

Case Report

Terminal deoxynucleotidyl transferase negative T-cell lymphoblastic lymphoma from heterotopic Warthin's tumor in cervical lymph nodes: a case report and review of literature

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Abstract: Collision of lymphoma and Warthin's tumor (WT) is extremely uncommon, especially T-cell lymphoma. Here we present a 69-year-old woman who had terminal deoxynucleotidyl transferase (TDT) negative T-cell lymphoblastic lymphoma (T-LBL) from heterotopic Warthin's tumor in cervical lymph nodes, in which only cervical lymph nodes enlarged initially and quickly progressed to systemic lesions.

Keywords: Heterotopic Warthin's tumor, T-cell lymphoblastic lymphoma, terminal deoxynucleotidyl transferase negative, collision tumor, cervical lymph nodes

Introduction

Warthin's tumor (WT), also known as papillary cystadenoma lymphomatosum, a common benign neoplasm of salivary gland, exclusively occurs in the parotid gland or ectopic salivary gland in periparotid lymph nodes (LN). Tumors are typically composed of proliferative eosinophilic epithelium and lymphoid stroma. The epithelium consists of two layers of cells, of which the eosinophilic lumen cells are high columnar with uniform palisade-like nuclei, and there are often acrosomal secretory vesicles on the cell surface. The deep part is a layer of smaller flat or cuboid basal cells without obvious atypical cells or mitosis. The stroma comprises lymphoid tissue with varying degrees of reactivity, usually accompanied by obvious germinal centers [1, 2].

Approximately 1% of WT undergo malignant transformation, which can occur in either the epithelial or lymphoid components [1]. Uncommonly, the malignant lymphoma occurs in WT lymphoid stroma and the majority are B-cell lymphoma and Hodgkin's lymphoma [3-23]. There are only two English reports about the co-existence of WT and T-cell lymphoma in

parotid gland [24, 25] and as far as we know, this is the first report in the English literature describing TDT negative T-cell lymphoblastic lymphoma (T-LBL) in neck heterotopic Warthin's tumor.

Case report

A 69-year-old woman was admitted to hospital with a painless rapidly growing mass on the left neck.

One month ago, an oval mass about the size of a quail egg was unexpectedly found on the left side of her neck, and grew to egg size. She denied smoking and malignant tumor history and had no fever, night sweats, or weight loss (B symptoms). By physical examination, a non-tender nodule of about 6.6*3.5 cm could be palpated on the left side of the neck with a smooth surface and tough texture. No obvious abnormality was found in hemogram indexes. PET-CT showed multiple enlarged LN shadows in bilateral cervical region II, left cervical region III and V accompanied by increased FDC metabolism and SUVmax was 9.1. These were malignant lesions, but there were no obvious malignant symptoms in other parts of the body. The

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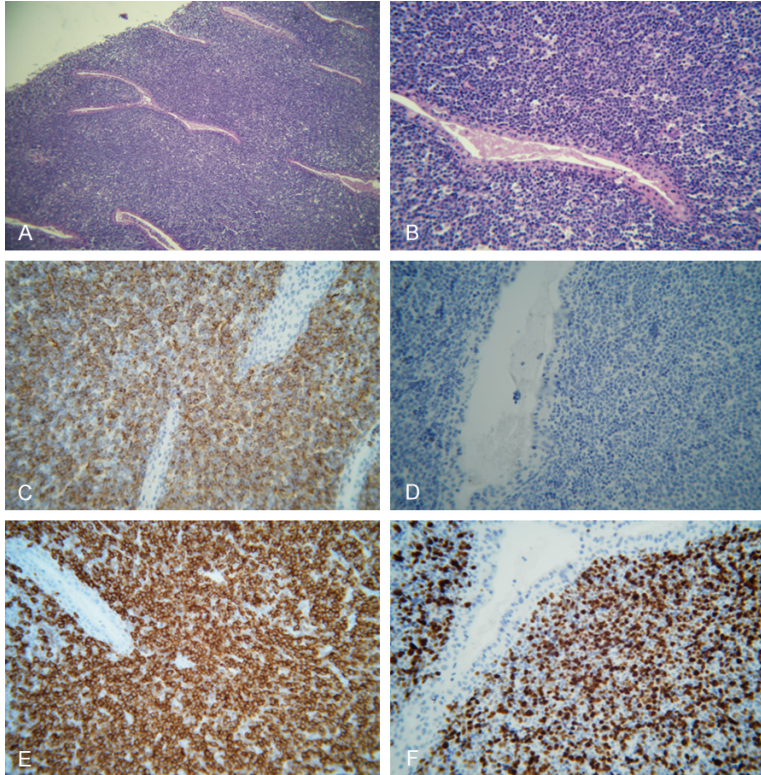


Figure 1. (A) (H&E $\times 10$) and (B) (H&E $\times 40$). The epithelium was not markedly atypical and the stroma was filled with atypical lymphocytes. (C) CD34+ ($\times 40$). (D) TdT- ($\times 40$). (E) CD7+ ($\times 40$). (F) The positive rate of Ki67 was more than 60% ($\times 40$).

patient underwent surgical resection of two nodules from left neck. The specimen received in formalin consisted of two gray-red soft nodules measured 3*2*1.5 cm and 5*3*2 cm. The cut surface was translucent, slightly leafy with clear boundary. Microscopically, tumors had a thin envelope and were composed of cysts covered by typical WT epithelial and diffuse lymphoid components (**Figure 1A**). The epithelium was eosinophilic two-layer architecture without heterotypic cells. There were numerous large cells in the diffuse lymphoid matrix with focal or sheet distribution, which had abundant cytoplasm, irregular nuclei, finely dispersed chromatin, and mitotic figures visible (**Figure 1B**). Immunohistochemical examination showed that the atypical lymphocytes expressed strong positivity for CD5, CD7, CD34, partly CD4 and were negative for TdT, CD8 and PAX5. The Ki-67 proliferation fraction was approximately 85% (**Figure 1C-F**). A diagnosis of T-LBL with coexistent WT was based on the findings described above. Unfortunately, the patient was discharged without any treatment. Two months later, the patient suffered from

fatigue and loss of appetite accompanied by dizziness, rash, sometimes nausea, and weight loss of 3 kg. Routine blood test showed HGB 114 g/L, PLT 63×10^9 /L, WBC 12.44×10^9 /L, and immature cells 58%. The patient was hospitalized with acute leukemia in the Department of Hematology. Flow cytometry of bone marrow showed acute T-lymphocytic leukemia (T-ALL), and neck LN biopsy and skin biopsy showed involvement by tumor. The patient received chemotherapy with COPD regimen.

Discussion

WTs are benign neoplasms composed of a salivary gland epithelial component and lymphoid stroma, which arise from heterotopic salivary gland epithelium within intraparotid and periparotid LNs. Approximately 1% of WT transform to malignant tumors, which can occur either in the epithelial or the lymphoid components [1].

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Cases of lymphoma and WT collision had been reported, most of which were Hodgkin's lymphomas and B-cell-derived non-Hodgkin's lymphomas (NHLs). Up to now, there have been 7 cases of Hodgkin's lymphoma and 25 cases of B-cell lymphoma with clear classification in the English literature, of which follicular lymphoma (10 cases) was the major type [3-23].

However, there were only two reports on T-cell lymphoma in WT. One was about the T-LBL associated with WT in parotid gland and the other was peripheral T-cell lymphoma, NOS in WT of right cervical LNs (**Table 1**) [24, 25]. The unusual TdT negative T-LBL occurring in heterotopic WT of neck, without signs of leukemia initially, made this case rare and interesting.

T-cell acute lymphoblastic leukemia/lymphoma (T-ALL/LBL) is an aggressive neoplasm derived from T-cell progenitors and TdT is the major marker for the confirmation of the precursor cell lymphoma. This rare case was diagnosed

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Table 1. Summary of T-cell lymphoma in Warthin's tumor

Author (year)	Sex	Age	Site	Mass size (cm)	LDH (U/L)	Diagnosis	Stage before treatment	Follow-up
Giaslakiotis (2009) [24]	M	81	right parotid	5.8×4.7×4.0	2072	T-LBL	IVB	DOD, 3 months
Pescarmona (2005) [25]	M	66	right cervical LN	NA	NA	peripheral T-cell lymphoma, NOS	IV	DOD, 5 months
Present case	F	69	left neck node	5*3*2 3*2*1.5	NA	T-LBL	IV	DOD, 5 months

M, male; F, female; LN, lymph nodes; DOD, died of disease; NA, not available.

as TdT-LBL, because it showed the typical morphology of precursor cell neoplasms in addition to the expression of CD34 and T cell biomarkers. Cases of TdT-negative T-ALL/LBL are rare and patients have a significantly higher rate of disease progression and shorter overall survival [26]. The patient in this case progressed to acute leukemia in less than two months and died five months later because of poor response to chemotherapy, which was in line with the literature.

The pathogenesis of lymphoma and WT in combination is not clear and many factors might be involved in the pathogenesis, of which age and gender may play roles in tumorigenesis. Most reported cases of WT and lymphoma coexistence reported have happened in elderly males. Among 33 patients previously reported and our case, 5 were female and 28 were male, aged from 49 to 102 with the median age being 68 years and the average age being 71.28 years, so the disease is predominantly in elderly men [3-23].

In conclusion, this is the first case report that illustrates TdT-LBL arising from heterotopic Warthin's tumor cervical lymph nodes and reminds us to examine the lymphatic stroma components of WT carefully.

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The case report and any accompanying report pictures were signed with informed consent from the patient's family members.

Disclosure of conflict of interest

None.

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