tions fall to a low level. The accelerated development of dental caries is also noted. Enlargement of the lacrimal glands is uncommon. Even when the salivary glands are not enlarged, they always exhibit lymphohistiocyte-mediated acinar destruction (Marx 1995). When enlarged, however, they show features of the benign lymphoepithelial lesion (BLL) in almost all cases. These lesions may occur in patients who do not have Sjogren's syndrome. Furthermore, they may undergo malignant transformation to lymphomas in patients with or without Sjogren's syndrome (Figure 6.2). This concept, as well as the entity Mikulicz's disease, is clearly worthy of additional discussion.

MIKULICZ'S DISEASE AND THE BENIGN LYMPHOEPITHELIAL LESION

The pathologic entity known as the benign lymphoepithelial lesion was once referred to as Mikulicz's disease. The German surgeon Johann Mikulicz first described the benign lymphoepithelial lesion in 1888 in a report of a single case of lacrimal gland involvement (Daniels 1991). The lacrimal gland enlargement was followed by enlargement of the submandibular and parotid glands, as well as minor salivary gland tissue. The term "Mikulicz's disease" was subsequently applied to a variety of cases of bilateral salivary or lacrimal gland enlargement, including those caused by sarcoidosis, lymphoma, tuberculosis, or syphilis. The term "lymphoepithelial lesion" was proposed by Godwin in 1952 to describe parotid gland lesions previously called Mikulicz's disease, adenolymphoma, chronic inflammation, lymphoepithelioma, or lymphocytic tumor (Godwin 1952). One year later, Morgan and Castleman observed numerous similarities of the benign lymphoepithelial lesion to the histopathology of Sjogren's syndrome and proposed that Mikulicz's disease is not a distinct clinical and pathologic entity but rather one manifestation of the symptom complex of the syndrome (Morgan and Castleman 1953). The benign lymphoepithelial lesion may become large enough to present as a mass resembling a parotid tumor (Figure 6.3).

Acinar degeneration and hyperplasia and metaplasia of the ducts led to the formation of the pathognomonic epimyoepithelial islands, which define the condition. Whether myoepithelial cells or ductal basal cells are responsible for these islands has been questioned. An immunohistochemical investigation has shown that myoepithelial cells do not play a role in the formation of these islands and they should be designated lymphoepithelial metaplasia (Ihrler, Zietz, and Sendelhofert et al. 1999). The condition is often a manifestation of Sjogren's syndrome or other immunological abnormality but may occur outside the Sjogren's disease process. Usually the lesion starts unilaterally but becomes bilateral in the parotids (Figure 6.4). It is less common in the submandibular and minor salivary glands (Figure 6.5).

The lesion may reach a large size, although it is usually asymptomatic. It may be diagnosed by fine needle aspiration if the etiology is uncertain and may require removal by parotidectomy for aesthetic reasons. Sudden growth or pain may be an ominous feature, as a benign lymphoepithelial lesion can undergo malignant change and is perhaps not as benign as its name suggests. The lymphocytic component can undergo change to MALT lymphoma (see chapter 11), particularly in Sjogren's syndrome (Abbondanzo 2001) but also in HIV infections (Del Bono, Pretolesi, and Pontali et al. 2000). Recurrent benign lymphoepithelial lesion may also undergo malignant change of its epithelial component to become an undifferentiated carcinoma with lymphoid stroma (see chapter 8) (Cai, Wang, and Lu 2002).