Case Report

Extranodal natural killer/T-cell lymphoma, nasal type: A great pretender

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Abstract

Extranodal natural killer/T-cell lymphoma, nasal type (ENKTCL) is a rare Epstein–Barr virus associated lymphoma seen predominantly in Asian population with a 5 years survival rate ranging from 10% to 75% depending on the stage of presentation. In this case report, we describe an unusual presentation of ENKTCL, which in its early stages was clinically misdiagnosed as buccal space infection and later on histologically as inflammatory myofibroblastic pseudotumor owing to manifold reasons. Postoperative biopsy specimen showed characteristic feature of ENKTCL both histologically and immunophenotypically. This case report underlines the importance of adequate sampling and the unusual presentation of ENKTCL nasal type with oral manifestations.

Key words: Epstein–Barr virus, inflammatory myofibroblastic pseudotumor, lymphoma

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Introduction

Head and neck is a common locale for extranodal lymphomas, mostly of B-cell origin. However, cases of T-cell lymphomas are also reported in the literature. Extranodal natural killer (NK)/T-cell lymphoma, nasal type (ENKTCL) is now acknowledged as a distinct Epstein–Barr virus (EBV) associated clinicopathological entity.[1]

WHO classification of tumors of hematopoietic and lymphoid tissues classifies it under mature T-cell and NK-cell neoplasms.[2] It is a fast growing, aggressive tumor that leads to cataclysmic necrotising lesion affecting the midface.[3,4]

Nasal and paranasal areas constitute up to 4/5th of all the cases of ENKTCL. Less commonly involved areas include skin, liver, spleen, lungs, gastrointestinal tract. The neoplasm presents with initial nonspecific nasal symptoms, nasal discharge, obstruction, rhinitis, sinusitis, cellulitis, hemifacial pain, and edema.[5-7]

We report a case of ENKTCL, nasal type with deceptive initial clinical and histological features that lead to misdiagnosis and proved fatal.

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Case Report

A 49-year-old male came for evaluation of an ulcerated lesion over the right nasolabial fold and right upper labial vestibule. Patient underwent extraction of upper right canine and was treated for right buccal space infection 1-month ago with no evidence of improvement. There was a history of intermittent fever, nasal stuffiness, epistaxis and hemifacial pain. Patient was a known case of uncontrolled diabetes mellitus type 2 since 10 years and was on oral hypoglycemic.

Extraorally, a diffuse erythematous swelling was present over right maxillary region with an ulcerated area over the right nasolabial fold region [Figure 1a] measuring approximately 2 cm × 3 cm. Intraorally, an ulcerated lesion with sloughing was evident in the right upper labial vestibule. Sutures were seen at the site of nonhealing extraction socket [Figure 1b] and overall oral hygiene was poor. Bilateral submandibular lymph nodes were palpable and tender.

Patient was HIV seronegative. Fine needle aspiration cytology of the submandibular lymph nodes was suggestive of reactive hyperplasia. Computed tomography (CT) of the face and paranasal sinuses revealed mild thickening of the mucosa of right maxillary sinus and posterior ethmoidal air cells. The foregoing findings favored an inflammatory/infectious etiology, probably fungal or bacterial.

Incisional biopsy revealed small to medium sized hyperchromatic round cells and spindle-shaped cells proliferating with in an eosinophilic amorphous background. Periodic acid-Schiff staining revealed fungal hyphae [Figure 1c and d]. Histopathological findings were suggestive of an inflammatory myofibroblastic pseudotumor. Thereafter the lesion was excised under general anesthesia. Postoperatively patient developed a low-grade intermittent fever and progressive clinical deterioration. Blood investigations showed a reduction in hemoglobin (12.3–8.6 g%), total leucocyte count (4800–1400/μl), platelet count (1.8 lakh to 40,000) and a rise in erythrocyte sedimentation rate (20–33 mm/h). Bone marrow biopsy did not reveal any significant pathology. Histopathological examination of the excised tissue showed perivascular cuffing of lymphoid cells [Figure 2a] (angioinvasion pattern), areas of angiodestruction and necrosis. Immunophenotypically the tumor cells were positive for CD3, CD7, CD30, CD45, CD56, granzyme B and negative for CD4, CD8, CD20 [Figure 2b-i]. *In-situ* hybridization revealed tumor cells harboring EBV-RNA. The histological and immunohistochemical analysis were consistent with the postoperative diagnosis of ENKTCL, nasal type.

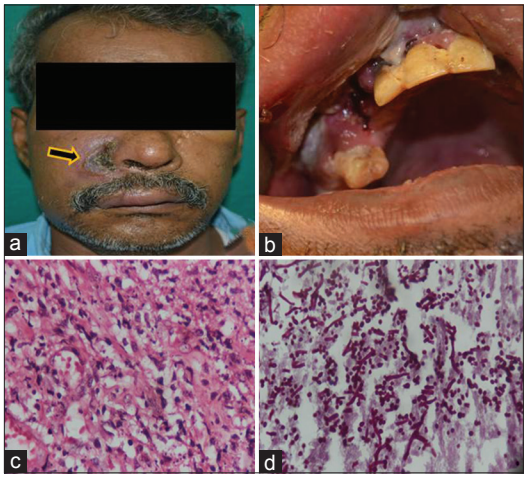

Figure 1: (a and b) Preoperative extraoral and intraoral view. (c) H and E stained section of preoperative incisional biopsy specimen. ×400 (d) Periodic acid-Schiff positive fungal hyphae (×400)

In the postoperative period (2 weeks) patient showed feeble response to insulin (RBSL: 222 mg/dl) and there was no recovery in falling blood parameters. Patient had periodic stupor-like state with minimum recorded Glasgow coma scale score of 7 (E2 V1 M4) along with episodes of acute respiratory distress (respiratory rate: 36/min) and tachycardia (pulse: 120/min), followed by cardiac arrest from which he could not be resuscitated.

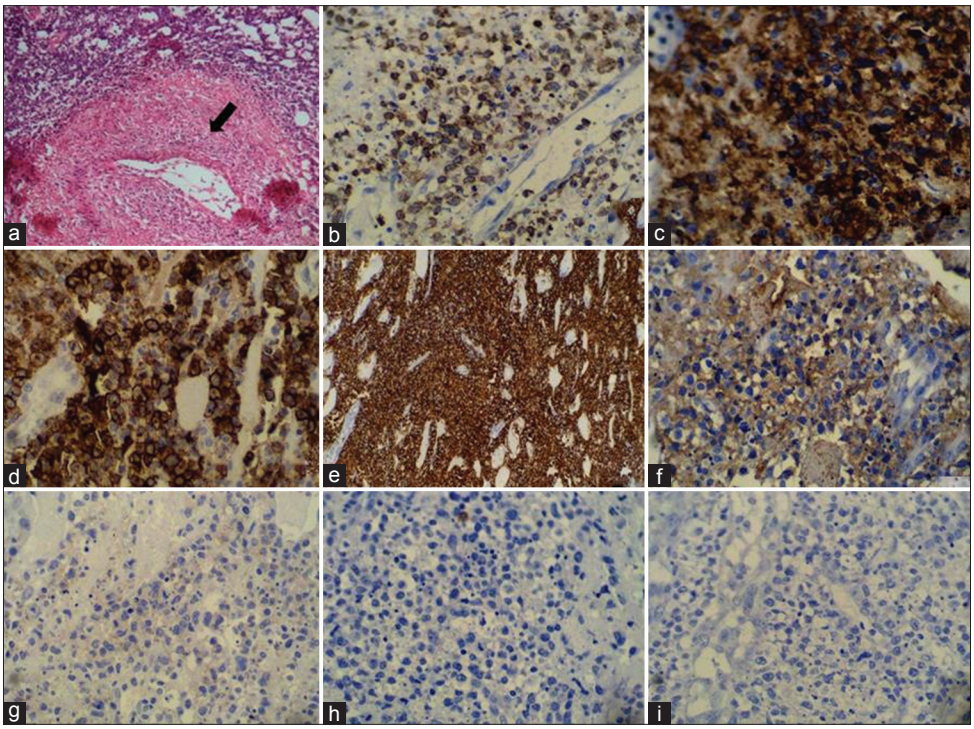

Figure 2: (a) H and E stained section of postoperative excised mass showing angiocentricity (arrow); ×100. Immunohistochemically tumor cells express CD3 (b), CD7 (c), CD30 (d), CD45 (e), and CD56 (f) and are immune negative for CD4 (g), CD8 (h), CD20 (i) ×100

Discussion

Extranodal natural killer/T-cell lymphoma is common in residents of South-East Asia, Central and South America with a male predominance.[4,5] EBV is considered as sine qua noncharacteristic in this type of lymphoma though this virus is usually linked with the etiology of B-cell lymphomas.[1]

Natural killer/T-cell lymphoma involves NK cell which are closely related to have features overlapping with T-cell lymphoma. WHO classification (2008)[2] replaced the older terminology of "angiocentric T-cell lymphoma" as proposed by REAL classification.[7] Previously it was recognized by different terminologies.[3,8]

Typically it presents as a granulomatous lesion around the nose accompanied by erythema and necrosis invading adjacent tissues including paranasal sinuses. Systemic spread can also occur.[4,6] ENKTCL has a very wide and vague clinical spectrum that can mimic a variety of reactive or nonreactive processes. An early diagnosis of ENKTCL is of prime importance as its spread to adjacent tissues, hinders the local function as well as attenuates the response to therapy. Both neoplastic and nonneoplastic entities should be considered in the differential diagnosis. Extensive necrosis is the characteristic feature of this tumor which is frequently misinterpreted as an infectious process.[7,9] This is also the cause of repeated biopsies.[4]

Extranodal natural killer/T-cell lymphoma has a variable histopathological spectrum. In the early stages, polymorphonuclear leucocytes, eosinophils and plasma cells can accompany lymphoma cells while in late stages tumor cells are masked by extensive necrosis and inflammation. Tumor cells vary in size and appearance. Cucumber-like cells are often seen. The nucleus often has an irregular nuclear folding and crumpled chromatin. Identification of tumor cells can also be done by tissue touch preparations for demonstrating cytoplasmic azurophilic granules.[4,6,9]

Angiocentricity, though a frequently noted feature of the ENKTCL, is not pathognomonic of this lymphoma. The prominent necrosis results from the angiodestructive effect of tumor cells and increased expression of chemokines in tumor cells-induced by EBV infection or release of cytotoxic proteins by NK cells.[5,7]

Immunophenotypically tumor cells are positive for cytoplasmic CD2, CD3 epsilon and CD56. CD43 and CD45RO can also be expressed. CD4, CD5, CD8, CD57 and surface CD3 are not expressed. Expression of T-cell intracellular antigen-1, granzyme B, perforin and EBV-RNA are also reported.[5,7,9] Expression of surface CD3, CD5 and T-cell receptor can be evaluated on lymphoma cells to differentiate NK cell from T-cell lymphoma.[6,7]

Cytogenetic studies have shown frequent deletion in chromosome 6 (q21-q25) along with rearrangement, loss and gain in other chromosomes.[4,10] Conventional radiological investigations, CT scan and magnetic resonance imaging are required to establish the true extent of the disease and to predict invasiveness.[4]

To conclude, our case is unusual in its initial presentation and histology, for both directed us toward the possibility of a reactive process. Although rare, ENKTCL should be considered in the differential diagnosis of infective/inflammatory processes refractory to conventional therapy.

Our case was misdiagnosed due to - earlier atypical clinical character and history, insufficient sampling, associated diabetes diverting diagnosis in favor of infective etiology and absence of bone marrow involvement.

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