

## Extranodal Natural Killer/T-cell Lymphoma, Nasal Type

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### To the Editor:

The term extranodal natural killer (NK)/T-cell lymphoma, nasal type, was adopted by the World Health Organization to replace angiocentric lymphoma.<sup>1</sup> These lymphoid neoplasms can appear on the head and neck,<sup>1</sup> affecting the mucosa of the nasal cavity, but they are uncommon in the central facial region.<sup>2</sup> They have also been described in other locations such as the skin, soft tissues, testicles, upper respiratory tract, and gastrointestinal tract.<sup>3</sup> The World Health Organization has classified them into 3 main categories<sup>1</sup>:

1. Extranodal NK/T-cell lymphoma, nasal type
2. Enteropathy-type T-cell lymphoma
3. Subcutaneous panniculitis-like T-cell lymphoma

Extranodal NK/T-cell lymphoma, nasal type, is closely associated with Epstein-Barr virus infection.<sup>4</sup>

The skin constitutes the second most common site in which primary extranodal lymphomas develop. In order to classify a lymphoma as a primary neoplasm of the skin, there must be no

evidence of disease at any other site for at least 6 months prior to the initial presentation.<sup>5</sup> Primary NK-cell lymphomas of the skin are rare. Infiltration by NK-cell lymphomas arising in the nasal mucosa has been reported<sup>6</sup>; these neoplasms have an aggressive behavior, leading to rapid destruction of the skin and adjacent tissues.

We present the case of a 73-year-old woman with no past history of interest, who presented a 6-month history of a painless tumor in the nasal vestibule. The tumor increased in volume until it ulcerated through the skin and extended to affect the whole nose and both cheeks. It had an ulcerated, necrotic appearance with well-defined borders (Figure 1). Helical computed tomography of the facial region revealed an extensive lesion that involved the left nasal fossa and affected the lateral cartilages on that side. There was no evidence of intraorbital or intracranial spread.

Biopsy revealed an ulcerated epidermis with abundant necrotic tissue and an infiltrate of pleomorphic cells with prominent, indented nuclei. The cells were found mainly in the walls of

the blood vessels of the dermis and subcutaneous tissue (Figure 2). Immunohistochemistry of the neoplastic cells was positive for CD56, CD45RO, and CD43, and negative for CD20, CD30, and CD57, leading to diagnosis of centrofacial non-Hodgkin NK/T-cell lymphoma. Polymerase chain reaction for Epstein-Barr virus was negative.

The rest of the physical examination and chest radiograph were normal.

The patient was referred to the hematology department, where chemotherapy and radiation therapy were prescribed, but this treatment was refused by the patient. She died 3 months later.

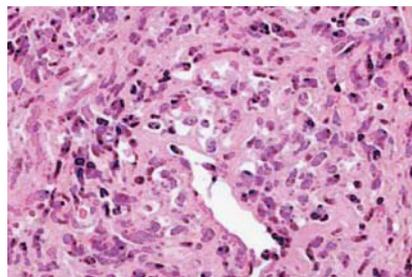
Extranodal NK/T-cell lymphomas are rare, accounting for around 12% of non-Hodgkin lymphomas,<sup>7</sup> and occur mainly in adults, with a peak in the fifth decade of life.<sup>3</sup> They are more common in individuals of Asian origin than in Europeans, and they are also relatively prevalent among individuals of Latin American and Mexican origin<sup>2</sup>; this would suggest that genetic factors may be important in the development of these lymphomas.<sup>3,4</sup>

The differential diagnosis of these disorders includes Wegener granulomatosis and infections such as mucormycosis in immunosuppressed patients.

NK cells are derived from pluripotent cells that express CD16, CD56, and CD57. They are initially related to T cells but later differentiate to form a distinct cell line. This new line is formed of lymphocytes that have cytotoxic activity despite there being no previous sensitization in the individual. They are cells with an abundant, clear cytoplasm containing azurophilic granules, and they express the CD56 surface antigen. NK-cell lymphomas are rare tumors



**Figure 1.** Painless tumor of the nasal vestibule. The tumor increased in size until it ulcerated the skin and spread to affect the whole nose and both cheeks.



**Figure 2.** Malignant lymphoid infiltrate with a predominantly angiocentric pattern. The malignant cells are small and have abundant, clear cytoplasm; they were CD56<sup>+</sup> on immunohistochemical study (×40).

with an aggressive course and are characterized by an angiocentric, angiodestructive, lymphoid infiltrate. Immunohistochemically these cells are CD2<sup>+</sup>, CD3<sup>-</sup>, CD7<sup>+/-</sup>, and CD56<sup>+</sup>.

In general, CD56<sup>+</sup> tumors have a poor prognosis, with a mean survival of 13 months.<sup>4</sup> It has been reported that lymphomas that overexpress the p53 gene have a worse prognosis.<sup>8</sup>

These tumors must be differentiated from blastic NK-cell lymphoma. This type of tumor was considered to arise from immature NK cells, but it is now known that the precursor cells are plasmacytoid dendritic cells.<sup>9</sup>

Due to their rarity, it is important to recognize the existence of highly aggressive lymphomas and to classify them correctly. Both pathologists and clinicians must keep these tumors in mind, make the correct diagnosis, and start specific treatment rapidly. Radiation therapy is the treatment of choice in localized disease and is usually combined with chemotherapy.<sup>3</sup> If patients are initially managed using chemotherapy, palliative or adjuvant radiation therapy is recommended, as its benefits persist even after chemotherapy.<sup>10</sup>

## References

1. Jaffe ES, Harris NL, Stein H, et al. Pathology and Genetics of Tumours of Haematopoietic and Lymphoid Tissues. World Health Organization Classification of Tumours. Lyon: IARC Press; 2001.
2. Mosqueda-Taylor A, Meneses-García A, Zarate-Osorno A, Ruiz-Godoy, Rivera LM, Ochoa-Carrillo FJ, et al. Angiocentric lymphomas of the palate; clinico-pathological considerations in 12 cases. *J Oral Pathol Med.* 1997; 26:93-7.
3. Nava VE, Jaffe ES. The Pathology of NK-Cell Lymphomas and Leukemias. *Adv Anat Pathol.* 2005;12:27-34.
4. Bekkenk MW, Jansen PM, Meijer CJL, Willemze R. CD56+ hematological neoplasms presenting in the skin: a retrospective analysis of 23 new cases and 130 cases from the literature. *Ann Oncol.* 2004;15:1097-108.
5. Cerroni L, Signoretti S, Hofler G, Annessi G, Pütz B, Lackinger E, et al. Primary cutaneous marginal zone B-cell lymphoma: A recently described entity of low-grade malignant cutaneous B-cell lymphoma. *Am J Surg Pathol.* 1997;21:1307-15.
6. Liu J, He Z, Xie Y, Fang K, Gao Z, Wang B. Nasal natural killer/T cell lymphoma with cutaneous involvement: case report and Chinese literature review reported in China mainland. *J Dermatol.* 2003;30:735-41.
7. Au WY, Ma SY, Chim CS, Choy C, Loong F, Lie AK, et al. Clinicopathologic features and treatment outcome of mature T-cell and natural killer-cell lymphomas diagnosed according to the World Health Organization classification scheme: a single center experience of 10 years. *Ann Oncol.* 2005;16: 206-14.
8. Meneses-García A, Herrera J, Mohar A, García-Cuellar C, Suchil-Bernal L. [Metalloproteinase [MMP-1,2 and 11], tissue inhibitor of metalloproteinase-1 (TIMP-1, and p53 expression in nasal-type angiocentric T/NK-cell lymphoma: an immunohistochemical study)]. *Gac Med Mex.* 2005;141:291-6.
9. Calvo M, González C, Martín E, Marqués A, Jaén P. [Blastic NK-cell lymphoma]. *Actas Dermosifiliogr.* 2006; 97:253-6.
10. You JY, Chi KH, Yang MH, Chen CC, Ho CH, Chau WK, et al. Radiation therapy versus chemotherapy as initial treatment for localized nasal natural killer (NK)/T-cell lymphoma: a single institute survey in Taiwan. *Ann Oncol.* 2004;15:618-25.

## Paraneoplastic Ichthyosis

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### To the Editor:

We report the case of a 63-year-old woman with a history of type 2 diabetes and hyperuricemia who presented with asthenia, weight loss (totalling 14 kg), pruritus, xerosis, and diffuse scaling. The symptoms had begun 4 months earlier. The patient also had a growth under her right arm that had been present for a month.

On examination, the patient was found to have marked xerosis and widespread scaling, with small, loosely adherent,

confluent scales that were whitish in color. The most severely affected areas were the extensor surfaces of the arms and legs; here the flakes were browner and there were also reticulated lesions reminiscent of eczema craquelé (Figure 1). Scaling was also evident on the flexor surfaces and on the face and scalp. Palpation revealed enlarged axillary lymph nodes under both arms (the node in the right axilla measured 5 cm) (Figure 2). Computed tomography showed masses in the mediastinum and in both



**Figure 1.** Small, widespread, partially adherent, whitish scales.