Abstract

Lymphoid tissue located in the head and neck region include multiple regional lymph node chains as well as mucosa associated lymphoid tissue of the conjunctiva, buccal and nasopharyngeal cavities (Waldeyer’s ring), and thyroid and salivary glands. This region is a rich source of antigenic stimuli including infectious agents coming from the outside environment. Many reactive conditions that affect lymphoid tissue in this region may mimic neoplasia. In fact, distinguishing between benign and malignant lymphoid proliferations in the head and neck region is a relatively frequent diagnostic challenge and in many instances, this distinction is not straightforward. It therefore behooves the practicing pathologist to be able to recognize the benign lymphoproliferative disorders that affect this region so as to effectively guide the appropriate clinical management of such patients. Kimura disease, Epstein Barr lymphadenitis, HIV associated salivary gland disease and chronic sialadenitis are benign conditions that not infrequently affect
lymphoid tissue in the head and neck region and that share certain overlapping features with malignant lymphoma. In this brief review, we discuss these conditions and highlight clinicopathological features that may help distinguish them from neoplastic lymphoproliferations that may share similar features.

Keywords: Kimura, HIV, EBV, chronic sialadenitis, MALT
Introduction
The head and neck region represents about 10% of the total body surface area and contains several mucosal surfaces, including buccal, nasopharyngeal and ocular, that can serve as ports of entry for antigens into the body’s internal environment. Consequently, this region is rich in lymphoid tissue that is strategically located to survey, process and eliminate potentially harmful antigens. Head and neck lymphoid tissue includes mucosa associated lymphoid tissue (MALT) of the buccal and nasopharyngeal cavities (Waldeyer’s ring), conjunctiva, and thyroid and salivary glands. There are also multiple regional lymph node chains. These are constantly bombarded by external antigenic stimuli and are frequently enlarged or tender in response to viral, bacterial and other infectious lymphadenitis. Non-neoplastic lymphadenopathy such as those associated with autoimmune diseases and iatrogenic causes (such as certain drugs) also frequently affect head and neck lymphoid tissue. In fact, it is not uncommon for the practicing pathologist to be faced with the challenge of distinguishing between reactive and neoplastic lymphoid proliferations in this region.(1) From a histopathological stand point, it is important to consider both the overall architecture of the lymphoid tissue as well as the cytological features of the proliferating cells in order to help make the distinction between a reactive and neoplastic process. Reactive conditions generally show overall preservation of normal lymphoid architectural features including intact B-cell (lymphoid follicles) and T-cell (inter-follicular and paracortical) areas, even if there is overall expansion (lymphoid hyperplasia) or partial distortion of one or more of the components. Neoplastic processes, on the other hand, frequently disrupt or replace the normal architecture.

Here we review four selected non-neoplastic entities that affect head and neck lymphoid tissue and can mimic lymphoid neoplasia.
Kimura Disease

Kimura disease is a rare chronic inflammatory disorder with a predilection for the head and neck region. First described in the Chinese literature in 1937 as “eosinophilic hyperplastic lymphogranuloma”, the disease acquired its current eponymous designation from Kimura who published a series in the Japanese literature in 1948. However, the true incidence of Kimura disease is not known. Most cases have been described in mainland China and Japan where the disease occurs predominantly in young males. Sporadic cases have been described in most geographic regions around the world including North and South America, Europe and Africa. The largest series reported in the United States by Chen et al from The Armed Forces Institute of Pathology (AFIP) included 21 patients of different ethnicities including Caucasian, Black, Asian, Hispanic and Arabic (1 each) with a male: female ratio of 6:1 and a mean age of 31 years (range 8 to 64). These findings are comparable to those described in similar case series reported in the Japanese and Chinese literature.

The etiology of Kimura disease is unknown. It is considered to represent a chronic inflammatory disorder, possibly due to a hitherto unidentified antigenic stimulus. Infectious agents such as viruses, parasites and Candida albicans and toxins have been proposed as possible triggers, but there is no conclusive evidence to support any specific inciting factor. Patients usually present with single or multiple painless subcutaneous masses in the head and neck region, including the face, neck and periauricular areas. Enlarged regional lymph nodes are frequently present and the reported frequency of clinically detectable regional lymphadenopathy ranges from 32 to 100%. Subcutaneous tissue and lymph node groups outside of the head and neck region may also be involved, at times without apparent head and neck disease. Unilateral or bilateral involvement of parotid and submandibular salivary glands may lead to swelling and lacrimal gland involvement has been reported in at least one patient. In addition, peripheral blood eosinophilia, frequently above 10%, and elevated serum IgE and eosinophil cationic protein levels are invariably present. Renal disease, usually in the form of nephrotic-level proteinuria, is seen in up to 16% of patients. The histopathologic correlate includes a number of patterns including mesangioproliferative
glomerulonephritis, membranous nephropathy and minimal change disease, among others. (1316)

Historically, Kimura disease has been confused with angiolymphoid hyperplasia with eosinophilia (ALHE). However, it is now well established that these two represent separate unrelated entities with distinct clinicopathological features. (10, 17) ALHE, renamed epithelioid hemangioma, is a benign vascular tumor characterized by proliferation of small, capillary-sized vessels with plump, epithelioid endothelial cells (in contrast to Kimura disease) which can be highlighted with immunohistochemical stains for CD31, CD34 and factor VIII. Furthermore, ALHE is usually localized to the skin without regional lymph node involvement and despite the frequent presence of a rich inflammatory milieu including eosinophils and lymphocytes, peripheral blood eosinophilia and elevated IgE are not seen. Several malignant lymphomas including classical Hodgkin lymphoma (CHL), peripheral T-cell lymphomas, especially angioimmunoblastic T-cell lymphoma (AITL) and non-Hodgkin B-cell lymphomas may be accompanied by prominent eosinophilia and should always be considered in the differential diagnosis of Kimura disease. These lymphoid neoplasms in early stages may not demonstrate significant disruption of the normal lymph node architecture, or easily identified neoplastic cells such as Hodgkin/Reed-Sternberg (HRS) cells in CHL and clear cells in AILT. Particularly, differentiating Kimura disease from early forms of AILT and interfollicular CHL can be extremely challenging. If interfollicular CHL is suspected, IHC for CD30, CD15, and Pax5 will be helpful to identify HRS cells. On the other hand, if early AITL is suspected, IHC for CD3, CD4, CD8, CD10, PD-1 will help to identify proliferation of neoplastic cells with a follicular T-help immunophenotype, and in situ hybridization may highlight EBER positive cells. Molecular studies may show clonal T-cell receptor rearrangement, in contrast to Kimura disease which would typically show a polyclonal pattern.

The natural history of Kimura disease is not well described. In most patients, the disease shows a prolonged, indolent clinical course. In the AFIP series, the majority had complete remission with no evidence of disease even with long term follow up while one
patient still had evidence of disease more than 12 years after initial presentation. Long-term oral corticosteroids seem to be the mainstay of treatment of Kimura disease whereas surgical resection and radiation have limited roles in localized disease. Multifocal disease outside of the parotid glands, eosinophils > 50% and IgE levels >10,000 IU/ml have been shown to be associated with recurrent disease.(7) More aggressive therapy with immunosuppressive agents like Cyclosporine and azathioprine may play a role in the treatment of patients with renal disease (18,19)

HIV associated Lymphoepithelial Cysts

The term HIV-associated salivary gland disease usually refers to lymphoproliferative disorders that lead to parotid gland enlargement in HIV infected patients.(20, 21) The overwhelming majority of these lesions are lymphoepithelial cystic lesions.(20-23) The term lymphoepithelial cyst (LEC) was first introduced by Bernier and Bhaskar et al. in 1958 and the first report of bilateral multicystic lesions in HIV-infected patients was in 1987 by Morris et al. (24, 25) Like many other HIV/AIDS-related disorders, the incidence of HIV-related salivary gland disease has progressively declined since the introduction of highly active antiretroviral therapy (HAART). Nevertheless, LEC remains the most common cause of parotid gland enlargement in HIV-positive patients and is estimated to occur in up to 10% of this patient group, which is more than ten times the incidence of sporadic LECs in the general population (<1%). (23, 26, 27) Therefore, the discovery of parotid gland LECs in any patient should trigger an investigation into their HIV status. Any age group may be affected, and HIV-related LECs have been reported in patients as young as 2 months of age.(26, 28)

Over the years, there has been much controversy regarding the pathogenesis and appropriate terminology for these lesions. Some terms previously used include benign lymphoepithelial cyst (BLEC), benign lymphoepithelial lesion (BLEL), AIDS-related lymphadenopathy and cystic lymphoid hyperplasia.(27) Historically, most authors have
suggested that the cystic lesions arise in hyperplastic intraparotid lymph nodes affected by persistent generalized lymphadenopathy as part of the spectrum of the HIV-associated syndrome, while others have suggested that the changes represent an autoimmune process akin to that seen in Sjögren’s syndrome. (26, 29, 30) In 1996, however, Ihrler et al used immunohistochemistry and 3-D reconstruction of histologic sections to show that LECs represent an advanced stage of generalized lymphocytic infiltration and lymphoepithelial lesions of the salivary parenchyma. They showed that the cystic lesions represent dilated striated ducts which develop due to compression by markedly hyperplastic lymphoid tissue. (26, 31) It is unclear why such prominent lymphocytic infiltration of the parotid glands occurs in only a subset of HIV-positive patients, and although an infectious trigger has been postulated, definitive evidence is lacking. HIV p24-antigen can be found in follicular dendritic cells and multinucleated giant-cells but not in lymphocytes in lymphoepithelial cystic lesions; however, the significance of this is unclear. (32) Other viruses like EBV and CMV do not seem to play a pathogenic role. (32) Given the morphologic similarities with the salivary gland changes seen in Sjögren’s syndrome, a chemokine-mediated autoimmune reaction has also been proposed by some. Itesco et al. even demonstrated an increased prevalence of HLA-DR5 in a series of patients with HIV-related LECs. (30, 33) However, to date, a clear etiology remains unknown.

Patients with HIV-related LECs typically present with slow growing, painless, bilateral parotid gland swelling. (26) Unilateral involvement can also be seen, but this is more common in sporadic LECs not related to HIV infection. Submandibular gland involvement has also been rarely reported. (34) In most cases, the disorder is brought to the attention of the patient or physician because of the cosmetic effect of an enlarging mass in the neck. However, more serious complications like xerostomia or facial nerve compression may rarely occur. (35) By ultrasound, computerized tomography or magnetic resonance imaging, multiple thin cysts are usually identified. (27) Enlarged regional lymph nodes may accompany parotid gland enlargement, but these do not usually show cystic formations. (36)
Histologically, HIV-related LEC is characterized by atrophic glands, follicular lymphoid hyperplasia and cystic ductal dilatation with squamous metaplasia. Histiocytes and plasma cells are usually present in the cyst walls and multinucleated giant-cells may also be seen. However, the full spectrum of histopathological changes in LEC is rarely seen because salivary glands with these lesions are rarely completely excised. In the elaborate study by Ihrler et al., the authors used computer-assisted reconstruction of autopsy and surgical specimens to show that the lesions are composed of complex three-dimensional cystic structures with numerous peripheral branches that communicate with preserved intercalated ducts and salivary acini. They showed that well developed LECs in fact represent an advanced stage of a generalized lymphoid infiltration with lymphoepithelial lesions of the salivary gland parenchyma. Earlier stages without cystic development were demonstrated in autopsy specimens, and showed similar features with Sjögren disease such as lymphoepithelial duct lesions and follicular hyperplasia with atrophic salivary gland parenchyma. Please refer to below “chronic sialadenitis and early extranodal marginal zone lymphoma (ENMZBCL)” to see the distinction of lymphoepithelial lesions and ENMZBCL. Immunohistochemical stains highlight preservation of intact B- and T-cell areas and polytypic plasma cells by Ig kappa and lambda light chain expression. HIV p24 antigen may be detected in multinucleated giant-cells. LECs frequently undergo fine needle aspiration for cytologic evaluation. This typically shows desquamated squamous cells associated with a polymorphous population of lymphocytes, histiocytes and plasma cells in an amorphous, proteinaceous background.

Benign LECs may also occur in the setting of several non-HIV related disorders such as chronic sialadenitis (Sjögren disease), sarcoidosis, and Hashimoto disease. The histologic appearance of these lesions may be virtually indistinguishable from that of HIV-associated LEC. However, some features such as the presence of squamous metaplasia and bilateral lesions, although not entirely specific, are more characteristic of HIV-related LECs. In addition, some authors suggest that a markedly decreased interfollicular CD4:CD8 T-cell ratio may help to distinguish HIV-associated LEC from HIV-negative cases. Warthin’s tumor (or papillary cystadenoma lymphomatosum) is
the most common bilateral neoplasm of the parotid glands. Histologically, Warthin’s tumor is characterized by a double layer of oncocytic epithelium growing in a cystic or papillary pattern and a dense stromal lymphoid infiltrate. Malignant squamous cell cystic lesions, unlike benign LECs, show cytologic atypia of the squamous epithelial cells. It is important to note that p16 appears to be intrinsically expressed by the squamous cells of LECs and therefore immunohistochemical expression for this protein seems to play a limited role in differentiating LECs from malignant cystic squamous cell lesions.(40)

Surgical resection, frequently by enucleation of the cystic lesions of HIV-related LECs usually results in resolution. Aspiration of the cystic contents may also result in partial relief. There have been reports of complete regression with antiretroviral treatment only, and there is no increases risk for malignancy. (41)

Lymphoepithelial Sialadenitis and Extranodal Marginal Zone B-cell Lymphoma (ENMZBCL)

Lymphoepithelial Sialadenitis is an autoimmune lesion and a component of Sjogren syndrome, featured by a benign lymphoid infiltrate of salivary glands with lymphocytic epitheliotropism. Sjögren syndrome affects women 3:1 over men, in the fourth to seventh decades of life and affects parotid glands in about 90% of cases(42). Bilateral disease is typical, but one gland may be more severely affected than the other. Patients with Sjögren syndrome have a markedly increased risk of developing secondary lymphoma, which may be 44 times greater than in the general population(43). Lymphoepithelial sialadenitis is characterized by lymphocytic infiltrate, parenchymal atrophy, and foci of epithelial proliferation. The lobular architecture of the salivary gland is usually preserved. In the early stages, the extent of lymphocytic infiltrate varies among lobules of gland, but in late stage disease, nearly all of the lobules are infiltrated. The number of reactive follicles varies from few to numerous. Within the lymphoepithelial lesions, lumens are sometimes evident, but most are irregularly shaped islands of polygonal and spindled cells. The hyperplastic epithelium is predominantly ductal basal cells that lack immunohistochemical markers specific to myoepithelium. The lymphocytic infiltrate
belongs to acquired mucosa-associated lymphoid tissue (MALT) in salivary gland, with predominance of T-cells, but the lymphocytes in and around the lymphoepithelial lesions are mainly of B cells with monocytoid features or centrocyte-like cells.

Extranodal marginal zone B-cell lymphoma (ENMZBCL) of the parotid gland usually arises in the context of lymphoepithelial sialadenitis of Sjögren syndrome. The distinction between benign lymphoepithelial sialadenitis and early ENMZBCL can be challenging and in some cases not possible, implying a histologic, immunophenotypic and genotypic continuum that develops from a polytypic lymphoid proliferation to ENMZBCL. In lymphoepithelial sialadenitis, monocytoid and centrocyte-like B-cells are present within lymphoepithelial lesions, which are frequently accompanied by immunoblasts, plasmacytoid lymphocytes and plasma cells, which are similar to ENMZBCL. Reactive follicles can be seen in both conditions. In up to 50% cases of benign lymphoepithelial sialadenitis, some foci of intraepithelial B-cell infiltration are clonal, as demonstrated by PCR immunoglobulin heavy chain gene rearrangement; and in some cases, focal plasmacytoid lymphocytes or plasma cells within the lymphoepithelial lesions show kappa or lambda light chain excess by in situ hybridization or immunohistochemistry (IHC). Therefore, demonstration of clonality in the absence of an expansion of these B-cell clones, it is controversial whether they represent the very early manifestation of lymphoma, and a diagnosis of ENMZBCL is discouraged.

In early ENMZBCL, there is an expansion of monocytoid cells to form broad halos and bands around the lymphoepithelial islands, and clonality is demonstrated either by PCR gene rearrangement study or flow cytometry light chain restriction. If clonality is absent, a diagnosis of early ENMZBCL is also discouraged, and patients will be recommended for a close follow-up. As early ENMZBCL progress, monocytoid B cells form coalescing wide strands, expand the interglandular spaces, replace acini and ducts, alter the normal lobular salivary gland architecture, surround nerves, and infiltrate into fat and interlobular and periglandular connective tissues. The monocytoid B cells are positive for pan-B cell marker CD20, CD79a and Pax5; negative for CD5, CD10, cyclin D1; and positive for CD43 in a significant percent of cases (60-70%), and demonstrate clonal plasma cells in 50% cases. Overall, salivary ENMZBCL lymphoma is rather
indolent and usually remains localized. However, as disease progress, regional lymph node involvement or other extranodal site involvement may occur. t(14;18)(q32;q21) involving IGH and MALT1 may be demonstrated in ENMZBCL by fluorescence in-situ hybridization.(48) Gene translocations t(11;18)(q21;q21) and t(1;14)(p22;q32) are frequent in gastric and pulmonary marginal zone lymphomas but rare in ENMZBCL of salivary glands.

Epstein-Barr Virus Lymphadenitis and Lymphoproliferative Disorders

Epstein-Barr Virus (EBV) is a ubiquitous gamma herpes virus with a double stranded DNA genome and is exclusively found in humans. Over 95% of adults worldwide are infected with EBV. The virus is primarily transmitted in saliva by direct human contact, hence the colloquial term “kissing disease” for Infectious Mononucleosis (IM).(49) After a 2 to 7-week incubation period, a lytic phase of infection leads to high levels of viral shedding in saliva which can persist for up to 18 months. Although EBV can infect epithelial cells, it is unclear whether infected oropharyngeal epithelial cells play a role in this phase of infection, since several authors were unable to detect EBV infection in tonsillar epithelium in patients with IM.(50, 51) Within the immune system, B-cells are preferentially infected and results in a striking secondary increase of CD8+ suppressor T-lymphocytes. In developing countries, primary infection of EBV almost always occurs in early childhood and is either asymptomatic or manifests itself as a mild nonspecific upper respiratory tract viral infectious syndrome. In more developed countries, the majority of primary infections occur during adolescence or early adulthood and about 30% to 50% of patients develop IM syndrome.(51) IM is a self-limited lymphoproliferative disorder characterized by pharyngitis and lymphadenopathy associated with fever, fatigue and malaise.(52) Non-tender enlargement of anterior and posterior cervical lymph nodes is most frequently observed. But diffuse lymphadenopathy may also be seen. Splenomegaly and hepatomegaly may be seen in about 50% of patients.(53, 54) A fatal or nearly-fatal clinical course of IM with fulminate multiorgan failure is usually associated with
immunodeficient states such as AIDS, congenital immunodeficiency syndromes, most notably X-linked lymphoproliferative disorder and treatment with immunosuppressive drugs, (55) and only rarely occurs in previously healthy patients.

Chronic active Epstein-Barr virus (CAEBV) disease has been defined as a systemic EBV-positive lymphoproliferative disease (LPD) characterized by fever, lymphadenopathy, and splenomegaly developing after primary virus infection in patients without known immunodeficiency (56). Antibody titers show evidence of primary EBV infection with anti-EBV viral capsid antigen IgG $\geq 5120$, anti-EBV early-antigen IgG $\geq 640$, or anti-EBNA $< 2$; and high levels of EBV DNA in the blood, histological evidence of organ disease, and elevated levels of EBV RNA or viral proteins in affected tissues. In CAEBV, EBV can affect B-, T-, and NK-cells. The term CAEBV should be applied to systemic LPDs that are not frank lymphomas and that arise during primary infection and persist for over 6 months(57). CAEBV of B-cell origin has also been referred to as chronic (or persistent) IM. Ohshima K et al(58) described the spectrum of CAEBV of T- or NK-cell origin as polymorphic LPD without clonal proliferation of EBV-infected cells; polymorphic LPD with clonal proliferation of EBV-infected cells; monomorphic LPD (either peripheral T-cell lymphoma or NK cell lymphoma/leukemia) with clonal proliferation of EBV-infected cells. The term ‘systemic EBV-positive T-cell LPD’, as adopted by the WHO classification, is the preferred pathologic designation over CAEBV for those cases that are clearly clonal (polymorphic LPD with clonal proliferation of EBV-infected cells and monomorphic LPD), as they are generally associated with an aggressive clinical course and require aggressive treatment.

In recent years, it has been appreciated that defective immune surveillance for EBV may develop late in life and be associated with the development of EBV-positive B-cell LPD in individuals who otherwise have no apparent immune deficiency. These are often due to EBV reactivation as demonstrated by increased anti-EBV viral capsid antigen IgG, anti-EBV early-antigen IgG, and positive anti-EBNA. The spectrum of EBV-associated B-cell LPD as described by Jaffe ES et al include(57): (i) lymph node-based reactive hyperplasia with increased EBV-positive B cells, (ii) EBV-positive nodal B-cell
lymphoproliferations resembling post-transplant LPD (PTLD), (iii) EBV-positive extranodal B-cell lymphoproliferations resembling PTLD, (iv) EBV-positive diffuse DLBCLs, and (v) EBV-positive B-cell proliferations resembling CHL. The reactive hyperplasia process-category (i) is often self-limited in most patients, with only rare patients showing progression to a more aggressive lymphoproliferative process.

Although there are no evidence-based or consensus guidelines for the clinical work-up of possible EBV infection, a combination of clinical, serologic data and possible tissue biopsy is necessary.(54) Laboratory evaluation of EBV infection includes EBV-specific serologic analysis for anti-viral capsid antigen (VCA)-IgG and IgM, anti-early antigen IgG and anti-EBNA, EBV DNA and RNA. Pathologic evaluation of a tissue biopsy specimen in order to rule out another etiology or a malignant process may be performed when there are atypical clinical features such as absence of atypical lymphocytosis or high titers of EBV antibodies, an enlarging neck mass and age >30 years.(59)

Histologically, EBV lymphadenitis (IM) is characterized by a prominent interfollicular/paracortical expansion associated with variable degrees of follicular hyperplasia and distended sinuses. The paracortex has a mottled or “moth-eaten” appearance with increased high endothelial venules and a mixed population of small, medium and large lymphocytes, histiocytes, and variable numbers of plasma cells and eosinophils. Increased large immunoblasts are a characteristic feature and may be polylobated or show prominent nucleoli reminiscent of HRS cells. Immunoblasts may sometimes form confluent sheets, closely mimicking large B-cell lymphoma. Single cell or confluent necrosis may also be seen. Follicles may be hyperplastic or relatively atretic and usually contain prominent germinal centers with numerous mitoses and tingible body macrophages. Marginal zone monocytoid B-cell hyperplasia is also occasionally observed. Sinuses are frequently distended with histiocytes and/or lymphocytes and plasma cells or with acellular eosinophilic proteinaceous fluid. It is not uncommon for the lymphoid proliferation to extend beyond the lymph node capsule into extranodal fat. However, the overall lymph node architecture, with preservation of B- and T-cell areas as highlighted with immunohistochemical stains, is generally preserved.
Immunohistochemical stains also show that immunoblasts represent a mixture of B- and T-cells and also express CD45 and CD30. Analysis for EBV small-encoded RNA (EBER) by in situ hybridization shows a variable number of positive cells and is usually more sensitive than immunohistochemical staining for EBV LMP1. Molecular studies show polyclonal B and T-cells by immunoglobulin and T-cell receptor gene rearrangements respectively. Furthermore, Southern blot analysis usually shows a polyclonal pattern of EBV. Of note, however, fatal IM (sporadic or associated with immunodeficiency) may show monoclonal EBV in association with monoclonal B- or T-cell proliferations. In one series, histologic evaluation of autopsy specimens from these patients demonstrated marked infiltration of polymorphous lymphocytes and histiocytes in lymph nodes, spleen, liver and bone marrow, occasionally associated with prominent hematophagocytosis and necrosis.

IM-like syndromes can be caused by several other infectious agents including cytomegalovirus (CMV), HIV, adenoviruses, hepatitis A virus, adenoviruses, diphtheria and Toxoplasma gondii. Serologic testing is an important tool to help distinguish these etiologies. CMV mononucleosis is probably the most common mimicker of EBV infection and can show a clinical and hematologic picture indistinguishable from EBV-related IM. CMV lymphadenitis typically shows paracortical expansion with immunoblastic and perivascular monocytoid B-cell proliferation. However, scattered large atypical cells with pleomorphic nuclei and characteristic “owl’s eye” intranuclear viral inclusions are unique to CMV infection. In addition, immunohistochemical or in situ hybridization analysis for CMV can be helpful. Toxoplasma infection most commonly presents in the general population as localized posterior cervical lymphadenopathy associated with mild constitutional symptoms. Toxoplasma lymphadenitis is characterized by a triad of reactive follicular hyperplasia, intrasinusoidal monocytoid B-cell hyperplasia and singly scattered and clusters of inter and intra-follicular epithelioid histiocytes. Paracortical expansion with immunoblastic proliferation is not a prominent feature. The atypical immunoblastic proliferation of EBV lymphadenitis may mimic diffuse large B cell lymphoma (DLBCL), or HRS cells of classical Hodgkin lymphoma. Prominent intrasinusoidal immunoblastic proliferation may mimic anaplastic large cell
lymphoma (ALCL). In cases of EBV reactivation in elderly, CAEBV infection, and EBV infection in congenital immunodeficiency, it requires hematopathology expertise in interpretation, in conjunction with immunophenotyping and molecular studies for B-, T-cell or EBV clonality, as well as correlation with clinical manifestation in order to reach an accurate diagnosis.

Summary

In head and neck region, biopsy specimens containing lymphoid tissue are commonly encountered in our daily practice. The lymphoid tissues may represent normal lymphoid tissue in the oral pharyngeal regions, reactive lymphoid hyperplasia or a malignant lymphoma. As a surgical pathology, it is important to recognize if the lymphoid proliferation is benign, as a portion of other ongoing processes, such as Warthin’s tumor and nasopharyngeal carcinoma; or reactive lymphoid hyperplasia secondary to viral infection, autoimmune disease, drug/toxin or idiopathic that may explain the clinical manifestation of a mass-like lesson or enlargement of organs; or a lymphoproliferative disorder, which requires hematopathologic consultation, further comprehensive immunophenotyping and molecular studies.

References


