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Case Report

ALK-positive large B-cell lymphoma presenting as oropharyngeal mass: A rare case report

Kavitha Bali Nagendrappa[1]*, Ramakrishna Reddy[1], Kalyan Rao[1], Reshma Stanly[1], Rajesh Bendre[1]

[1]Dept. of Histopathology, Apollo Diagnostics GRL, Hyderabad, Telangana, India

Abstract

Anaplastic lymphoma kinase-positive large B-cell lymphoma (ALK+ LBCL) is an exceedingly rare and aggressive subtype of diffuse large B-cell lymphoma characterized by distinctive clinical and immunophenotypic features. It predominantly affects younger individuals and often presents with extranodal involvement, which can pose diagnostic challenges due to its diverse morphology and overlapping immunoprofiles with other hematologic malignancies. This case report describes a 46-year-old male presenting with a progressive oropharyngeal mass originating from the right tonsillar fossa, an uncommon site for ALK+ LBCL. Histopathological examination revealed a diffuse infiltrate of medium-sized lymphoid cells, with immunohistochemistry demonstrating positivity for ALK1, MUM1, CD138, and BOB1, alongside a high proliferative index, while lacking expression of classical B-cell markers such as CD20 and PAX5. Differential diagnosis included ALK+ ALCL, plasmablastic lymphoma, DLBCL-NOS, and plasma cell neoplasms; however, immunophenotypic and molecular features confirmed ALK+ LBCL. This case underscores the essential importance of thorough immunohistochemical profiling in diagnosing atypical presentations of ALK+ LBCL and highlights the need to include this entity in the differential diagnosis of CD20-negative lymphoid tumors in extranodal locations. Identifying such rare manifestations is crucial for accurate diagnosis and for informing appropriate targeted treatment approaches.

Keywords: Anaplastic lymphoma kinase-positive (ALK+), Large B-cell lymphoma, Extranodal involvement, Differential diagnosis.

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1. Introduction

Anaplastic lymphoma kinase-positive large B-cell lymphoma (ALK+ LBCL) is a rare and highly aggressive subtype of diffuse large B-cell lymphoma (DLBCL), first described in 1997.[1] It is distinguished by the abnormal expression of the ALK protein, typically resulting from chromosomal translocations involving the ALK gene, most frequently t(2;17)(p23;q23), which produces a CLTC-ALK fusion gene.[2] Unlike other ALK-expressing lymphomas, such as ALK-positive anaplastic large cell lymphoma, ALK+ LBCL lacks CD30 expression and shows a distinct immunophenotypic profile, typically expressing plasma cell-associated markers such as CD138 and MUM1, while being negative for traditional B-cell markers like CD20.[3,4]

This lymphoma predominantly affects younger individuals and follows an aggressive clinical course with poor response to conventional chemotherapy regimens.[5] Due to its rarity, ALK+ LBCL is often under-recognized, and diagnosis requires a high index of suspicion along with detailed immunohistochemical and molecular studies.[6] In this case report, we present a rare instance of ALK+ LBCL, highlighting its clinical presentation and diagnostic challenges.

2. Case Summary

A 46-year-old male presented with progressive dysphagia over several weeks. Contrast-enhanced computed tomography (CECT) of the neck revealed an ill-defined heterogeneously enhancing soft tissue mass measuring 2.5 x

*Corresponding author: Kavitha Bali Nagendrappa
Email: drkavithabali@gmail.com

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2.2 cm in the right tonsillar fossa, protruding into the oropharyngeal cavity. Associated para-pharyngeal fat stranding was noted. Multiple subcentimetric lymph nodes were identified in level IA, bilateral IB, and level II cervical chains, with the largest node measuring 6 mm in short-axis diameter.

An incisional biopsy of the right tonsillar mass was performed. Histopathology demonstrated a diffuse and nodular infiltrate of medium-sized cells with moderate cytoplasm, round vesicular nucleus and prominent nucleoli.(**Figure 1**A-D)

Immunohistochemistry (IHC) demonstrated positivity for CD45, MUM1, BOB1, and diffusely for ALK1, with focal or patchy expression of CD138 and CD10. The tumor cells were negative for CD20, CD3, CD2, PAX5, TdT, CD34, BCL2, CD30, and EBV. The proliferative index, assessed by Ki-67, was greater than 90%. Based on the morphological and immunophenotypic characteristics, the diagnosis was aligned with ALK-positive large B-cell lymphoma.(**Figure 1**E-O)

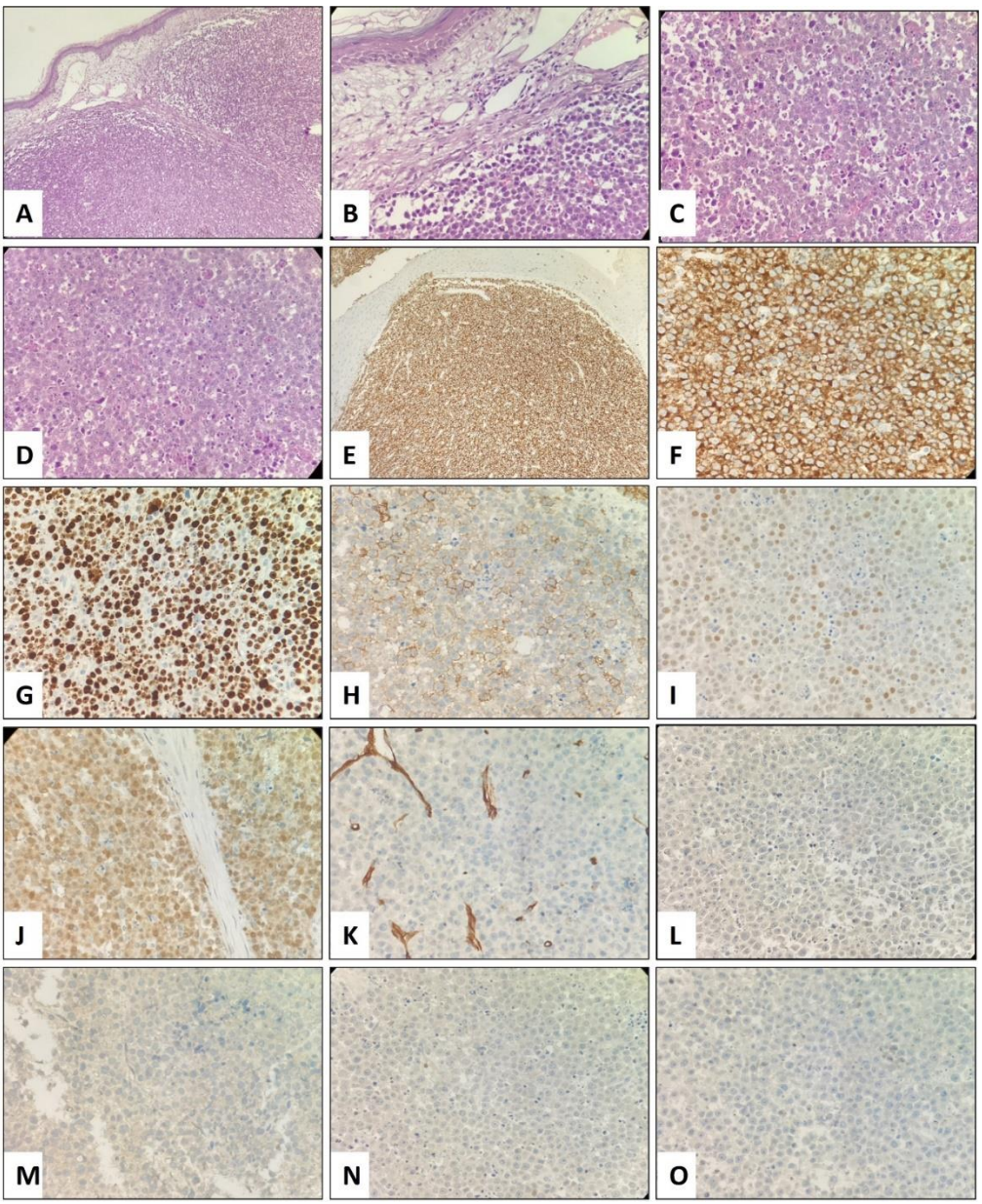

Figure 1: A, B): H&E-stained sections reveal stratified squamous epithelium overlying a lesion. **C, D):** The lesion is composed of medium-sized plasmacytoid cells arranged in a diffuse pattern. These cells exhibit moderate cytoplasm, round vesicular nuclei, and prominent nucleoli. **E):** Immunohistochemistry (IHC) for CD45 shows diffuse positivity. **F):** IHC for ALK demonstrates diffuse positivity. **G):** IHC for Ki-67 reveals a proliferative index exceeding 90%. **H):** IHC for CD138 shows patchy positivity. **I, J):** IHC for BOB1 and MUM1 shows nuclear positivity. **K–O):** IHC for CD34, TdT, CD20, CD79a, and CD3 are negative.

3. Discussion

ALK+ LBCL is a rare and highly aggressive subtype of diffuse large B-cell lymphoma. It primarily affects younger to middle-aged individuals and often presents with extranodal involvement, including in rare sites such as the nasopharynx or oropharynx, as seen in this case. Dysregulated expression of anaplastic lymphoma kinase (ALK), most often caused by a chromosomal translocation t(2;17)(p23;q23) that creates the CLTC-ALK fusion gene, leads to the constitutive activation of ALK tyrosine kinase. This activation drives oncogenic transformation and unchecked proliferation of B-cells.[1,7]

Immunophenotypically, ALK+ LBCL demonstrates plasmablastic differentiation, with tumor cells expressing plasma cell-associated markers such as CD138 (syndecan-1) and MUM1/IRF4, while lacking classical B-cell lineage markers such as CD20 and PAX5. This phenotype contributes to diagnostic challenges, particularly in distinguishing ALK+ LBCL from other aggressive hematologic malignancies.[8]

In this particular case, the disease was presented as a tonsillar mass, an atypical site for ALK+ LBCL. The tumor is more frequently encountered in lymph nodes, the nasopharyngeal region, and the gastrointestinal tract.[9] The extranodal tonsillar presentation emphasizes the necessity for comprehensive immunohistochemical and molecular evaluation to avoid misdiagnosis.

3.1. Differential diagnostic considerations

The unusual IHC profile observed in this case required careful differentiation from several morphologically and phenotypically overlapping entities:

1. ALK-positive anaplastic large cell lymphoma (ALK+ ALCL): ALK+ ALCL typically shows strong CD30 positivity, epithelial membrane antigen (EMA) expression, and a T-cell immunophenotype (frequently CD3 positive). However, it lacks MUM1 and CD138 expression, markers that are present in our case. Additionally, this tumor was CD30 and CD3 negative, arguing against a diagnosis of ALK+ ALCL.[10]
2. Plasmablastic lymphoma (PBL): PBL often arises in HIV-positive individuals and shows plasmablastic features, with expression of CD138 and MUM1, and frequent Epstein-Barr virus (EBV) positivity. However, PBL characteristically lacks ALK expression, which was positive in our case, and the patient was EBV-negative, excluding this possibility.[11]
3. Diffuse large b-cell lymphoma, not otherwise specified (DLBCL-NOS): DLBCL-NOS is usually CD20 and PAX5 positive, reflective of its mature B-cell origin. In our case, lesional cells however, showed absence of both markers, supporting exclusion of DLBCL-NOS in favor of ALK+ LBCL.[12]
4. Extramedullary plasmacytoma / multiple myeloma: These plasma cell neoplasms typically express CD138, MUM1, and CD38, and may mimic ALK+ LBCL in morphology and phenotype. However, they usually lack ALK expression, exhibit a plasma cell dyscrasia, and do not demonstrate lymphoid architecture. The presence of ALK and the absence of systemic plasma cell disease further argue against these diagnoses.[13]

4. Conclusion

This case highlights the critical need for thorough immunohistochemical analysis in diagnosing atypical oropharyngeal masses. Although rare, ALK-positive large B-cell lymphoma should be included in the differential diagnosis of CD20-negative lymphoid neoplasms, especially when involving extranodal locations. Prompt recognition and diagnosis are essential to guide appropriate management and explore targeted therapeutic options.

5. Source of Funding

None.

6. Conflict of Interest

None.

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