

Hydroa vacciniforme-like cutaneous T/NK-cell lymphoma, nasal type

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Abstract

Hydroa vacciniforme-like cutaneous T/NK-cell lymphoma is a rare lymphoma mainly affecting Asian and Latin American indian children. It starts with swelling, vesicles, crusts, and vacciniform scars of extended evolution. Its severity increases with time and may cause disfigurement, thus physically and psychologically affecting patients.

Generally, these patients have poor prognosis due to late detection of the lymphoma. A 20-year-old female patient with nasal-type NK-cell lymphoma starting with hydroa vacciniform (HV) of poor evolution at the age of 13 years is reported. The authors suggest that patients with atypical HV may improve with treatment at an early stage (*Dermatol Argent* 2009; 15(5):350-353).

Key words: *T/NK-cell lymphoma, nasal type; hydroa-like cutaneous T/NK-cell lymphoma.*

ABREVIATURAS

AFB: acid-fast bacillus.

ALP: alkaline phosphatase.

ANCAs: antineutrophil cytoplasmic antibodies.

Anti-EBNA: anti-Epstein-Barr virus nuclear antigen antibody.

Anti-MPO: antimyeloperoxidase antibody.

Anti-PR3: antiproteinase 3 antibody.

Anti-VCA: anti-Epstein-Barr virus capsid antigen antibody.

CAT: computerized axial tomography.

CHOP: cyclophosphamide, doxorubicin, vincristine, and methylprednisone.

EBER: small size EBV nuclear RNA.

EBV: Epstein-Barr virus.

GOT: glutamic-oxalacetic transaminase.

GPT: glutamic-pyruvic transaminase.

H-E: hematoxylin-eosin.

HV: hydroa vacciniforme.

LDH: lactic dehydrogenase.

LMP-1: latent membrane protein 1.

NK: natural killer.

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Introduction

HV-like T-cell cutaneous lymphoma is a rare lymphoma that mainly affects children and is associated with Epstein-Barr virus (EBV). Patients, almost exclusively from Latin America and Asia, develop HV-like papulovesicular lesions associated with swelling, bullae, ulcers, crusts, and scars involving both areas exposed and not exposed to solar radiation. We report a HV-like NK lymphoma, nasal type.

Clinical case

A 20-year-old female Bolivian patient residing in the Province of Buenos Aires since she was 13 years old, without significant inherited-familial history. Personal history: measles. According to the patient, it started at the age of 6 years with facial erythema and swelling which increased with solar exposure and did not totally remit in winter. She consulted at several hospitals and reached HV diagnosis; she was treated with chloroquine and subsequently with methylprednisone. She was admitted at our hospital in July 2007 with left basal pneumonia. Interconsultation with Dermatology was requested for facial erythema and swelling with vesicles, erosions, crusts, and smallpox-like scars affecting both cheeks, the forehead and the chin (**Figure 1**). There was no relation with solar exposure, and no reference to hypersensitivity to mosquito bites. With clinical diagnosis of HV, a skin biopsy was performed, which resulted in the presence of epidermal vesicles containing fibrin and inflammatory cells, and perivascular inflammatory infiltrate in dermis consistent with HV (**Figure 2**). Laboratory: blood cell count within normal limits. ESR 101 mm/h. Liver function tests: GPT 36 U/L, GOT 42 U/L; ALP 334 U/L. Treatment with methylprednisone 8 mg/day was instituted, with improvement of the clinical picture. The patient referred events of chronic sinusitis and hemoptysis, and we requested facial bone and chest CATs, which showed mucosa thickening in paranasal areas and irregularities of mucosa in nasal fossae and turbinate bone; and bronchial ectasia at lung basal segments. In October, she presented intense facial swelling and an ulcerated crusty lesion at left nasal lateral level (**Figure 3**), which evolved into perforation of the nasal wall. It was accompanied with fever, rinorrhea and left sinusopathy, and was treated with levofloxacin 500 mg/day and methylprednisone 40 mg/day. A new laboratory test showed slight decrease in hematocrit and neutrophilia. EBV serology: anti-EBNA IgG +; anti-VCA IgG +; anti-VCA IgM -. ANCA_s++. Anti-PR3 0.1 U (N < 3.5 U). Anti-MPO 7.5 U (N < 9 U). Sputum AFB: negative. Normal porphyrin test. LDH 822 U/L. Beta 2 microglobulin 6.41 mg/l. The clinical picture worsened and suspecting a diagnosis of HV-like T-cell lymphoma, biopsy was obtained from the borders of the nasal ulcer and mucosa, with negative results for lymphoma. Therefore, a surgical biopsy from left side



Figure 1. Involvement of forehead, cheeks, and chin with swelling, erythema, vesicles, crusts, and smallpox-like scars.

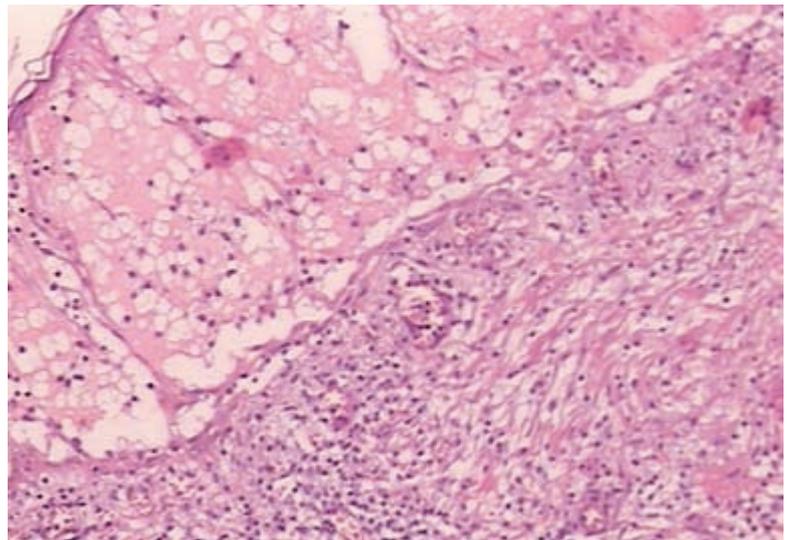


Figure 2. Presence of epidermal vesicle and dermal perivascular infiltrate with lymphocyte dominance (H-E).

of nasal septum was obtained and analyzed with H-E, resulting in the identification of a small-to-medium size monomorphic lymphoid cell population (**Figure 4**) involving all the dermis and partly migrating to epithelium, with the presence of atypical mitosis, angiocentricity, and areas of necrosis. Immunomarkers: weak intracytoplasmic CD3; positive CD56 (**Figure 5**); positive TIA-1 (**Figure 6**), and negative LMP-1. She was referred to the Hematology Department with diagnosis of T/NK lymphoma and treated with a cycle of cyclophosphamide, doxorubicin, vincristine, and methylprednisone (CHOP), but the patient developed septicemia and died. No autopsy was performed.

Comments

HV is a chronic photosensitive disorder characterized by the presence of recurrent vesicles and necrotic ulcerations which heal with smallpox-like scars, located on photoexposed areas; starting in childhood, it usually resolves spontaneously during adolescence and does not affect the general condition.¹

In 1986, Oono et al.² reported HV associated with cutaneous lymphoma in a 16-year-old patient, where HV lesions had appeared at 6 years of age; evolution was atypical, since lesions were not photoinduced, did not improve with age and affected general health.

Subsequently, several similar cases were reported, mostly in Asian and Latin American Indian children.³⁻⁵ Recently, some authors suggested that these cases were related to lymphoproliferative processes leading to the development of a cutaneous T-cell lymphoma.³⁻⁸ Chen et al.⁷ reported in 2002 a case of CD8+ T-cell cutaneous primary lymphoma with lesions similar to HV; these authors suggested that lymphoma may appear with early HV-like lesions, or develop years after their occurrence. Likewise, Feng et al.⁹ report a case of CD8+ T-cell lymphoma in a 12-year-old girl with hypersensitivity to mosquito bite since her first years of life; and they believed this hypersensitivity to insect bite was a nonspecific expression of altered immune response. A HV-like form associated to Hodgkin's lymphoma and node lymphoma has also been described in adults.^{10,11}

The presence of EBV has been mentioned in HV, HV-like and other lymphoproliferative processes; this suggests that this virus may trigger such processes in genetically predisposed patients and in a specific environment. Early exposure to EBV may cause immunotolerance of infected cells, allowing their continuous proliferation. This is possibly caused by loss or reduced expression of LMP-1 by neoplastic cells, thus becoming non-detectable by the immune system. It was also found that EBER (EBV-encoded small nuclear RNA) becomes more positive as the disease progresses; thus whether it is the cause or a consequence of the disease remains uncertain.¹² For some authors, this association of virus and lymphoproliferative processes possibly reflects endemic EBV distribution and may not suffice to justify virus association with lymphoma.¹³ However, others believe that EBV infection in a genetically susceptible population would firstly induce hypersensitivity to mosquito bite and hydroa vacciniforme, and later progress in a small number of cases to atypical hydroa vacciniforme or centrofacial lymphoma, possibly causing death by hemophagocytic syndrome.¹⁴

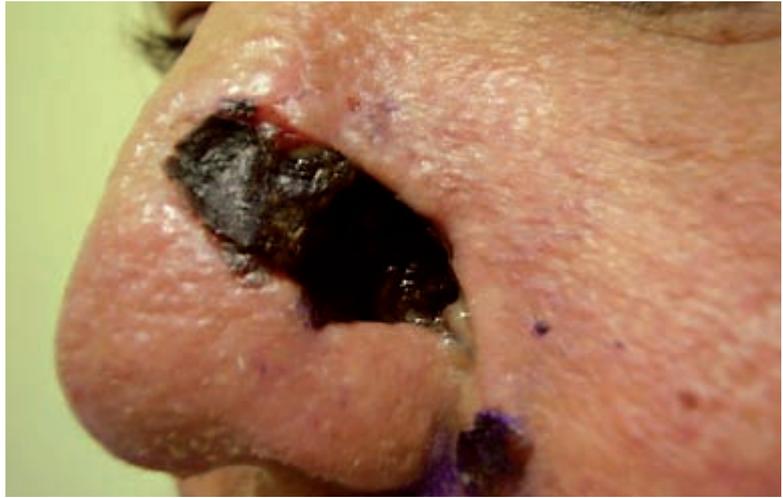


Figure 3. Ulcerated crusty lesion at the level of the left nasal side.

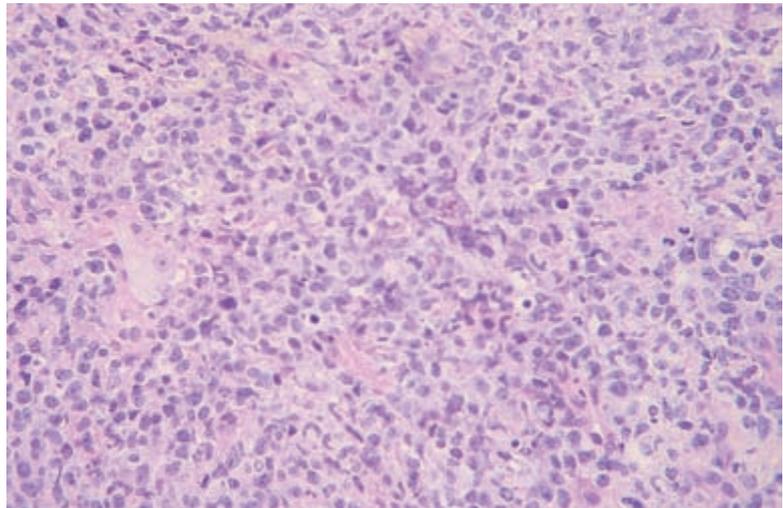


Figure 4. Small-to-medium-size lymphoid tissue pleomorphic infiltration with atypical mitosis (H-E).

Thus, typical and atypical forms of HV are included in the scope of cutaneous disorders induced by EBV-infected T-cells.¹⁵

In relation to the therapeutic approach of atypical HV, some authors suggest maintaining an expectant behavior, and others suggest treatment with thalidomide, cyclophosphamide, or corticosteroids.⁴

This case clearly manifested clinical and atypical HV, where the presence of lymphoma could be identified in the nasal septum biopsy specimen, with positive immunohistochemical markers for NK lymphoma.

Nasal type T/NK lymphoma, formerly known as midline malignant granuloma, is an aggressive neoplasia that may derive from NK-cells (CD56+) or T-cells (CD56-); incidence is higher in Asia and Central and South America, predominantly in young males. It appears as a rapid-growing destructive centrofacial tumor tending to ulcerate; in addition to its nasal and oropharyngeal location, the skin is the second site of involvement. By histology it is proved to consist of small to large cells with pale cytoplasm and irregular nucleus, which constitute a dense infiltrate in dermis, and occasionally in hypodermis. Immunohistochemistry generally marks positive CD2+, CD56+, CD3-, CD3 cytoplasmic +, TIA1+, Granzima B+, Perforin+, LMP-1+ and EBV usually. Internal organ dis-

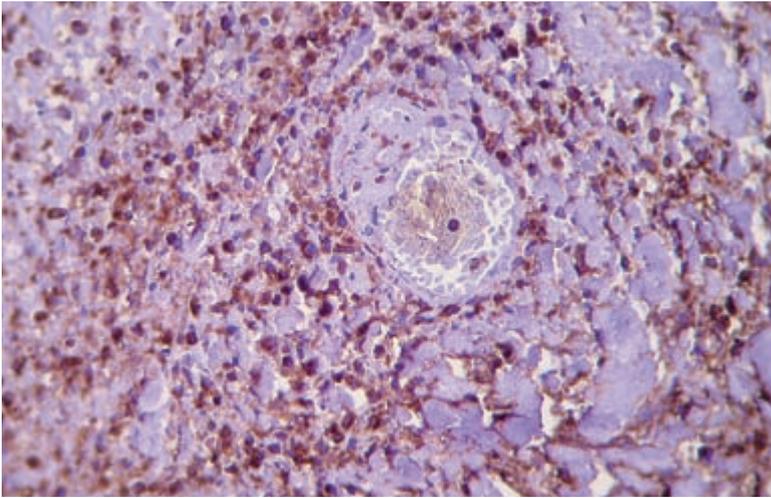


Figure 5. CD56+ immunomarkers.

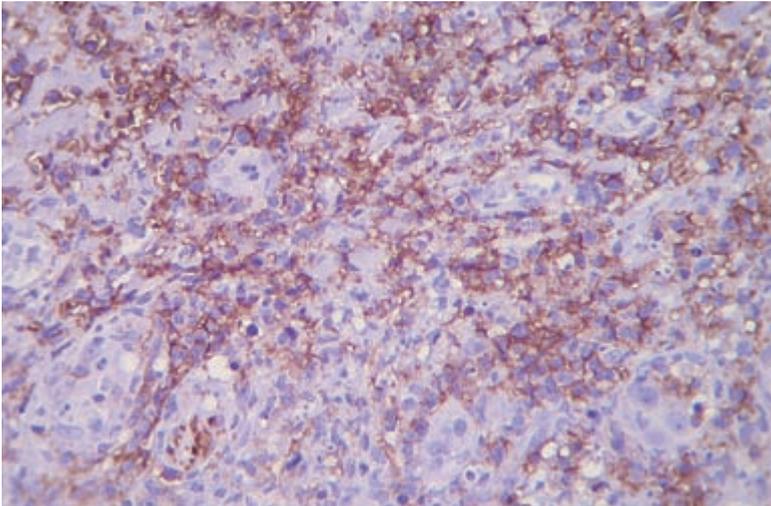


Figure 6. TIA-1+ immunomarkers. Angiocentricity is identified.

semination is common, with poorer prognosis. Treatment of nasal T/NK lymphoma includes cyclophosphamide, doxorubicin, vincristin and prednisone.¹⁶

Conclusions

Evidence exists that the presence of EBV in lymphoproliferative processes is an important factor in etiopathogenesis of such processes, with direct correlation. Thus, when cells were scarce, a spontaneous involution occurred; while a larger amount of infected cells correlated with development of lymphoma.¹² Like other authors, we believe that atypical HV falls within the scope of lymphoproliferative processes^{6,9,14} and is a lymphoma from the start. Consequently, we suggest that polychemotherapy treatment is justified in early stages of the cases of extended evolution affecting general condition and causing intense physical and psychological suffering due to this disfiguring disease, thus allowing the improvement of the currently severe prognosis with late treatment of these patients. We believe this case report is relevant, since no reports of this rare lymphoma have been found in the national literature.

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