Antibodies to nuclear antigens in three patients with scleroderma and asthma

We read with interest the report of Martin et al regarding autoantibodies to centromere and histone in patients with scleroderma and severe pulmonary and vascular disease. During the past two years we have been following in our practice female patients with scleroderma (two with localised scleroderma and one with diffuse scleroderma) and asthma, aged 40, 48, and 77, respectively; the onset of scleroderma had been preceded by asthma in each case. The first two patients had been atopic. Accompanying diseases were acne rosacea (first patient), thyroid adenoma (second), and diabetes mellitus type II (third patient). The diabetes in the last patient had begun 30 years ago after a pregnancy. A typical of asthma and radiographic evidence of pulmonary emphysema were found in all patients; none had symptoms suggestive of Sjögren’s syndrome. The serum IgE values were increased in the first two patients. All patients had positive antinuclear antibodies (ANA) by the linked immunosorbent assay (ELISA), and the second and third patients positive antibodies to histone 2A (ELISA). None of the three had Ro(SS-A) or La(SS-B) antibodies. The second patient was a smoker.

The cases can be included in the group of any overlap syndromes. The question is whether asthma is a manifestation of fibrosis, or the two diseases are independent entities. The scleroderma involves only the skin in two of the patients. Spirometry showed an obstructive defect of ventilation in all three patients. The increase in IgE in the sera of two patients suggests involvement of reaginic type reactions. The ANA positivity suggests type II and III immune reactions. We could find no published reports of a combination of scleroderma, asthma, and positive ANAs. The presence of two diseases—scleroderma and asthma—raises the following issues:

1. The role of scleroderma as a cause for the development of asthma in these patients. The pulmonary involvement in scleroderma is very common. It is of a restrictive type, while in asthma, obstruction of the airways is a characteristic feature. Our data support the notion of an independent development of asthma.

2. The role of the endocrine system in the development of scleroderma. It is well known that rheumatic diseases are more frequent in females. Asthma also suffer from rosacea more often and the appearance of the disease may be linked to the climacteric. It is notable that two of our patients had accompanying endocrine diseases, thyroid adenoma and diabetes. The combination of asthma with scleroderma and endocrine disorders in our three patients warrants further investigation of this association.

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LETTERS TO THE EDITOR

Ehlers Danlos syndrome and osteoporosis

Ehlers Danlos syndrome (EDS) is a group of inherited connective tissue disorders with extreme genetic and clinical variability. The clinical manifestations of EDS are a result of abnormalities in collagen types 1 and 3, the main proteins of skin, ligaments, tendons, blood vessels, and internal viscera. Type I collagen is also the main protein constituent of the bone matrix and its abnormalities form the molecular basis of osteogenesis imperfecta (OI). EDS is therefore quite closely linked to OI and the two conditions are known to coexist. In spite of this there are no detailed studies available on bone mineral content and bone turnover in EDS.

In the past three years we have seen seven patients with EDS and assessed bone densities in the lumbar spine and hip using dual energy x ray absorptiometry. A 65 year old lady, referred from the orthopaedic department for investigations of a wedge fracture of the L2 vertebra. She did not have any obvious precipitating causes for osteoporosis in her past medical, menstrual, 

AUTHOR’S NOTE: Dr Nikolov and his colleagues raise interesting questions. The three patients that describe asthma diagnosed on clinical grounds and confirmed by spirometry. We also are not aware of any reports of asthma co-existing with scleroderma, but as asthma occurs in 4-6% of the population, it is not surprising that the two diseases coexist. However, as Nikolov et al imply, a key question is whether scleroderma and asthma may have a common pathogenic basis.

In addition to the observations offered in their letter, it is interesting that scleroderma and asthma do share certain pathogenic features; for example increased dermal mast cells and increased ability of mast cells to release histamine have been reported in scleroderma. Both these findings suggest that the pro-angiogenic properties of EDS collagen may include a hypersensitive reaction similar to that described in asthma. It is not clear if a similar process involving mast cells occurs in the lung in scleroderma, although circumstantial evidence suggests that it does.

Our report suggested that scleroderma patients with centromere and histone antibodies had more severe disease characterised by pulmonary and vascular involvement. It is not clear if the patients referred to by Nikolov et al had centromere antibodies, but two did have antibodies to histone H2A. Although review of our charts has not identified asthma as a clinical feature in our patients, based on the observations of Nikolov et al, in future studies it may be important to determine if there are clinical correlations between the two diseases.

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