Primary nodular lymphocyte predominant Hodgkin lymphoma of the palate: A rare incidence which was also associated with progressive transformation of germinal centres of cervical lymph node

Hanan Ali a, Kikkeri Naresh b, Nayef M. Aqel a,*

a Department of Cellular Pathology, Northwick Park Hospital, Harrow, Middlesex HA1 3UJ, United Kingdom
b Department of Histopathology, Hammersmith Hospital, London W12 0HS, United Kingdom

Received 22 March 2013; accepted 15 April 2013
Available online 27 June 2013

Keywords
Nodular lymphocyte predominant Hodgkin lymphoma;
Palate;
Mouth;
Extranodal manifestation;
Progressive transformation of germinal centres

Abstract
Primary manifestation of nodular lymphocyte predominant Hodgkin lymphoma in oral cavity is very rare. We are describing such a case which was associated with progressive transformation of germinal centres in a cervical lymph node.

© 2013 Production and hosting by Elsevier B.V. on behalf of National Cancer Institute, Cairo University.

Hodgkin lymphoma (HL) is classified as classical HL and that of nodular lymphocyte predominant Hodgkin lymphoma (NLPHL). Typically, both types present in the form of nodal disease and primary involvement of extranodal tissue, by Hodgkin lymphoma is rare [1,2]. NLPHL is an uncommon type of HL representing about 5% of overall HL cases [3,4]. The 2008 WHO lymphoma classification [4] defines NLPHL as a “monoclonal B-cell neoplasm characterised by a nodular, or a nodular and diffuse, proliferation of scattered large neoplastic cells known as popcorn or lymphocyte predominant cells (LP cells). These LP cells are monoclonal B cells of germinal centre (GC) origin. They reside in large spherical meshworks of follicular dendritic cell (FDC) processes that are filled with non-neoplastic lymphocytes and histiocytes.” LP cells stain positive for CD45 and other B lymphocyte antigens, including, CD20, and CD79a. They also express Pax-5 (a B cell-specific activator protein), transcription factors OCT-2 (B-cell Oct-binding protein 1) and B-cell specific transcription co-activator (BOB-1). LP cells express GC marker (BCL-6), although they appear to stain negative for CD10 [5,6]. LP cells stain negative for antigens of Reed Sternberg cells of classical HL (CD15 and CD30), However reactive CD30 positive immunoblasts can be found outside the neoplastic nodules of NLPHL. Most LP cells express J chain and they frequently express epithelial membrane antigen (EMA) [7].

* Corresponding author.
E-mail address: nayef.aqel@nhs.net (N.M. Aqel).
© Peer review under responsibility of The National Cancer Institute, Cairo University.
We have recently looked after a 68-year-old female who presented with severe headache. Clinical examination showed a hard palate mass hidden under a loosely fitted denture. Magnetic Resonance Imaging (MRI) of the head demonstrated a solid mass in the hard palate which was at the right of the midline. This mass measured 33 mm in diameter and invaded the adjacent bone without extending into the maxillary alveolus or the nasal cavity. There were also abnormally enlarged right cervical lymph nodes (levels 1–4) measuring up to 21 mm in level 4.

Blood cell counts, renal and liver function tests, serum lactate dehydrogenase (LDH) were all within normal range. Serological tests for Hepatitis A, B and C, and HIV were negative. The palatal tumour was excised. The tumour measured 25 × 22 mm in maximum dimensions and had a maximum thickness of 14 mm. On histology, a dense nodular lymphocytic infiltrate was found beneath the squamous epithelium. The nodules were identified as abnormal follicles by the presence of dense FDC meshworks (CD21, CD23 positive). No diffuse areas were seen. The nodules were composed predominantly of a mixture of follicular T-helper lymphocytes (CD3, CD5, CD4, and PD-1 positive) and small B-lymphocytes of mantle zone phenotype (positive for CD20, CD79a, surface IgD, and IgM). These nodules contained scattered LP/popcorn cells. The LP cells demonstrated large irregular nuclei with vesicular chromatin pattern and prominent nucleoli (Fig. 1). They stained positive for CD45, CD20, OCT2, BOB-1 (weak), immunoglobulin J chain and EMA. They stained negative for CD3, CD5, CD4, PD1, CD15, CD30, IgM, IgD and BCL2. They also showed Kappa light chain restriction by RNA in-situ hybridisation. PD-1 positive T-lymphocytes formed rosettes around the LP cells (Fig. 2). No classical Reed Sternberg cells were seen.

Excision of the largest right level 4 cervical lymph node showed reactive hyperplasia with numerous secondary follicles. Present also were a few discrete larger nodules/follicles with diameters 3–5 times larger than that of the secondary follicles. They were rich in meshworks of FDCs (positive for CD21 and CD23). They showed blurred mantle zone with mantle zone cells infiltrating the centre of nodules discretely and in sheets; these cells were positive for CD20, CD79a, IgM and IgD. Some residual centroblastic cells were identified which stained negative for EMA, immunoglobulin J chain and RNA in situ hybridisation failed to demonstrate light chain restriction in these cells. They lacked cytological features of LP cells. A diagnosis of progressive transformation of germinal centres (PTGC) was made on this lymph node. Bone marrow aspirate and trephine biopsy showed no evidence of

![Figure 1](image1)  A neoplastic nodule containing mixed sheets of small B and T lymphocytes with discrete larger neoplastic “popcorn” cells. Haematoxylin and eosin stain.

![Figure 2](image2)  Upper three images of “popcorn” cells demonstrating their complex nuclear features. The nuclei are large, vesicular and irregular and contain a few discrete small nucleoli. Lower left image: A “popcorn” cell showing cytoplasmic positivity for J chain. Right lower image: A “popcorn” cell is surrounded by small T lymphocytes, as demonstrated by PD-1 antibody.
infiltration by NLPHL. This finding was also confirmed by immunocytochemistry. The association between PTGC and NLPHL has been known for many years. Some studies have suggested that as high as 30% of PTGC patients are associated with antecedent, concurrent or subsequent NLPHL, while others have not demonstrated such a strong correlation [3,8].

In conclusion; primary manifestation of NLPHL in oral cavity is very rare. Using modern immunohistochemistry in recent years, there has been description of a single case of primary NLPHL in the floor of the mouth [9] and 3 cases in the tonsils [10] (2 in the palatine tonsils and one in the lingual tonsil). Our case is an addition to these extremely rare cases.

References