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EDITORIALS

Multiple autoimmune syndrome

M. COJOCARU, MD, PhD[a]; Inimioara Mihaela COJOCARU, MD, PhD[b]; Isabela SILOSI, MD, PhD[c]

[a]"Titu Maiorescu" University, Faculty of Medicine, Department of Physiology, Bucharest, Romania
"Dr. Ion Stoia" Center for Rheumatic Diseases, Bucharest Romania
[b]"Carol Davila" University of Medicine and Pharmacy, Clinic of Neurology, Colentina Clinical Hospital, Bucharest, Romania
[c]"University of Medicine and Pharmacy, Discipline of Immunology, Craiova, Romania

ABSTRACT

The co-occurrence of autoimmune diseases has been epidemiologically studied and has aided in our understanding of autoimmunity. The combination of at least three autoimmune diseases in the same patient has defined as multiple autoimmune syndrome (MAS). About 25 percent of patients with autoimmune diseases have a tendency to develop additional autoimmune diseases. MAS is recognized with increasing frequency. Several associations have been proposed as a form of MAS. Multiple autoimmune syndrome can be classified into three groups according to the prevalence of their associations with one another: type 1, type 2 and type 3. Genetic, infectious, immunologic and psychological factors have all been implicated in the development of MAS. In MAS, patients often have at least one dermatological condition, usually vitiligo or alopecia areata. The pathogenesis of multiple autoimmune disorders is not known yet, perhaps environmental triggers and genetic susceptibility are involved. Abnormalities of both humoral and cell-mediated immunity have been described. However, as new perspectives develop on the pathogenesis and natural history of autoimmune diseases, a refinement in the methodology for the study of the co-occurrence of disease is warranted in order to maximize the information that one may realize from such studies. This paper presents some recent results of studies in light of current understanding of the natural history of autoimmune diseases.

Key words: multiple autoimmune syndrome, classification, pathogenesis

The paper highlights multiple autoimmune syndrome (MAS), presenting a new classification according to the association of the disorders, and focusing modern immunologic investigations in order to diagnose these conditions. The issue is addresses to immunologists, to internal medicine physicians, to rheumatologists, to dermatologists, to neurologists. It is of interest, the presence of one autoimmune disorders

Address for correspondence:
Univ. Assoc. Prof. Manole Cojocaru, MD, PhD, 67A Gheorghe Petrascu Street, District 3, Zip Code 031593, Bucharest, Romania
email address: manole_cojocaru@yahoo.com

leading to the discovery of other autoimmune conditions and improving their therapeutical measures.

MAS is the coexistence of three or more autoimmune diseases. In this unusual condition, dermatological autoimmune diseases and especially vitiligo have an important place. Disorders of autoimmune pathogenesis occur with increased frequency in patients with a history of another autoimmune disease. At least one of them is usually a skin disease, such as psoriasis or scleroderma. The coexistence of five autoimmune diseases is extremely rare. Familial or genetic, infectious, immunologic and psychological factors have been implicated in the development of MAS (1,2).

Environmental triggers in a genetically susceptible individual are believed to cause disorders of immune regulation. Cytomegalovirus, for instance, is shown to cause the development of multiple autoantibodies. Certain autoantibodies are found in disorders affecting multiple organs. Disorders of an autoimmune nature are known to occur with increased frequency in patients with another autoimmune disease. About 25 percent of patients with autoimmune diseases have a tendency to develop additional autoimmune disorders (3).

The pathogenesis of multiple autoimmune disorders is not known. Environmental triggers in a genetically susceptible individual are believed to cause disorders of immune regulation.

Multiple autoantibodies can be found in a patient and some of the specific mono- or polyclonal autoantibodies may be multiple organ reactive.

Autoimmune phenomena may be prominent in inflammatory bowel disease. Ulcerative colitis, in particular, exhibits a high incidence of associated autoimmune diseases, including hypothyroidism, primary sclerosing cholangitis, vitiligo, and alopecia areata.

Multiple autoimmne syndrome can be classified into three groups that correspond with the prevalence of their being associated with one another in patients with two autoimmune diseases, this classification is helpful when signs of a third disorder emerge.

1. type 1 MAS includes myasthenia gravis, thymoma, polymyositis and giant cell myocarditis
2. type 2 MAS includes Sjögren's syndrome, rheumatoid arthritis (RA), primary biliary cirrhosis (PBC), scleroderma, and autoimmune thyroid disease
3. type 3 MAS groups together autoimmune thyroid disease, myasthenia gravis and/or thymoma, Sjögren's syndrome, pernicious anemia, idiopathic thrombopenic purpura (ITP), Addison's disease, type 1 diabetes mellitus, vitiligo, autoimmune hemolytic anemia (AIHA), systemic lupus erythematosus (SLE), and dermatitis herpetiformis.

This classification helps to detect a new condition liable to appear in a patient who has had two previous autoimmune diseases. It provides a basis for analysis of the pathophysiological mechanisms of autoimmunity (4).

Multiple sclerosis is occasionally present in type 3 MAS. In this unusual conditions, dermatological autoimmune diseases and especially vitiligo have an important place. Type 2 of MAS can be described as an association of Reynolds syndrome and the lupus erythematosus/lichen planus-overlap syndrome. Reynolds syndrome is a rare autoimmune disease, consisting of the combination of primary biliary cirrhosis and progressive systemic sclerosis. In some patients this syndrome has also been associated with Sjögren syndrome and hemolytic anemia (5,6).

In many cases of MAS reported in the medical literature, vitiligo is the first autoimmune disease to be diagnosed. In these cases, vitiligo is usually bilateral and symmetrical (occurring in the same places on both sides of the body), and in most cases of vitiligo that occurred in MAS, autoimmune thyroid disease was also present (7).

Bullous pemphigoid is the most common autoimmune blistering skin diseases. The significance of the association of bullous pemphigoid with other autoimmune diseases is still unknown. The most frequent associations are those with PBC, psoriasis, and an unusual condition termed MAS, defined as the combination of at least three autoimmune diseases in the same patient. This association is probably not fortuitous and suggests a pathogenic relationship (8,9).

Sjögren's syndrome is a systemic autoimmune disease that frequently presents concomitantly with other systemic connective tissue or organ-specific autoimmune diseases. This association is well described for SLE and RA. The presence of Sjögren's syndrome influences the expression of the other autoimmune disease to

some degree, for instance by increasing fatigue and lymphoma risk. The underlying mechanisms for this syndrome are not yet understood, but it may be more prevalent than currently recorded (10).

The association of bullous pemphigoid, vitiligo and autoimmune thyroid disease is not reported and it show that conditions do not have to be standardized in groups because of its variability. Other conditions found in various combinations in MAS are: pemphigus and autoimmune thyroid disease in type 1 MAS; chronic active hepatitis (CAH), SLE, pemphigus, bullous pemphigoid, AIHA, ITP, alopecia areata and Addison's disease in type 2 MAS; and acquired primary hypogonadism, hypophysitis, RA, PBC, relapsing polychondritis, multiple sclerosis, CAH, ulcerative colitis, and scleroderma in type 3 MAS (11).

Patients with a clustering of autoimmune diseases may help to delineate the pathogenesis of ulcerative colitis. Researchers note that in many cases, the presence of one autoimmune disorder helps lead to the discovery of other autoimmune conditions. The literature reports overlap syndromes in various combinations; however, the coexistence of five autoimmune diseases is extremely rare (12,13).

Concurrent autoimmune diseases are common in patients with autoimmune hepatitis (AIH) and mirror the full range of known autoimmune diseases. An extended diagnostic screening for accumulating autoimmune diseases, especially autoimmune thyroiditis, seems reasonable in patients with AIH (14,15). ❑

CONCLUSION

Multiple autoimmune syndrome is a condition in which patients have at least three distinct autoimmune conditions. Multiple autoimmune disorders occur with increased frequency in patients with a previous history of another autoimmune disease.

The underlying mechanisms for this syndrome are not yet understood, but it may be more prevalent than currently recoded.

The presence of one autoimmune disease should alert one to watch for another one. The occurrence of multiple autoimmune phenomena indicates the need for continued surveillance for the development of new autoimmune disease in predisposed patients.

In many cases, the presence of one autoimmune disorder helps lead to the discovery of other autoimmune conditions.

People with one autoimmune disease, or with a family history of autoimmune diseases, should be aware of a tendency to develop additional autoimmune disorders. ❑

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