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Case Report

Indolent T-lymphblastic proliferation: report of a case involving the upper aerodigestive tract

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Abstract: T-lymphoblastic lymphoma (T-LBP) is a high-grade malignant lymphoma, which possesses the characteristic of high metastasis and high mortality without treatment. We are presenting a special T-lymphoblastic proliferation involving in the oropharynx, nasopharynx, sinus and trachea in a patient with local involved about 15-years without systemic dissemination. The immunophenotype of this case was similar to T-LBP. The proliferous cells were positive for terminal deoxynucleotidyl transferase (TdT), CD3, and appeared co-expression CD4 and CD8. No clonal rearrangements of TCRγ and/or TCRβ gene were detected. Indolent T-lymphoblastic proliferations rarely occurred or unusually could not be diagnosed, combing with the relevant literature and clinically indolent manifestation, we interpreted this case as indolent T-lymphoblastic proliferation (iT-LBPs). So far, the mechanism of the T-lymphoblastic proliferations is still uncertain and requires further study.

Keywords: T-lymphoblastic lymphoma, indolent T-lymphoblastic proliferation, upper aerodigestive tract

Introduction

T-lymphoblastic lymphoma is a high-grade malignant lymphoma characterized by an immature T-precursor phenotype, occurrence in male adolescents, and high incidence of mediastinalinvolvement [1]. It closely related to T-cell acute lymphoblastic leukemia; indolent T-lymphoblastic proliferations are not generally recognized to occur [1]. Velanker [2] and his team firstly reported an indolent T-lymphoblastic proliferation in 1999. The patient had an over 16-year history of T-lymphoblastic proliferation located at the upper aerodigestive tract with frequent recurrences but without evidence of systemic dissemination. The patient only received surgical resection but not received chemotherapy or radiation therapy. Since then nearly 10 detailed case reports of indolent T-lymphoblastic proliferation have been noted in the literature with increasing frequency in recent years [3]. Robert S. Ohgami [3] and his team had summarized specific criteria used to diagnose indolent T-lymphoblastic proliferation, notably: (1) Confluent groups of TdT^+ T cells in a biopsy specimen. (2) Relative preservation of surrounding normal lymphoid architecture. (3) TdT^+ T cells without morphologic atypia. (4) Absence of thymic epithelium. (5) Non clonal TdT^+ T cells. (6) Immunophenotype of developmentally normal immature thymic T cells and (7) Clinical evidence of indolence (follow-up >6 mo without progression) [3]. The biopsy of pharyngeal tissue of these patients had histologic similarity with expression of TdT, CD3, and co-expression of CD4 and CD8. However, no clonal T-receptor rearrangement was detected. In our case, the patient had a 15-year history of T-lymphoblastic proliferation located at the pharynx, sinus, trachea with frequent recurrences but without evidence of systemic dissemination. The patient was not performed any chemotherapy or radiation therapy. Like the previous cases, there was no clonal T-receptor rearrangement detected. The immature cells of indolent T-lymphoblastic proliferations exhibited polyclone. It resembled to teratoma, possibly derived from residual layer cells remaining stay at the oropharynx and nasopharynx, evolving to a kind cell like thymus cells. However, the

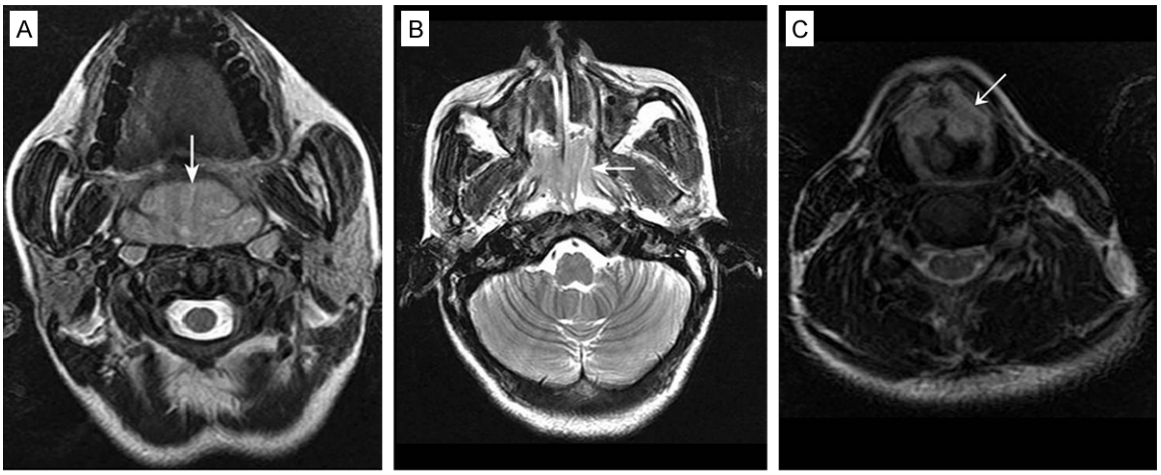

Figure 1. MRI scan of the mass indicated by an arrow; regions as follows: A. The throat; B. The nasopharynx; C. Close to the trachea.

mechanism of the T-lymphoblastic proliferations was still uncertain.

Case report

The patient was a 37-year-old female, who was in good condition until the age of 22 when she experienced the onset of hoarseness without a sore throat, but with a stuffy nose and dry throat at the same time. Although she was given anti-inflammatory therapy at the junior hospital, any remission of her hoarseness after a rest or being silence. Over the next few years, the patient was stricken with hoarseness all the time and performed intermittent treatment. At the age of 37, the nasal stuffiness was aggravated with white ropy snots. Physical examination revealed neoplasms blocking the back end of double nasal common meatus, nasopharyngeal mucosal hyperemia, the lymphoid follicles hyperplasia at the latter margin of pharynx and the palatine tonsil swollen at the grade of 1. However, no systemic lymphadenopathy was discovered. Biopsy of the pharyngeal tissue was interpreted as “mucosal chronic inflammation”. 18 days later, MRI demonstrated the nasopharynx and oropharynx were populated by palingenetic masses, and interpreted as “nasopharyngeal carcinoma with cervical lymph node along with cancerometastasis, not excepting for inflammatory lesions” (**Figure 1A-C**). Electronic laryngoscope revealed multiple masses uplifted in the nasopharynx blocking the choanae, and pedicle neoplasm involving epiglottis blocking the laryngeal cavity. At that time, the patient suffered from respiratory distress. Tumorectomy and tracheostomy were performed for airway obstruction. The removed gross tumor samples were observed. The nasopharynx tumor was solid, unencapsulated with the size of 2.0×1.0×0.5 cm and gray-tan cut surface. Glottides tumor was in irregular shape with the size of 1.0×0.5×0.5 cm. Throat tumor was also in irregular shape with the size of 2.0×2.0×1.0 cm. Bloods counts were negative. Bone marrow aspiration and biopsy were performed. Chemotherapy and radiation therapy were never given. The family history of lymphoma had no clue. The patient was currently well and close follow-up would be required to ascertain the behavior.

Materials and methods

Glass slides and paraffin blocks were available from the specimens of tumorectomy. The use of these human tissue samples has been reviewed and approval by our institutional ethics board. Immunohistochemical studies were performed on formalin-fixed, paraffin-embedded sections by the avidin-biotin-complex immunoperoxidasetechnique [1]. Paraffin sections stained with H&E were viewed with an upright microscope and photographed by DP2-BSW. Antibodies were used as follows: TDT, CD20, Bcl-2, Bcl-6, Kappa, Lambda, CD4, CD8, CD1a, CD3, CD79a, CD21, PAX-5, Ki-67, CD10, TIA-1, GZB, CK, CD56. All antibodis were purchased from Maixin China. T-cell antigen receptor gene rearrangement studies were per-

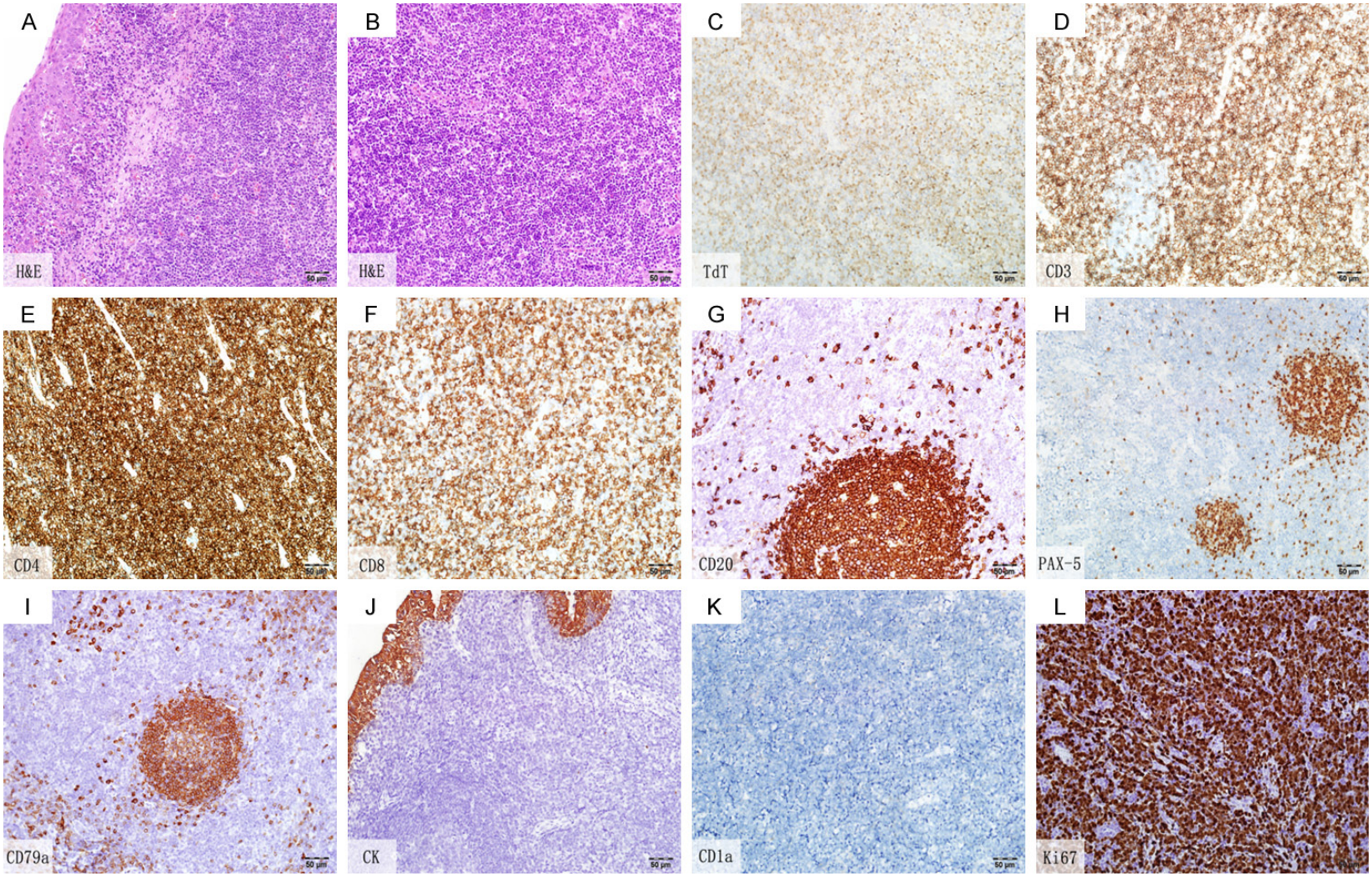

Figure 2. Microscopic features of tumors involved by It-LBP. (A, B) H&E staining presented preserved epithelium architecture and numorous small to medium-sized cells in the interfollicular zone. (C-L) Immunohistochemical staining appearance of the tumors. The proliferous cells in the interfollicular zone were positive for TdT, CD3, CD4, CD8 (C-F). The reactive follicles were positive for CD20, CD79a, Pax-5 (G-I). On the contrary, these proliferous cells presented CK^- and $CD1a^-$ (J, K). The Ki67 proliferative index is very high (L).

formed as previously described. In brief, DNA isolated from formalin-fixed paraffin-embedded tissues was digested overnight using HPA II restriction enzyme, then used as template for polymerase chain reaction using 5'-TCCAGAATCTGTTCCAGAGCGTGC (forward) and 5'-TGGGCTTGGGGAGAACCATCCTC (reverse) as primers [4]. The forward primer was fluorescently tagged with carboxyfluorescein (FAM) [4]. The polymerase chain reaction products were analyzed by an ABI7500 with data analysis using a Peak scanner 2 (Life Technologies) [4].

Results

Histopathology

The samples showed preserved epithelium architecture, and the base cell was sharply delineated. There were reactive lymphoid follicles but the architecture was distorted, with marked expansion of the interfollicular zone. In the interfollicular zone, there was a spectrum of lymphocytes, small to medium-sized cells with features of lympholasts (thin nuclear membrane, fine chromatin, scanty cytoplasm), cells with features intermediate between small lymphocytes and lympholasts and large lymphoid cells (**Figure 2**). Mitotic figures could be identified.

Immunohistochemical studies

Pharyngeal mass immunohistochemistry demonstrated that $CD20^+$ cells were confined mostly to the reactive follicles (**Figure 2**), where $CD79a^+$ and $PAX\text{-}5^+$ cells always were found (**Figure 2**). The interfollicular zone was populated mostly by $CD3^+$ T cells (small cells tend to be weaker) (**Figure 2**). Many of the interfollicular cells were TdT^+, forming sheets-positive cells medium-sized cells and small cells (**Figure 2**). There was co-expression of CD4 and CD8 (**Figure 2**). The Ki67 proliferative index was very high (70-90%) (**Figure 2**). And there was negative expression for CD1a and CK (**Figure 2**).

Molecular studies

T-cell antigen receptor gene rearrangement studies were performed using Biomed-2 primers, followed by differential fluorescence detection [5]. There was no clone rearrangement detected in the TCRγ gene and TCRβ gene (**Figure 3**).

Discussion

Lymphoblastic lymphoma is recognized as a high-grade lymphoma closely related to T-cell acute lymphoblastic leukemia [1]. However, in our case, it has a relative long-term history, preserved tissues architecture, presence of a spectrum of cells (like the normal thymic cortex), we are inclined to the interpretation of indolent T-lymphoblastic proliferation. This is a very rare condition with only nearly 10 cases reported in the literature-the clinical scerarios were practically identical with this case. T-lymphoblastic proliferations of these patients have common clinical features: predilection for involvement of the oropharynx/nasopharynx, a long-term clinical course, remaining located with frequent recurrences and no clue of systemic dissemination.

Besides this condition, it has also been reported that aggregates or sheets of TdT^+ T cells can occur in hyaline-vascular types but the TdT^+ lymphoid cells in these conditions appeared as small lymphocytes.

The mechanism of the T-lymphoblastic proliferation is still not well understanding. The immature cells are T-lineage, expressing TdT, CD3 and CD4/CD8, consistent with an intermediate stage of thymocyte development that is not normally present in lymph nodes [1]. However, we do not considered the possibility of a case of ectopic thymus or thymoma, because the immature cells are negative expression for CD1a, suggesting the shortage of thymic epithelium. To our knowledge, the thymus is embryologically derived from the third and fourth pharyngeal pouches [1], it is possible that the pharyngeal epithelium in these cases retains thymic potential, resulting in migration and proliferation of bone marrow-derived T-lymphoblasts [2]. In addition, we noticed that is resembled to teratoma. Teratoma is derived from residual layer cells in the process of embryonic development. A teratoma is an encapsulated tumor with tissue or organ components resembling normal derivatives of more than one germ layer. Therefore, it is possible that residual layer cells remain stay at the oropharynx/nasopharynx, evolving to a kind cell

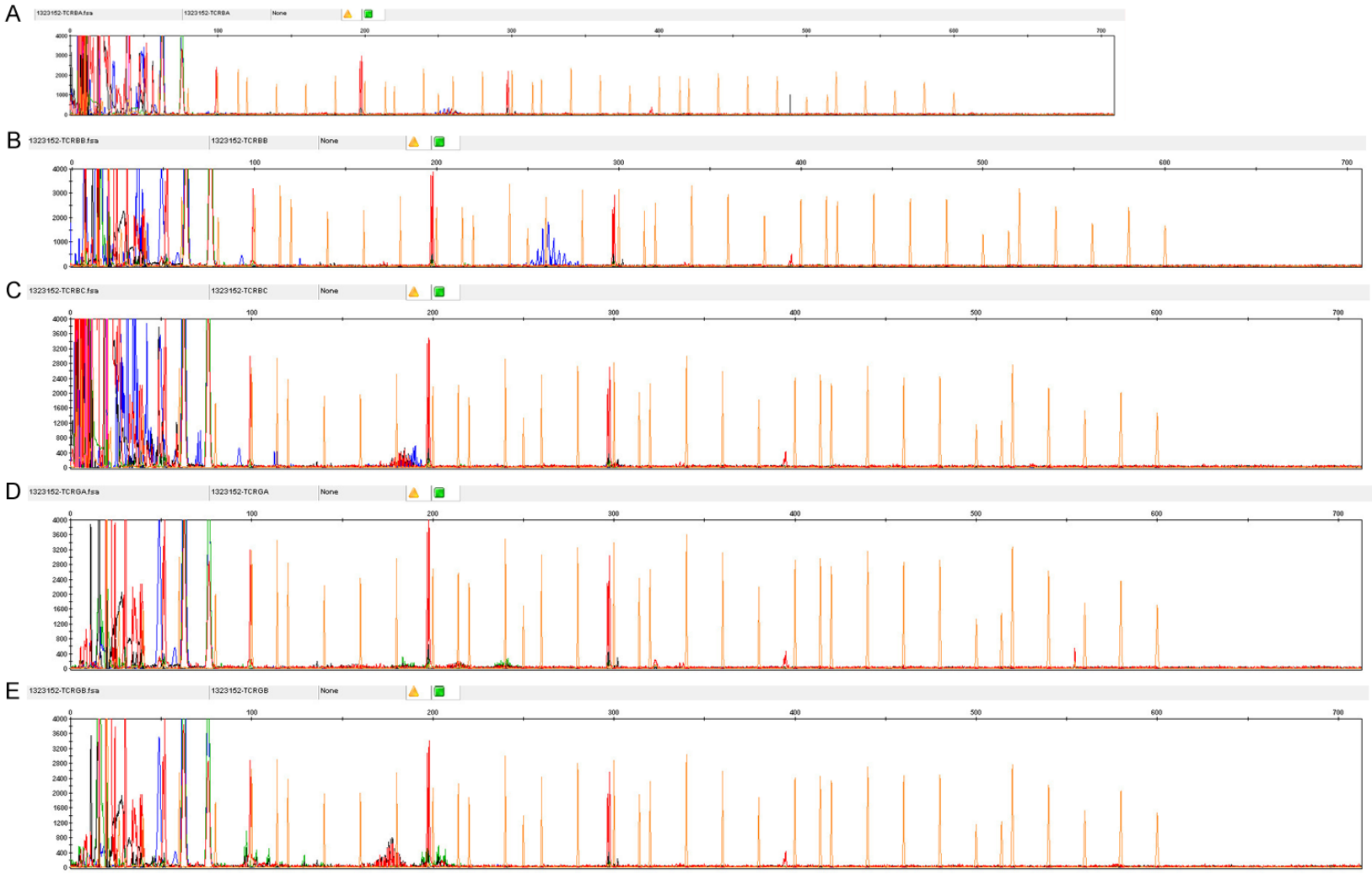

Figure 3. Pictures of TCR gene rearrangenment detection. Results presented no clonal rearrangements of TCRβ (A-C) and/or TCRγ (D, E) gene were detected.

like thymus cells, but differing from biological behavior.

Because of lack of prior biopsies for documentation, it may be prudent to label this as T-lymphoblastic proliferation of uncertain significance for the time being. Staging would be helpful, to determine if there is no marrow involvement (which if positive, would indicate a malignancy instead). Close follow-up is required to ascertain the behavior.

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Disclosure of conflict of interest

None.

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