2. Sjögren’s Syndrome with Systemic Lupus Erythematosus/Mixed Connective Tissue Disease

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Introduction

The co-existence of Sjögren’s syndrome (SS) with systemic lupus erythematosus (SLE) has been alluded to since 1959 (Heaton 1959). Since that report, numerous studies on comparing and contrasting these two diseases have been reported (Bencze 1970; Heaton 1959; Kassan 1977; Moutsopoulos 1980a; Moutsopoulos 1980b; Steinberg 1971). Many of the clinical, serological and immunogenetic features of SS and SLE often make precise diagnosis difficult and suggest similar (Moutsopoulos 1980a, 1980b), possible common pathophysiologic features.

In 1959, Heaton reviewed the pathologic and clinical features of SS and SLE and came to the conclusion that SS was a benign form of SLE. This was on the basis of many overlapping systemic symptoms and the presence, grossly, of similar pathologic findings in the two diseases (“oedema, early destruction of the elastic tissue, hyalinization, infiltration with lymphocytes and plasma cells, fibroblastic proliferation, and thickening of blood-vessel walls with hyaline tissue”) (Heaton 1959). Since that time, more precise data based on better clinical definitions, serologic and immunologic methods have allowed for critical descriptions of similarities and differences between primary SS, secondary SS with SLE/mixed connective tissue disease (MCTD) and SLE alone.

Incidence

Primary SS evaluated retrospectively (Pavlidis 1982) had an average age at onset of 44 years (±15 years) as contrasted to 29.3 years (range 2–76 years) (Dubois 1964) for SLE alone. The incidence for the development of SLE following an initial diagnosis of primary SS is between 1% and 9% (Alarcon-Segovia 1974; Moutsopoulos 1980a; Sharp 1975; Shearn 1952). In contrast, features of SS in SLE (secondary SS) are found more frequently with an incidence varying from 6% (Grennan 1977b; Steinberg 1971) to 90% (Alarcon-Segovia 1974b). This enormous variation is explained by the lack of standardized criteria for the diagnosis of SS. In our experience using recommended criteria outlined in chapter II.E.1, the true incidence probably is around 25%.

The presence of SS in MCTD has been found to vary from 7% (in one multicenter study) (Sharp 1975) to approximately 50% in one clinic (Alarcon-Segovia 1974a) of 25 patients with MCTD. The latter study found symptomatic xerostomia and/or ocular symptoms of keratoconjunctivitis sicca in 12 of 25 patients where confirmation of these findings was accomplished by objective methods.
Clinical Studies

Patients with primary SS and those with SLE may have similar disease manifestations including features of arthritis (usually nonerosive and nondeforming), rash, vasculitis, central nervous system involvement and glomerulonephritis (Moutsopoulos 1980a). A report by Heaton in 1959 postulated on purely clinical grounds that SS may be a milder form of SLE. Clinical experience over the last 25 years suggests that SS and SLE are different diseases although precise diagnosis on clinical grounds alone can be difficult in certain rare patients. Features of lymphadenopathy, hepatosplenomegaly, interstitial renal disease, pulmonary involvement, cutaneous and peripheral nerve vasculitis appear with greater frequency and severity in primary SS than in SLE (Alexander 1983a, 1983b; Bloch 1965; Moutsopoulos 1980a).

The clinical manifestations of SS in SLE patients are often mildly symptomatic or subclinical (Alarcon-Segovia 1974b). Lip biopsy is positive for SS in 50% (Moutsopoulos 1980b) to 94% (Alarcon-Segovia 1974b) of SLE patients in two studies reported. In these same groups, parotid scans were abnormal in 58% (Moutsopoulos 1980b) and 90% (Alarcon-Segovia 1974b) yet clinical symptoms were present in only 30% (Moutsopoulos 1980b) and 42% (Alarcon-Segovia 1974b) respectively.

Grennan et al. (1977a) reported a higher incidence of SS in a group described as overlapping SLE and rheumatoid arthritis (RA) with erosive polyarthritis where an 83% incidence (five of six patients) of SS was found. This was compared with a 13% and a 24% incidence of SS in subsets of patients with SLE/scleroderma and typical SLE respectively. No differences in the incidence of clinical renal disease was noted among the “typical” SLE patients with SS (50%) and those without SS (45%).

Clinical reports of MCTD with SS (Alarcon-Segovia 1974a; Sharp 1975) are limited. Symptomatic SS was found in 50% of 25 patients in one study (Alarcon-Segovia 1974a) where it was postulated that subclinical SS in this disease may be more prevalent as noted in SLE (Alarcon-Segovia 1974b) and scleroderma (Alarcon-Segovia 1976). Overall, the clinical features of MCTD patients with secondary SS did not differ from those with MCTD alone. Symptomatic SS was found to be the presenting symptom in two of twelve patients who later developed other clinical features of MCTD. This is not often seen in other forms of secondar SS (Moutsopoulos 1980a; Moutsopoulos 1979b).

Three cases of childhood MCTD (Fraga 1978) were noted to be associated with secondary SS. Parotid enlargement was also reported in one other case of childhood MCTD (Sanders 1973) and has been seen in one other case by one of the authors (Kassan SS, unpublished data). This is quite significant owing to the fact that both childhood MCTD and childhood SS are both relatively infrequent disorders (Fauci 1980).

Serologic Studies

Patients with primary SS, secondary SS with SLE, and secondary SS with RA all manifest features of B-cell hyper-reactivity as evidenced by the findings of polyclonal hypergammaglobulinemia, non-organ specific autoantibodies, (i.e. rheuma-