Primary lymphoplasmacytic lymphoma of the larynx mimicking extramedullary plasmacytoma: A case report

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Abstract. Primary haematological neoplasms of the larynx are uncommon; therefore, information regarding their epidemiology is limited and the diagnosis of histological types requires careful consideration. The current study describes the case of a 72-year-old male patient with primary laryngeal lymphoplasmacytic lymphoma (LPL) that was difficult to distinguish from plasmacytoma. Imaging examinations of the neck revealed a mass in the right laryngeal folds, 25x12x25 mm in size, which was surgically resected by direct laryngoscopy. Histopathologically, the mass showed diffuse proliferation of plasma cells with CD138 (+) and IgG (+) in the submucosal stroma. Flow cytometry revealed the tumour was positive for CD19 and negative for CD56. Based on these findings, the final diagnosis was confirmed as LPL, albeit similar to plasmacytoma regarding phenotypic features. There was no evidence of local or systemic recurrence following surgery, and the patient has been followed up without additional treatment. This case highlights the unique presentation of laryngeal lymphoma mimicking solitary plasmacytoma. The key factor in the diagnosis was the expression pattern of surface antigen markers.

Introduction

Haematological neoplasms such as lymphoma or plasmacytoma rarely develop in the larynx (1,2). With regard to lymphoma, fewer than 100 cases have been reported in the literature (1). Therefore, information regarding their epidemiology is limited and the determination and diagnosis of histological types requires careful consideration. As for laryngeal lymphoplasmacytic lymphoma (LPL), there have been very few reports to date (3). LPL is composed of small lymphocytes, plasmacytoid cells, and plasma cells that express high levels of surface immunoglobulin, generally of IgM type and occasionally of IgG or IgA type. While the diagnosis of LPL is commonly straightforward, particularly for those composed of small lymphocytes that express surface IgM, some cases of LPL with plasmacytic differentiation are difficult to distinguish from extramedullary plasmacytoma. According to previous reports describing laryngeal plasmacytoma, some case reports diagnosed plasmacytoma based solely on its pathologic features, including the presence of CD138-positive cells (4), which could lead to misdiagnosis. In the present case, we encountered a patient with primary laryngeal neoplasm, diagnosed as LPL mimicking plasmacytoma.

Case report

A 72-year-old male with a history of hypertension and reflux esophagitis visited an otolaryngologist in September 2021, complaining of dysphagia that had persisted for three years. A fiberscopic examination of the larynx revealed a pedunculated mass in the right aryepiglottic fold, but a biopsy did not reveal any neoplastic changes. The mass gradually increased in size over the seven months of follow-up, and then the patient developed respiratory distress in the left lateral recumbent position. As surgery was deemed necessary, the patient was referred to the Department of Otolaryngology at our institution in June 2022. Additional fiberscopic examination revealed a mass with a stalk in the right laryngeal folds (Fig. 1A), which showed pendulum-like motion during speech and breathing, and the glottis was barely observable. Narrow-band light observation revealed no abnormal findings in the mucosa. Contrast-enhanced computed tomography (CT) revealed a 25x12x25 mm oval of soft tissue structure bordering the right lamina propria, with a homogeneous interior and an enhancement effect comparable to that of the pharyngeal mucosa and tonsils (Fig. 1B). Contrast-enhanced MRI showed a uniform enhancing effect from early after contrast (Fig. 1C). The

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Table I. Antigen expression patterns of LPL and plasmacytoma.

Marker	CD10	CD19	CD20	CD38	CD56	CD138	Immunoglobulin	(Refs.)
LPL	-	+	+	+/-[a]	-	+/-[a]	IgM > IgG ≈ IgA	(13,14)
Plasmacytoma	-	-	+/-	+	+/-	+	IgG > IgA > IgM	(5,14)
The present case	-	+	+	+	-	+	IgG	-

[a]They are positive in cases of plasmacytic differentiation. LPL, lymphoplasmacytic lymphoma.

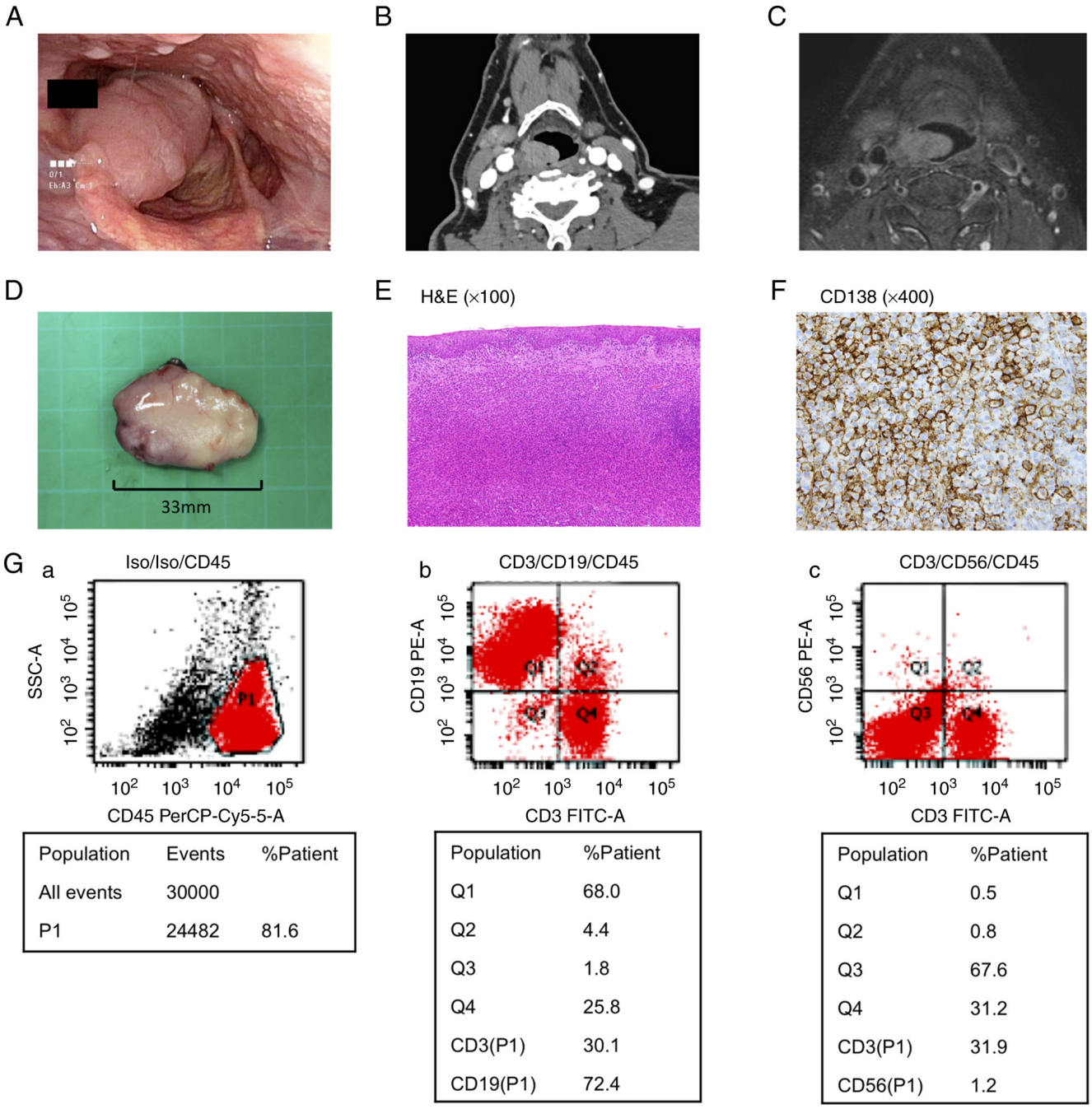

Figure 1. Imaging, pathology, and flow cytometry. (A) Fiberscopic examination: A large mass is shown in the right aryepiglottic fold with airway construction. (B) Contrast-enhanced CT: A lightly enhanced 25x12x25 mm oval structure composed of soft tissue is shown bordering the right arytenoid mucosa. (C) Contrast-enhanced MRI: A mass showing a uniform enhancing effect from early after contrast is shown. (D) Resected laryngeal mass: The 33-mm mass was completely removed. No residual tumour was observed macroscopically. (E) H&E staining of tissue from the laryngeal mass; magnification, x100: The tumour contained atypical plasma cells. (F) Immunohistochemical analysis of CD138 in the tissue from the laryngeal mass; magnification, x400: Neoplastic plasma cells were positive for CD138. (G) Flow cytometry of the laryngeal mass (a) lymphocytes (red dots) accounted for 81.6%; (b) lymphocytes positive for CD19 (72.4%); (c) lymphocytes negative for CD56 (1.2%). H&E, haematoxylin and eosin.

preoperative differential diagnoses were cancer, lymphoma, soft-tissue tumour, and amyloidosis. We first performed a tracheotomy under local anaesthesia. After that, we removed the tumour by direct laryngoscopy in July 2022. The intraoperative pathological diagnosis was malignant lymphoma. The surgery was concluded with complete resection of the mass (Fig. 1D).

Haematoxylin and eosin staining showed diffuse proliferation of plasma cells in the submucosal stroma and the presence of germinal centres in the lesion (Fig. 1E). Immunohistochemical analysis showed CD138 (+) (Fig. 1F), IgG (+), IgA (-), and IgM (-) cells within the entirety of the pathological specimen, and some CD20 (+) tumour cells. In situ hybridization showed light chain restriction with a predominance of kappa light chains. Direct fast scarlet 4BS (DFS) staining showed no amyloid deposition, and the specimen was negative for epithelial cell markers AE1/AE3. The pathological diagnosis was plasma cell neoplasm including plasmacytoma or low-grade lymphoma with marked differentiation into plasma cells. Flow cytometry revealed the laryngeal tumour to be positive for CD19 and negative for CD10 and CD56 (Fig. 1Ga-c). No tumour cell infiltration was found in the bone marrow. Blood examination showed no abnormalities in serum IgA, IgM, and IgG, or in the κ/λ ratio. Cytogenetic testing of the laryngeal tumour showed a normal karyotype.

Based on the above clinical findings, the final diagnosis was confirmed as LPL, based particularly on the fact that it was positive for CD19 and negative for CD56. The laryngeal lesion was completely resected, leading to an improvement in the patient's symptoms of dyspnoea and dysphagia. Whole body CT revealed no residual lesions or visible lesions in other parts of the body. The patient has been followed up every 3-6 months over one year without any additional treatment. The last visit was in late August 2023, and there has been no evidence of local or systemic recurrence.

Discussion

In the present case, the first impression obtained from the pathological findings was solitary extramedullary plasmacytoma, IgG-type, as the tumour cells indicated plasmacytic differentiation and expressed CD138, a main marker of plasma cells. However, this was inconsistent with the presence of CD19, which is mostly negative in plasma cell neoplasm (5). Further, the tumour cells did not express CD56, which is positive in 60-75% of plasma cell neoplasm (5). On the other hand, LPLs with IgG or IgA paraprotein are mostly positive for CD19 (96%) and usually negative for CD56 (16%) (6). Therefore, this primary laryngeal neoplasm was diagnosed as LPL based on the antigen expression pattern as shown Table I.

As in this case, the differential diagnosis between LPL and solitary plasmacytoma can be difficult, based solely on the pathologic and phenotypic features of the tumour. Next-generation sequencing studies have identified a MYD88 mutation (L265P), a component of the Toll-like receptor signalling machinery, in approximately 90% of LPLs (7,8). On the other hand, the mutation was absent in all multiple myeloma (MM) patients, thus MYD88 mutation analysis can facilitate the differentiation of LPL from MM. Even in this case, mutation analysis should have been performed at the time of tumour resection; however, additional testing was impossible because the specimens are not stored.

Extramedullary lymphoma localized in the larynx is rare, with fewer than 100 cases of laryngeal lymphoma published in the literature, with only five other reports when of LPL (1,3,9-11). However, it is controversial whether the incidence of laryngeal LPL is truly very low or whether it has previously been misdiagnosed as other B-cell malignancies, such as MM. If MYD88 mutation analysis is used more commonly in the initial diagnosis of lymphoma, the number of laryngeal LPL cases is expected to increase.

Treatment options for primary laryngeal B-cell lymphomas are typically radiotherapy or chemotherapy, with a good prognosis reported (12). Tumour resection is for diagnostic purposes, and postoperative radiotherapy or chemotherapy is commonly performed. In the present case, the patient chose watchful waiting according to the GELF criteria for low-grade B-cell lymphoma as there was no evidence of residual lesions. As there has been no recurrence at more than one year post-surgery, no additional treatment has been required.

This case highlights the unique presentation of laryngeal lymphoma pathologically and phenotypically mimicking solitary plasmacytoma. The key factor in the diagnosis was the expression pattern of surface antigen markers, with the tumour being positive for CD19 and negative for CD56. MYD88 mutation analysis, which is not available in this case, would further aid LPL diagnosis. When examining cases of laryngeal tumours, haematological neoplasms should be included in the differential diagnosis regardless of their rarity.

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Availability of data and materials

All data generated and/or analysed during this study are included in this published article.

Authors' contributions

MM and TI conceptualized and designed the study, and drafted the manuscript. FS revised the manuscript. NI, HT, KS, KY and FS were involved in the treatment of the patient. NI, KY and FS confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

This study was exempt from ethical approval by the ethics committee of Sapporo City General Hospital.

Patient consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Competing interests

The authors declare that they have no competing interests.

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