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Case Report

Primary mucosal CD30-positive T-cell lymphoproliferative disorders of the head and neck rarely involving epiglottis: clinicopathological, immunohistomchemical and genetic features of a case

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Abstract: A case of primary mucosal CD30-positive T-cell lymphoproliferative disorder of the head and neck rarely involving epiglottis in a 59-year-old male was reported. Histologically, the ulcerative mucosa was affected by sheets of mixed inflammatory infiltration, with scattered large atypical lymphoid cells arranging in an individual or small clusters with focal epidermotropism. Immunohistochemically, tumor cells were uniformly immunoreactive to antibodies against CD2, CD3, CD7, CD43, CD4, TIA-1, with a heterogeneous expression of CD30, but negative for CD20, CD79a, CD21, CD8, CD56, ALK, EMA, granzyme B. Epstein-Barr virus encoded RNA (EBER) were detected. Genetically, T-cell receptor (*TCR*) γ gene showed an oligoclonal rearrangement. This first case developing in epiglottis demonstrates mucosal CD30-positive T-cell lymphoproliferative disorders are characteristic of a broad clinicopathologic spectrum similar to the counterpart in the skin with a favorable prognosis.

Keywords: T-cell lymphoproliferative disorder, head and neck, CD30, immunohistochemistry, TCR

Introduction

The umbrella term "primary cutaneous CD30-positive T-cell lymphoproliferative disorders ($CD30^+$ T-cell LPDs)" covers a wide spectrum running gamut from benign lesions to malignancies comprising lymphomatoid papulosis (Lyp), borderline lesions, primary anaplastic large cell lymphoma (ALCL) [1]. Notwithstanding the overlapping morphologic features and immunophenotypes resulting in diagnostic challenges, the typical clinical presentations tend to tell them apart. Recently, a series of in situ CD30-positive T-cell lymphoproliferations involving the mucosa of head and neck were reported and show similarities to the cutaneous $CD30^+$ T-ell LPDs with a anatomic predilection of oral cavity [2, 3]. But, as yet, the case of the laryngneal area involved was not appreciated. Herein, we add a case of primary mucosal $CD30^+$ T-ell LPDs developing in epiglottis principally adopting an indolent process to elaborate the clinicopathologic characteristics to further get insight to this complicated group.

Clinical history

A 59-year-old male was admitted for persistent pain and foreign body sensation in pharynx for 4 months without obvious cough, sputum, fever and any histories of trauma and cutaneous lesions, such as primary Lyp or ALCL in skin. An ulcerated nodule covered gray-white exudations with 1.0 cm in maximum diameter in left bottom of the epiglottis was found by the electron-nasopharyngolaryngoscopy and further confirmed by the computerized tomography scan (CT) (**Figures 1**, **2**). There were no significant laboratory markers. A positive remove of the neoplasm was performed and the patient had experienced a calm duration for 10 months without any evidence of recurrence or metastasis.

Materials and methods

The specimen was fixed by 4% formalin, and then embedded routinely in paraffin and stained with hematoxylin and eosin. Immuohis-

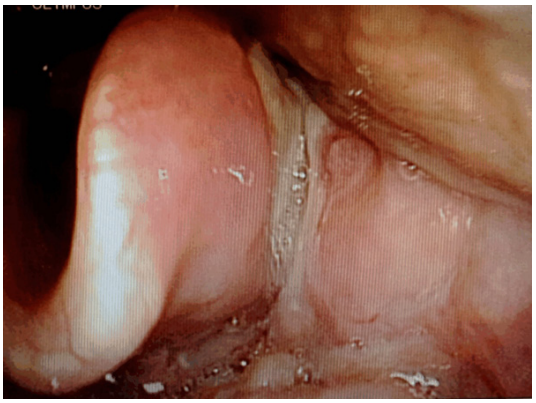

Figure 1. Electron-nasopharyngolaryngoscopy showed the lesion located in the in left bottom of the epiglottis and was covered by gray-white exudations.

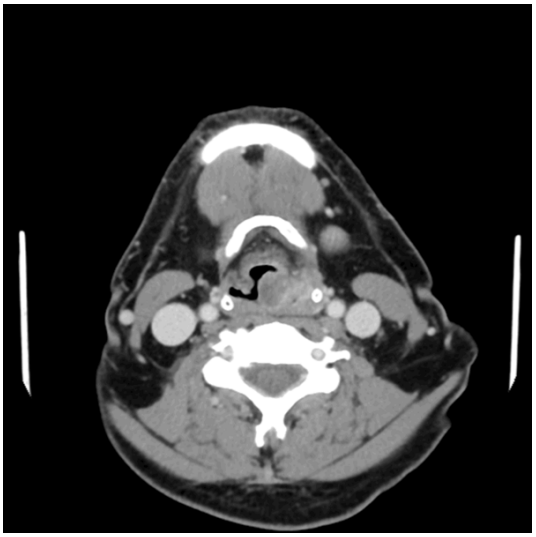

Figure 2. Enhanced CT scan (venous phase) showed a nodule protruding into the laryngeal cavity.

tochemical studies were performed using commercial antibodies in the Ventana BenchMark XT instrument (Ventana System, Tucson AZ). The antibodies included CD2, CD3, CD4, CD7, CD8, CD43, CD56, CD20, CD79a, CD21, CD30, ALK, TIA-1, granzyme B, EMA (all above from Ventana, prediluted).

Epstein-Barr virus encoded RNAs (EBER1/2) were detected on the paraffin section performed by in situ hybridization kits (Dako, Carpinteria, CA, USA) according to the manufacture's instruction.

T-cell receptor (TCR) gene rearrangement analysis was carried out with polymerase chain reaction (PCR) for TCRβ, TCRδ, TCRγ. Gene Clonality Assay kits (InVivoScribe Technologies,

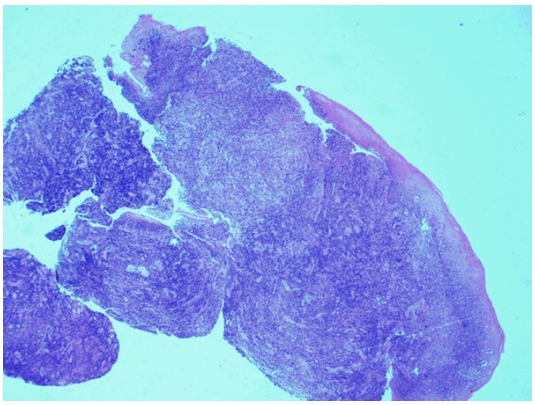

Figure 3. An intensive inflammatory infiltration with ulceration can be seen at low power.

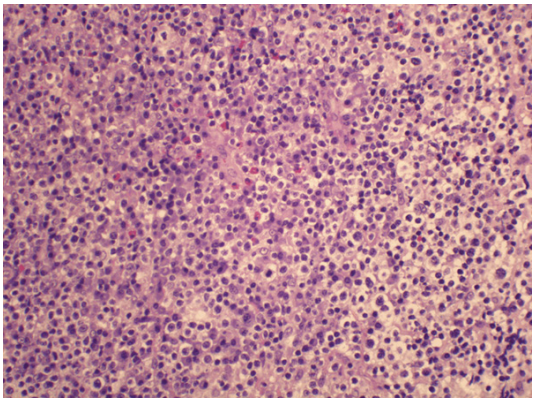

Figure 4. Medium to large typical cells arranged in aggregates with mixed inflammation; Note the scattered eosionphils.

San Diego, CA) was used in this study, and then products were separated by capillary electrophoresis by the automated sequencing system, ABI 3500 (Applied Biosystems Invitrogen, Foster City, CA) and analyzed by Genescan software (Applied Biosystems Invitrogen).

Results

Grossly, a small collection of grayish fragmented tissues measured 0.8 cm in diameter. Histologically, an intensive and mixed inflammatory milieu composed of numbers of small lymphocytes, plasma cells, histocytes, and eosinophils underlied the mucosa erosion (**Figures 3**, **4**), among which were the medium to large atypical cells scattered individually or arranged in small groups, with round or oval cell contour, irregular or multiple nuclei, abundant amphophilic or pale cytoplasm (**Figure 4**). Focally, epidermotropism and "hallmark cells" characteristic of eccentric kidney-, embryo-, or

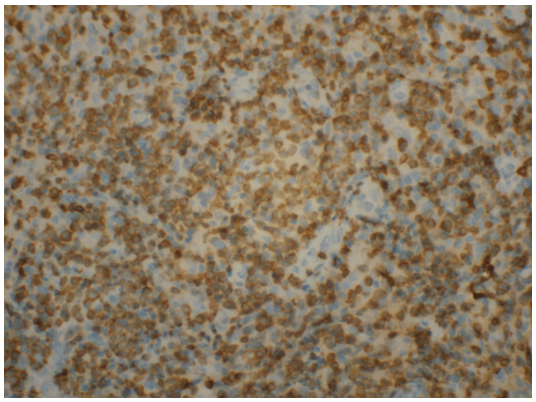

Figure 5. Tumor cells and some small lymphocytes expressed CD3.

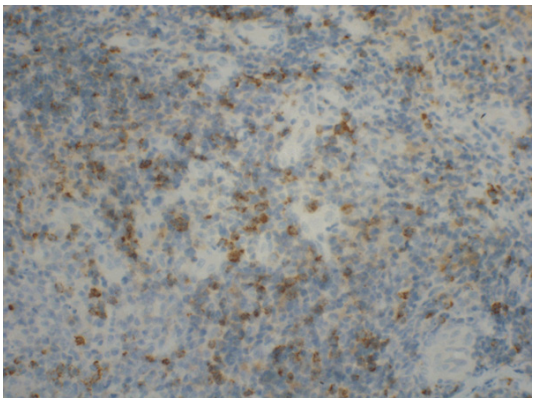

Figure 6. The atypical tumor cells expressed TIA-1.

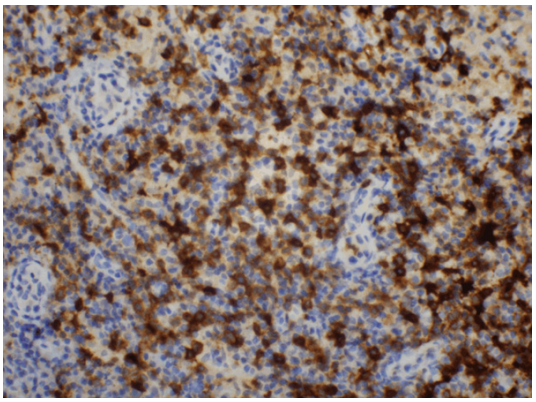

Figure 7. The medium to large atypical T cells arranged in groups heterogeneously expressed CD30.

horseshoe-like nuclei can be appreciated. Perivascular accentruation and coagulative necrosis were not found.

The tumor cells were uniformly positive for CD2, CD3 (**Figure 5**), CD7, CD43, CD4, TIA-1 (**Figure 6**), with a heterogeneous expression of CD30 (**Figure 7**), but negative for CD20, CD79a, CD21, CD8, CD56, ALK, EMA, granzyme B. EBER1/2 was detected in some large atypical T cells (**Figure 8**). T-cell receptor (TCR) γ gene showed an oligoclonal rearrangement, suggesting of the existence of clonal tumor cell population (**Figure 9**).

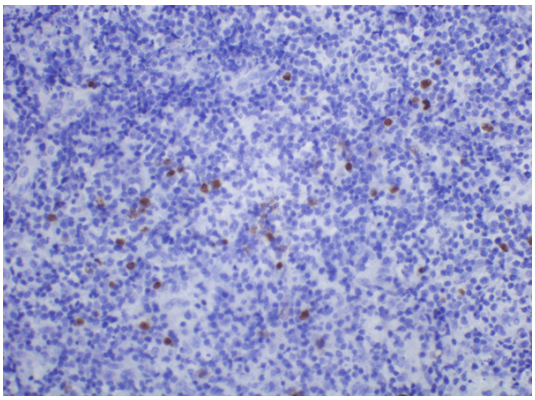

Figure 8. EBER1/2 was positive in some tumor cells.

Discussion

Without an exact and widely accepted diagnostic modality, however, the concept of primary cutaneous CD30$^+$ T-cell LPDs can be expanded to the lesion involving mucosal sites of head and neck, mainly because of the analogous structural and functional features in these two anatomic locations [3]. In addition, the juxtaposition of *DUSP22-IRF4* locus among some cases further supported the fact that primary mucosal CD30$^+$ T-cell LPDs of the head and neck can also be envisaged to lie on a similar morphologic continuum and have an indolent process in clinic [3]. Both the primary anaplastic large cell lymphoma (ALCL) and LPDs insufficient to totally situate the malignant extremity were reported by limited publications. The features of our case seemed to fall into the latter, some of which once were designated as "eosinophilic ulcer of the oral mucosa (EUOM)", "traumatic ulcerative granuloma with stromal eosinophilia (TUGSE)", "traumatic granuloma", and so on [2, 4]. But all of them share the features including the localized lesion, ulceration as a mainstay presentation, nonaggressive course, and presence of CD30-positive neoplastic T cells in variable number frequently with eosinophils [3].

Clinically, Primary mucosal CD30$^+$ T-cell LPDs of head and neck mainly affect the middle-aged and elderly people (range, 5-84 years;

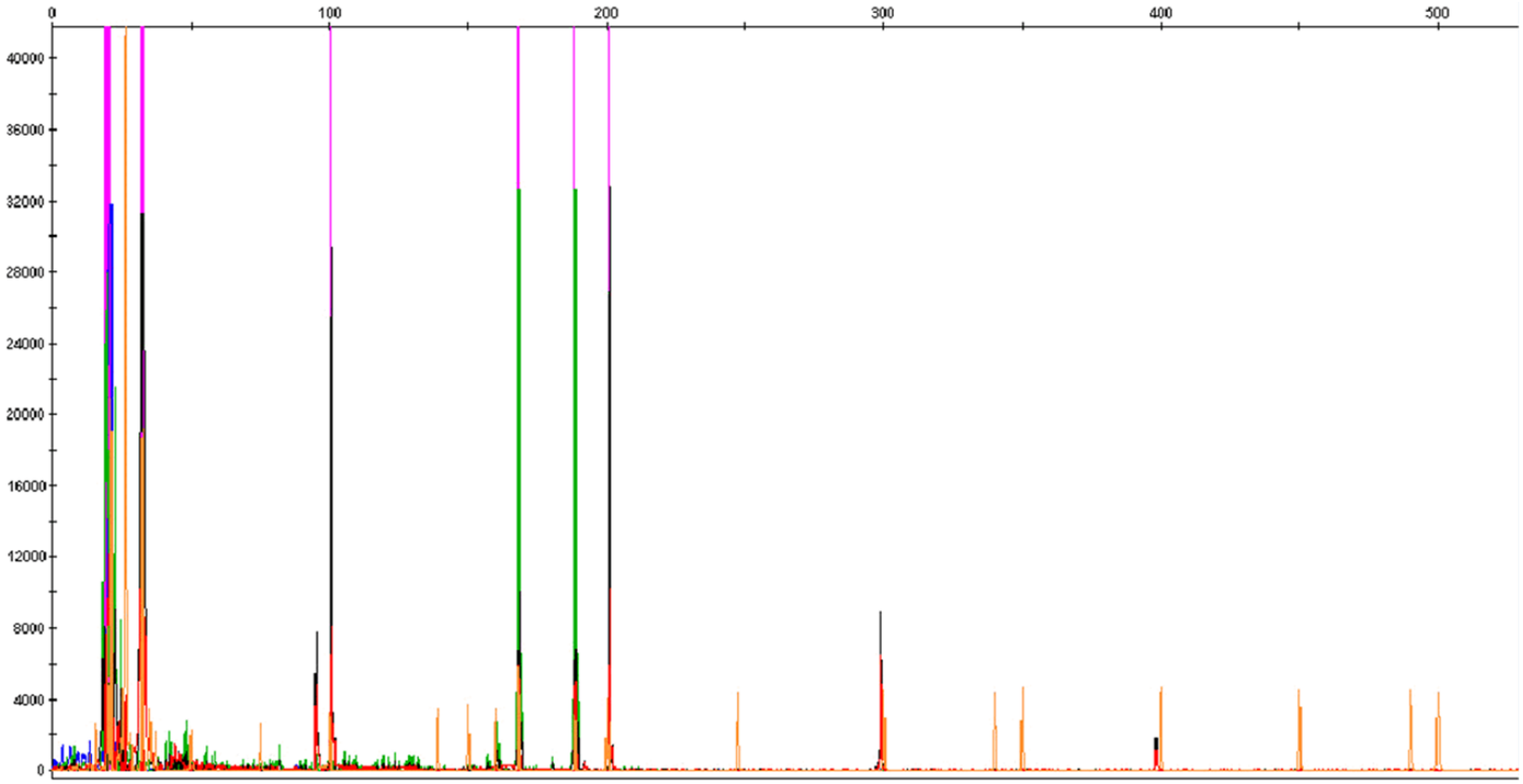

Figure 9. The two green peaks falling in the range between 145 bp-255 bp suggestive of an oligoclonal rearrangement of *TCR*γ gene.

mean, 57 years) with a female predilection [2, 3, 5]. Throat area affected is extremely scanty, and we first reported the epiglottis involved, however, which still belongs to the concept of head and neck in anatomy. The majority present with ulcer or ulcerated nodules in oral cavity including the tongue, lip, palate, gum and buccal mucosa; the surplus locations also comprise orbit, conjunctiva, nasal cavity, and sinuses [3, 6]. Some patients may feel pain and cause a significant food-intake impairment [4]. Histologically, akin to primary cutaneous $CD30^+$ T-cell LPDs, the lesions usually adopt a dense submucosal inflammatory infiltration with a varying proportion of medium to large T cells expressing CD30 scattered singly or arranged in clusters, aggregates, or sheets corresponding to various severity with or without epidermotropism [4]. These atypia lymphoid cells have round, oval or, typically but not pathognomonically, eccentrically placed embryo-like nuclei ("hallmark cell") with abundant amphophibic cytoplasm and multiple small nucleoli [5, 6]. Generally, ALCL is commonly characteristic of large lymphoid cells growing in a significantly sheet-like pattern with uniform and strong CD30 expression. Angiotropism can be appreciated with or without coagulative necrosis [5]. But the situation that atypical CD30-positive T cells merely take on the appearance of sparse or clustered growth pattern regardless of trauma in history tends to be considered as reactive or borderline lesion other than ALCL [2, 5]. Similar to our case microscopically, the patient also lived a persistent calm period without progression after neoplasm removed. The CD30-positive atypical cells were labeled by at least one T-cell antigen and CD4 or CD8 phenotype with or without EMA expression, but negative for B-cell antigens and ALK. Some cases may illustrate association with EBV in Asians in our routinely diagnostic practice, but it seems few correlation with the pathogenesis of primary mucosal $CD30^+$ T-cell LPDs of the head and neck [5, 6]. Amplification of *TCR* rearrangement can be detected, but not a conclusive criterion to give the diagnosis of ALCL. Presence of oligoclonal rearrangement of *TCR*γ in our case also showed there was a clonal lymphoid population. The accurate diagnosis should rule out several pertinent diseases including some infections, squamous cell carcinoma, salivary gland tumors and some autoimmune diseases. To combine the clinical, some distinctive histological and immnohistochemical features can prompt the diagnosis straight forward. Minor cases of both LyP and ALCL affecting oral cavity have been reported [4, 7]. Whether there are clinical histories of cutaneous lesions displaying a solitary or localized ulcer (ALCL) or chronic, recurrent, self-limited, multiple papulo-nodular lesions with different stages (LyP) is exceedingly crucial [4]. In light of the poor prognosis of systemic ALCLs, it is mandatory to exclude them involving the mucosal site by virtue of the careful clinical observation because other pathological features have little differential value except for ALK status in immunostain [5]. Primary mucosal $CD30^+$ T-cell LPDs of head and neck (include ALCL) have an indolent course, so conservative therapeutic schemes are recommended [3-5].

In conclusion, Primary mucosal $CD30^+$ T-cell LPDs of head and neck cover a broad continuum similar to the cutaneous counterpart with variable proportion of CD30-positive medium to large atypia T cells infiltration behaving an indolent clinical behavior. Laryngeal areas including epiglottis also can be affected. A careful clinical examination and relevant pathologic features help to secure the accurate diagnosis.

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Disclosure of conflict of interest

None.

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