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Monoclonal Gammopathies & Multiple Myeloma

IMMUNOSUPPRESSIVE AND BIOLOGICAL DRUGS DO NOT INFLUENCE PROGRESSION OF MGUS OR SMOLDERING MULTIPLE MYELOMA IN PATIENTS WITH CONCOMITANT AUTOIMMUNE DISORDERS: PRELIMINARY DATA FROM A RETROSPECTIVE, SINGLE-CENTER STUDY

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Introduction: Monoclonal gammopathies of undetermined significance (MGUS) and smoldering multiple myeloma (SMM) have been often reported coexistent to several autoimmune conditions in previous retrospective studies. Interestingly, in a recent cross-sectional, prospective, population-based screening study (Sverrisdottir I. et al. Ann Intern Med. 2024) of Icelandic persons aged 40 years or older, a diagnosis of an autoimmune disease was not associated with MGUS, although it was significantly more present in individuals with a prior clinical diagnosis of MGUS. Specific immunosuppressive therapies and "biologic" agents, including monoclonal antibodies, are frequently required in patients with autoimmune disorders. In this setting, however, limited data are available concerning whether these drugs may favour an increase of monoclonal protein (M-protein) or even the progression of these conditions to overt multiple myeloma (MM). On the other hand, in the clinical practice, hematologists are frequently asked to answer to this question. Methods. On this basis, we retrospectively evaluated the trend of M-protein in 37 patients with monoclonal gammopathy (34 MGUS; 3 SMM) followed at our institution and, at the same time, under treatment for autoimmune disorders (inflammatory bowel disease, rheumatologic, neurologic, cardiac/pneumological diseases). The protein change was calculated as the difference between the last and first M-protein values. Only patients with measurable M-protein and non-IgM isotype were included in the analysis; their clinical characteristics are summarized in Table 1. Results. The median age was 67 years (range 34-84), with a female predominance (67.6%). Regarding concomitant autoimmune diseases, 29 patients (78.4%) were affected by rheumatologic disorders, 4 (10.8%) by inflammatory bowel diseases, 2 (5.4%) by neurologic diseases and 2 (5.4%) by cardiac/pneumological disorders. Regarding M-protein, IgG kappa was the most frequent isotype (70.3%) reported. Specific treatments for these disorders included immunosuppressive drugs and biological agents, sometimes associated (Table 1). With a median time of observation of 48 months (range: 9-236), no significant difference (p-value = 0.4682, Kruskal–Wallis) was reported in M-protein concentration during follow-up and no patient developed clinical symptoms of active MM. Likewise, no decrease in M-component was observed, independently upon the efficacy of the treatments applied for the autoimmune disorders. Conclusions. Our still preliminary data suggests no evident relationship between MGUS/SMM evolution and underlying autoimmune disorders receiving immunosuppressive treatments. These data are certainly reassuring, as they would not support a link between plasma cell dyscrasia progression and treatments necessary for contemporary autoimmune diseases. Studies on a larger number of patients with extended follow-up are ongoing to achieve greater generalizability of our preliminary findings.

Table 1. Clinical and laboratory characteristics of patients with monoclonal gammopathy and autoimmune diseases

Median age, years (range)	67 (34-84)
Gender, n. (%)	
Female	25 (67.6)
Male	12 (32.4)
M-protein isotype, n. (%)	
IgG kappa	26 (70.3)
IgG lambda	5 (13.5)
IgG kappa + IgG lambda	3 (8.1)
IgA lambda	2 (5.4)
IgA kappa	1 (2.7)
Autoimmune disease	
Rheumatologic, n. (%)	**29 (78.4)**
Arthritis	
Rheumatoid arthritis	18
Psoriasic arthritis	4
Ankylosing spondylitis	1
Connectivities	
Systemic lupus erythematosus	2
Sjogren's syndrome	2
Still's disease	1
Systemic sclerosis	1
Inflammatory bowel disease, n. (%)	**4 (10.8)**
M. di Chron	3
Inflammatory bowel disease	1
Neurologic, n. (%)	**2 (5.4)**
Multiple sclerosis	2
Cardiac/pneumological, n. (%)	**2 (5.4)**
Asthma	1
Pleuropericarditis	1
Current autoimmune disease regimen	**n. patients according to first/second/third line**
-Contains immunosuppressive drugs	
Methotrexate	10/3/0
Hydroxychloroquine	3/1/0
Leflunomide	4/1/0
Sulfasalazine	1/1/0
Mesalazine	2/0/1
Colchicine	1/1/0
Ciclosporin	2/0/0
Dimethyl fumarate	1/0/0
-Contains biological drugs	
anti-CD20 (Rituximab, Ocrelizumab)	3/3/0
anti-TNF alfa (Adalimumab, Etanercept, Certolizumab, Infliximab)	5/10/1
anti-IL6 (Tocilizumab, Sarilumab)	1/1/3
anti-IL1 (Anakinra)	2/0/0
anti-IL-13 (Ustekinumab)	0/2/0
anti-IL-17 (Ixekizumab)	0/0/1
anti-IgE (Omalizumab)	1/0/0
anti-BlyS (Belimumab)	1/0/0
Median duration of follow-up, months (range)	48 (9-236)
Median variations in the M-protein level, between the beginning and the end of the follow-up (p-value according to Kruskal–Wallis test)	0.03 g/dL (0.4682)