Chapter 6

Systemic Diseases Affecting the Salivary Glands

Outline

Introduction

A number of systemic diseases result in infiltration of the salivary glands. These include immune-modulated or idiopathic diseases such as sarcoidosis, Sjogren's disease, sialosis, and lymphoepithelial lesions, as well as lymphoma, a malignant proliferation of B or T lymphocytes. Each of these processes involves multiple physiologic systems and may be diagnosed at an early stage with salivary gland biopsy. It is the purpose of this chapter to describe the clinical features of salivary gland involvement of systemic diseases.

Sjogren's Syndrome

Sjogren's syndrome is an inflammatory autoimmune disease that manifests as a chronic, slowly progressive disease characterized by keratoconjunctivitis sicca and xerostomia. Since 1965, it has been defined as a triad of dry eyes, dry mouth, and rheumatoid arthritis or other connective tissue diseases (Daniels 1991). This process may evolve from an exocrine organ–specific disorder to an extraglandular multisystem disease affecting the lungs, kidneys, blood vessels, and muscles (Table 6.1). These features are believed to be the result of immune system activation with the production of various autoantibodies with lymphocyte invasion of the salivary and lacrimal glands and other affected organs. The autoantibodies include those produced to the ribonucleoprotein particles SS-A/Ro and SS-B/La, and these are thought to interfere with muscarinic receptors (Garcia-Carrasco, Fuentes-Alexandro, and Escarcega et al. 2006). One study identified IgG from patients with primary Sjogren's syndrome containing autoantibodies capable of damaging saliva production and contributing to xerostomia (Dawson, Stanbury, and Venn et al. 2006). Other mechanisms of glandular dysfunction include destruction of glandular elements by cell-mediated mechanisms; secretion of cytokines that activate pathways bearing the signature of type 1 and 2 interferons; and secretion of metalloproteinases (MMP) that interfere with the interaction of the glandular cell with its extracellular matrix (Garcia-Carrasco, Fuentes-Alexandro, and Escarcega et al. 2006). In addition, increased MMP-3 and MMP-9 expression has been found to be responsible for acinar destruction in Sjogren's syndrome (Perez, Kwon, and Alliende et al. 2005). These substantial increases in MMP expression in diseased labial salivary glands may be potentiated by moderate decreases in tissue inhibitors of matrix metalloproteinases (TIMP).

Primary Sjogren's syndrome is designated when it is not associated with other connective tissue diseases. This notwithstanding, evidence exists that shows genetic aggregation of autoim-