis for late-stage disease remains poor, making early diagnosis and treatment crucial.[6,8,10] Here we describe a case of ENKTCL in a 79-year-old white man from the upper Midwestern United States.

Abbreviations used:

EBV:	Epstein-Barr virus
ENKTCL:	natural killer/T-cell lymphoma, nasal type
NHL:	non-Hodgkin's lymphoma
NK:	natural killer
PEG:	polyethylene glycol
TIA-1:	T-cell intracellular antigen 1

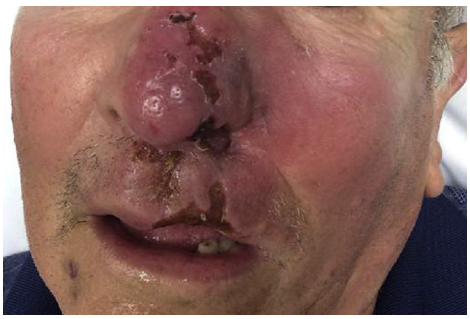

Fig 1. Clinical presentation in a patient with natural killer/T-cell lymphoma, nasal type. Erythematous indurated plaque involving the nose and upper cutaneous lip extending onto the cheek with overlying irregular crusted ulcerations. The left-upper lip and left nasal ala are retracted.

CASE

A 79-year-old white man was referred for evaluation of progressive facial erythema and ulceration. He had been in his usual state of good health until 1-year prior, when he was admitted to a hospital for meningitis, which was believed to be a secondary opportunistic infection. He subsequently developed recurrent episodes of facial erythema and swelling that failed to respond to multiple courses of antibiotics. Tissue cultures were repeatedly negative. Over the subsequent year, his condition worsened, and nasal septal and palatal perforation developed. He lost 30 pounds, which was attributed to an inability to chew. He was referred to our facility for further treatment.

Upon physical examination, the left and mid nasal bridge, nasal tip, nasal ala, and left cheek were erythematous, edematous, and indurated. Jagged ulcerations were present along the left nasal bridge, and an extensive, well-demarcated ulceration involved the upper cutaneous and vermillion lip, extending onto the mucosal lip. A lateral perforation connected the oral cavity with the nasal cavity. The

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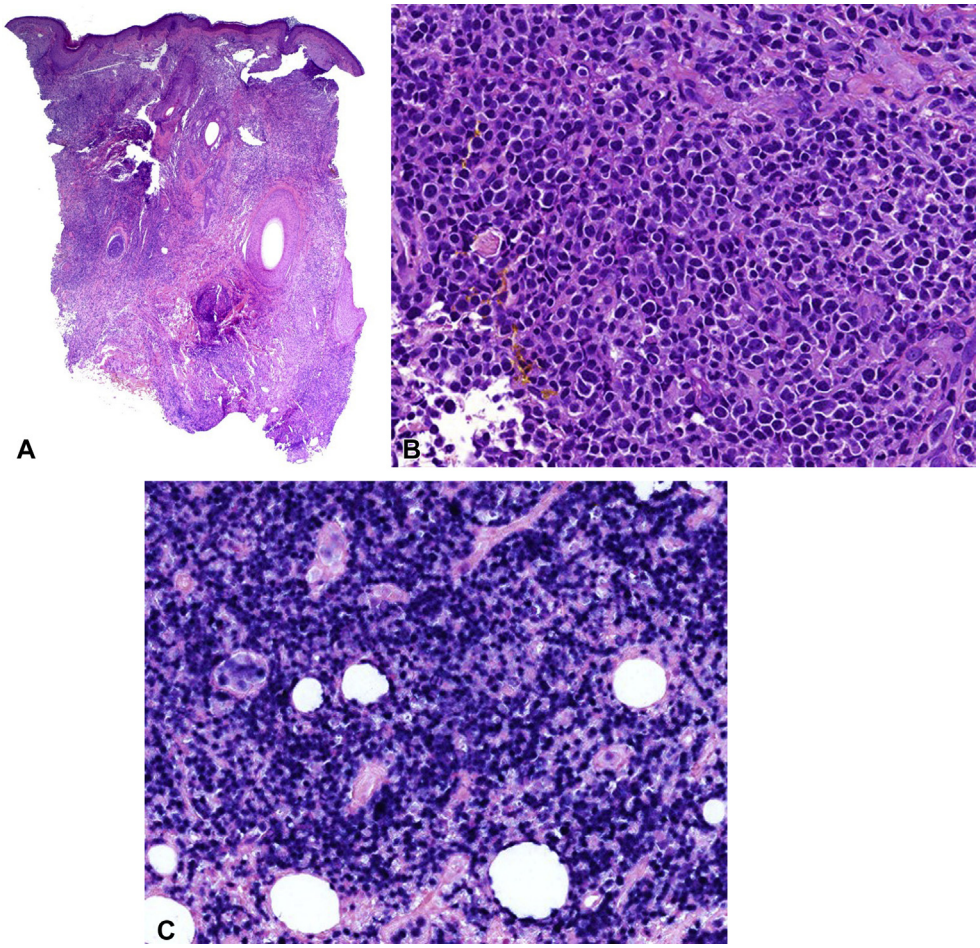

Fig 2. Histologic sections reveal a dense infiltrate involving the epidermis, dermis, and subcutaneous tissue. The infiltrate is composed of small-to-medium—sized lymphocytes with irregular nuclear contours and granular chromatin. In situ hybridization for Epstein-Barr virus—encoded RNA. Nearly all tumor cells show strong nuclear labeling. (**A-C**, Hematoxylin-eosin stain; original magnification: **A**, ×20; **B**, ×400; **C**, ×200.)

left nasal ala and left upper lip were retracted (Fig 1). Lesions were minimally tender to palpation, and the patient had no cervical lymphadenopathy.

Two punch biopsies were obtained from the affected skin of the left-upper lip for routine histology and tissue culture. Microscopic examination revealed an atypical lymphoid infiltrate diffusely involving the dermis and focally involving the epidermis (Fig 2, *A*). Lymphocytes were small to intermediate in size with convoluted nuclear contours (Fig 2, *B*). Atypical lymphoid cells were positive for CD2, CD3, CD56, T-cell intracellular antigen (TIA-1), and granzyme. In situ hybridization for EBV was diffusely positive in lesional cells (Fig 2, *C*). Given the clinical, histopathologic, and immunophenotypic features, a diagnosis of ENKTCL was made. A subsequent positron emission tomography-computed tomography scan showed involvement limited to the mid face. The patient was treated with concurrent radiotherapy, polyethylene glycol (PEG) asparaginase, vincristine, and prednisone. Although he experienced initial improvement in his cutaneous lesions and a decrease in EBV titers, his functional status rapidly declined. Three months after diagnosis, he entered home hospice care and died shortly thereafter.

DISCUSSION

The differential diagnosis for midline destructive lesions of the face includes a myriad of neoplastic, autoimmune, infectious and traumatic etiologies.[3] Those most commonly considered by the dermatologist include NHL (such as ENKTCL), leprosy, leishmaniasis, syphilis, rhinoscleroma, granulomatosis with polyangiitis, and cocaine use. Diagnosis of ENKTCL is usually based on a combination of epidemiologic, clinical, and histopathologic features.[4] Clinical features that suggest a diagnosis of

ENKTCL include nasal obstruction; epistaxis; and concurrent fever, malaise, and weight loss, although these are not specific for this diagnosis.[3] Skin biopsies display a dense, dermal, atypical lymphoid infiltrate; however, definitive interpretation can be challenging because of admixed reactive cells and necrosis.[2] Immunophenotypic evaluation can be helpful, with neoplastic T cells expressing CD56, TIA-1, and EBV.[1] A low threshold should be set for ordering a panel of these stains when working up a midline destructive lesion. Much of the data regarding ENKTCL is derived from patient populations in Asia, Latin America, and Central America; information on US patients with ENKTCL remains limited. Experts believe that this geographic variation might in part be explained by the increased prevalence of EBV in Asia and Latin and Central America.[2,6] ENKTCL remains rare in the United States; a population-based study in California found that the incidences in both Hispanics and Asians/Pacific Islanders were approximately 4 times higher than in non-Hispanic whites (0.05 per 100,000 person-years).[7] Rarely, the disease occurs in US-born white persons, as in our case.

We report a case of ENKTCL occurring in an elderly white man residing in the upper Midwest with no history of travel outside the United States or to areas where ENKTCL is more prevalent. Our case is also atypical in that the median age of diagnosis of ENKTCL is the 4th to 5th decade of life, whereas our patient was nearly 80 years. Diagnosis of this aggressive subtype of NHL was delayed for over a year as his symptoms progressed, resulting in significant destruction of nasal tissues and disfigurement of the face. While similar cases have been described in the literature, our case underscores the fact that ENKTCL can occur in any community, from private practices to academic medical centers. A high index of clinical suspicion for ENKTCL is necessary when evaluating a patient with midline facial lesions, as histologic findings can be nonspecific without the addition of appropriate immunohistochemical stains. Furthermore, the prognosis for patients depends heavily on the stage of their disease. Outcomes for early-stage ENKTCL have improved in recent years, with overall 5-year survival reaching 70%.[10] However, the prognosis for late-stage disease remains poor, with an overall 5-year survival as low as 30%.[6,8] Given this, early diagnosis and treatment are essential.

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