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T-Cell Acute Lymphoblastic Leukemia Camouflaged as Acute Tonsillitis: A Rare Case Report

Kuganathan Ramasamy,[1,2] Davina Stasia Teo,[1] Sai Guan Lum,[2] Farid Razali[1]

[1]Department of Otorhinolaryngology-Head & Neck Surgery, Hospital Shah Alam, Selangor, Malaysia
[2]Department of Otorhinolaryngology-Head & Neck Surgery, Faculty of Medicine, University Kebangsaan Malaysia, Kuala Lumpur, Malaysia

ABSTRACT

Background: Sore throat is a common complaint encountered in daily clinical practice. It is a defining characteristic of acute tonsillitis which is typically treated with symptomatic care and antibiotics in cases of bacterial infection. Despite being generally uncomplicated, acute tonsillitis can mask sinister pathologies such as diphtheria, infectious mononucleosis, and even malignancy.

Case Report: In this report, we present a case of a young adult with nonresolving acute exudative tonsillitis. Upon recognition of unusual alarming features, further investigations have led to the diagnosis of T-cell acute lymphoblastic leukemia (T-ALL).

Conclusion: Although unusual, hematological malignancies such as acute leukemia may manifest as acute tonsillitis. The significance of recognizing red flags that may occur in common symptoms such as sore throat is emphasized. It is necessary to be aware of this entity to prevent delayed diagnosis.

Keywords: Sore throat, tonsillitis, acute leukemia, T-cell lymphoblastic leukemia, hematology.

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Address for correspondence:
Kuganathan Ramasamy. Department of Otorhinolaryngology-Head & Neck Surgery, Hospital Shah Alam, Selangor, Malaysia
Phone: +603 5526 3000
E-mail:
kuganathan.ram@gmail.com

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INTRODUCTION

Acute tonsillitis is a frequently encountered diagnosis in a primary care and emergency department setting. It often arises due to viral or bacterial infection that does not necessitate extensive clinical investigations; therefore, it is best managed with supportive treatment and antibiotics as indicated. Nevertheless, acute tonsillitis may rarely manifest as a precursor to more serious conditions, such as hematological malignancies, namely, lymphoma, and leukemia. Herein, we describe a young adult who was referred to the Otorhinolaryngology (ORL) clinic due to nonresolving acute exudative tonsillitis and was eventually diagnosed with T-cell acute lymphoblastic leukemia (T-ALL). There are limited case reports describing acute tonsillitis as the sentinel presentation of acute leukemia; however, to the best of our knowledge, the current report would be the extremely rare conclusion in the diagnosis of T-ALL.

CASE REPORT

A 21-year-old male patient with no previous comorbidity was referred to the ORL clinic due to nonresolving exudative tonsillitis. He initially presented to the local health clinic with a primary complaint of a sore throat for 1 week associated with fever, odynophagia, and bilateral

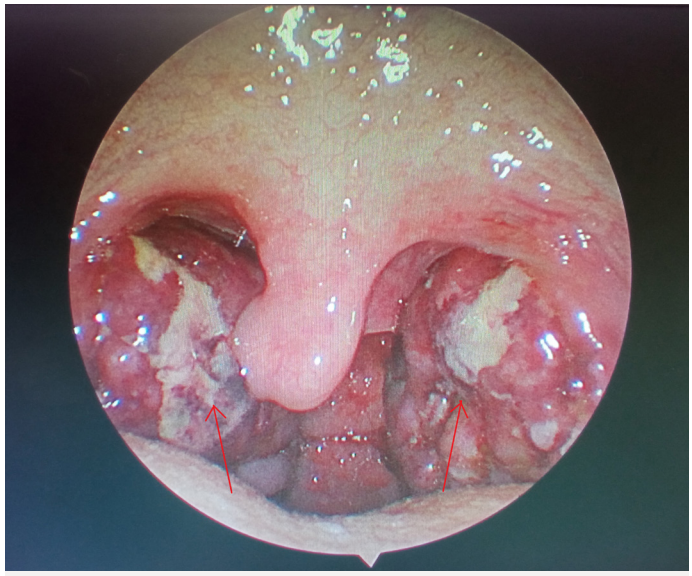

Figure 1. Inflamed bilateral tonsils (arrow) of grade III with an ulcerated surface, exudate formation, and areas of necrosis posteriorly.

neck swelling. Antibiotics were administered orally in order to treat his acute exudative tonsillitis. On further history, the patient denied tuberculosis contact, B-symptoms of lymphoma, or any high-risk behaviors. He is an active smoker with no family history of malignancy.

The oropharynx examination revealed inflamed and enlarged bilateral tonsils of grade III, with an unhealthy ulcerative surface and areas of necrosis (Fig. 1). There were multiple neck nodes involving bilateral levels II, III, and V, with the largest node at bilateral level II measuring 3 × 3 cm. Flexible nasopharyngolaryngoscopy showed an enlarged and inflamed adenoid with normal hypopharynx and laryngeal structures. Systemic examination revealed bilateral inguinal lymphadenopathy but no hepatosplenomegaly.

Due to the high suspicion of malignancy, biopsies were taken from both tonsils. The complete blood count revealed significantly elevated leucocytes at 370 × 10^3/uL with 93% lymphocytes. Urgent peripheral blood smear showed hyperleukocytosis with 88% blasts. Other significant results include hemoglobin 12.9 g/dL, platelet 45 × 10^3/uL, urea 3.7 mmol/L, creatinine 125 umol/L, lactate dehydrogenase (LDH) 2359 U/L, and uric acid 951 umol/L. The chest radiograph was normal with no mediastinal widening. He was admitted and immediately referred to the medical team for acute leukemia with tumor lysis syndrome. Further work-up with bone marrow aspirate and trephine biopsy along with immunophenotyping eventually confirmed the diagnosis of T-ALL. The histopathological examination of the tonsil biopsy was in keeping with the diagnosis by demonstrating infiltration of the leukemic cells into the tonsils (Fig. 2a). These atypical lymphoid cells were immunoreactive toward TdT, CD2, CD3, CD4, CD5, CD7, CD8, and CD79a (Fig. 2b,c). The ki67 proliferation index was approximately 80% (Fig. 2d). Following the resolved tumor lysis syndrome, the patient was commenced on the hyper-fractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone (hyper-CVAD) chemotherapy regime.

DISCUSSION

In the primary care setting, sore throat is a common presenting complaint that typically follows an upper respiratory infection. Acute tonsillitis, an inflammatory disorder of the tonsils, invariably manifests with sore throat as a hallmark symptom. Other usual accompanying symptoms include fever, odynophagia, dysphagia, and cervical lymphadenopathy. In adults, it is most often caused by a viral infection; approximately 5%–17% of the cases are due to bacterial causes, particularly Group A β-hemolytic streptococcus (GABHS).[1] Hence, the treatment is straightforward with supportive care and antibiotics as indicated. However, tonsillar inflammation can occur due to other sinister pathologies such as diphtheria, infectious mononucleosis, and worse, still, malignancies. These include carcinoma and hematological malignancies, namely, lymphoma and leukemia.

Palatine tonsils are part of Waldeyer's ring, which is a circular band of lymphoid tissue in the naso-oropharynx region. It is significant for being the most frequently involved extranodal site for head and neck lymphoma, followed by the nasopharynx and base of the tongue. Non-Hodgkin lymphoma of the B-cell lineage is the predominant entity, with diffuse large B-cell lymphoma being the most prevalent type.[2] However, leukemia with acute tonsillitis as its initial presentation is exceedingly rare with very few cases reported in the literature. Although oral manifestations are not rare, these are usually gingival enlargement and bleeding, oral ulcers, petechiae, and mucosal pallor.[3] These occurrences are either following direct infiltration of the leukemic cells or secondary to the impaired function of the hematopoietic cells. A recently published review article by Quispe et al.[4] concluded that oral cavity can harbor the initial manifestations of leukemia, particularly acute myeloid leukemia (AML). In fact, the limited case reports of leukemia presenting as tonsillitis were of acute myeloid type as well; thus, adding to the uniqueness and significance of our patient's presentation.[5,6]

ALL is more frequently diagnosed in children, whereas AML is the most prevalent acute leukemia in adults. Among ALL, T-ALL accounts for 15% of pediatric cases and 25% of cases in the adult population.[7] Lymphoid precursor cells pro-

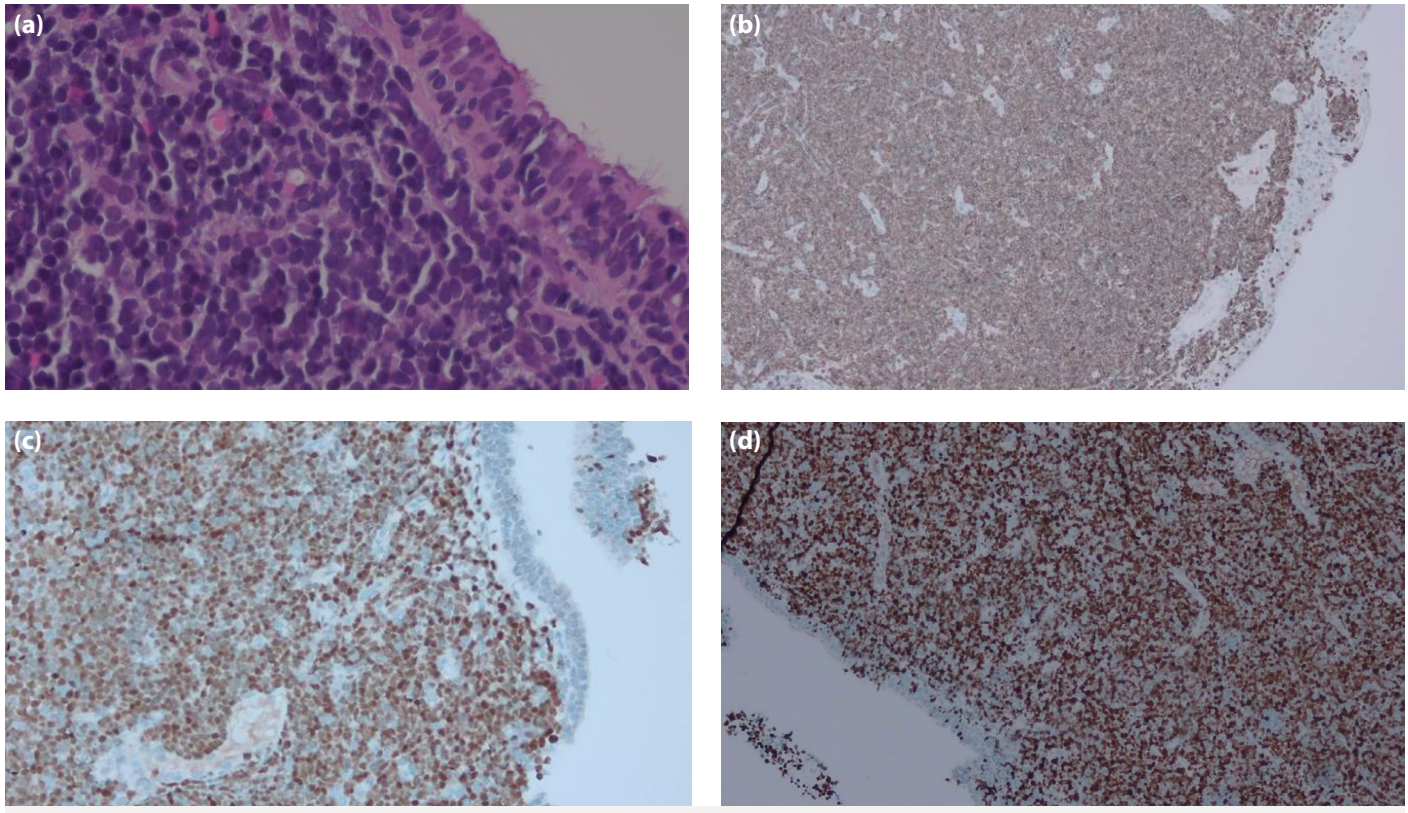

Figure 2. Microscopic images of tonsil tissue biopsy. **(a)** Diffuse infiltrate of atypical lymphoid cells displaying irregular nuclear contours, small nucleoli, and dispersed chromatin (H&E, ×400). Immunohistochemistry shows the neoplastic cells express **(b)** CD3 positivity and **(c)** TdT positivity. **(d)** Ki67 proliferative index of approximately 80%.

liferate and differentiate into T-cells in the thymus. T-ALL arises from the malignant transformation and proliferation of T-cell progenitors. T-ALL is differentiated from T-lymphoblastic lymphoma (T-LBL) by the presence of more than 25% marrow blasts.[8] T-ALL is more frequent in men than in women, and a retrospective study by Guru Murthy et al.[9] in 2018 reported an incidence of 0.13 cases per 100,000 adults in the United States.

Clinical manifestations of leukemia are expectedly due to bone marrow failure resulting in symptoms such as anemia, recurrent infections, fever, bleeding, purpura, and bone pain. These features can develop rapidly or rather insidiously over a variable period of time. Nevertheless, extramedullary manifestations can be the presentation of T-ALL and should therefore be familiar among clinicians to avoid delayed diagnosis. Among the extramedullary presentation of T-ALL are mediastinal masses potentially causing shortness of breath and superior vena cava obstruction, lymphadenopathy, hepatosplenomegaly, and central nervous system involvement.[9] As mentioned earlier, leukemic tonsillitis as an initial presentation of T-ALL remains elusive in the literature review.

The distinction between T-ALL and B-ALL is becoming more established with unique biological features and treatment options. The actively ongoing research into the genomics of T-ALL has nevertheless provided promising insights and outlook into the treatment aspect of this disease. Contemporary chemotherapy has resulted in marked improvement in the remission and overall survival rates of T-ALL patients, especially among younger patients.[9,10] Many clinical trials have reported 5-year disease-free survival rates of approximately 85%.[10] Contrary to B-ALL, age and leucocyte count at diagnosis are not independent prognosticators for T-ALL. Although chemotherapy remains the mainstay treatment, particularly the usage of pediatric-intensive regimens for adolescents and young adults, hemopoietic cell transplantation is an option for those patients who have adverse genetic features and/or minimal residual disease positive.[7]

CONCLUSION

Acute tonsillitis is a commonly encountered entity in daily practice. Despite its rarity, this case report highlights the possibility of acute tonsillitis being a precursor for acute leukemia. Clinical manifestations that deviate from the typ-

ical course of bacterial or viral tonsillitis should raise suspicions of a more sinister pathology. The unhealthy appearance of the tonsils with surface ulceration and the presence of multiple cervical lymphadenopathies are such alarming features. Awareness of such clinical manifestations will aid in avoiding delayed diagnosis and preventing potential morbidity and mortality.

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