EDITORIAL

The role of smoking in antineutrophil cytoplasmic antibody–associated vasculitis: time to highlight the importance of smoking cessation interventions

Micaela Gentile[1], Giovanni M. Rossi[1,2]

1 Renal Unit, Parma University Hospital, Parma, Italy
2 "Guido Erluison" Laboratory of Immunopathology, Parma University Hospital, Parma, Italy

RELATED ARTICLE

by Patel et al

As an entity grouping systemic autoimmune diseases, antineutrophil cytoplasmic antibody (ANCA)–associated vasculitis (AAV) is characterized by necrotizing inflammation of small to medium-size blood vessels without immune complex deposition and the presence of circulating ANCAs. Virtually any organ can be affected. There is a high prevalence of kidney involvement, which if not recognized in a timely manner can result in end-stage kidney disease.

The work of Patel et al,[1] published in this issue of *Polish Archives of Internal Medicine*, examines the role of smoking in the disease activity and mortality, based on a retrospective cohort analysis of 223 patients with AAV, that is, microscopic polyangiitis and granulomatosis with polyangiitis. In their study, the authors demonstrate that ever smoking is associated with increased disease activity as well as increased need for renal replacement therapy and immunosuppressive treatment, resulting in a reduced chance of survival.

AAV pathogenesis and evolution have already been investigated with controversial results regarding the role of smoking and other occupational exposures. According to a German study published in 2005, the proportion of active smokers among the patients with AAV was significantly lower than in the general population, indicating that smoke may play a protective role.[2] Maritati et al[3] confirmed this finding in an Italian cohort of 111 patients newly diagnosed with eosinophilic granulomatosis with polyangiitis (EGPA). However, the association with smoking was almost dichotomous based on the ANCA status: the association with smoking was stronger in ANCA-negative EGPA, that is, the patients with a more respiratory tract–limited phenotype than in the ANCA-positive patients with EGPA, that is, those with a more vasculitic phenotype. Of note, EGPA patients were excluded (and rightfully so) by Patel and colleagues. These discrepancies could be explained by regional differences in the studied populations, due to varied ethnicity and exposure to other risk factors. On the other hand, it is acknowledged that smoking is an independent risk factor for autoimmune diseases, such as systemic lupus erythematosus and rheumatoid arthritis,[4] with higher concentrations of circulating autoantibodies in smokers, despite the presence of other clinical conditions or additional risk factors.

It is unclear why ANCAs develop. The 2 main antigens (myeloperoxidase and proteinase 3) are found in the cytoplasm of neutrophils. By increasing the release of proinflammatory cytokines and reactive oxygen species, smoking may facilitate the release of these antigens on the surface of cells as well as bound ANCAs, and activate neutrophils, which results in NETosis, a form of cell death, where granules containing chromatin and ANCA antigens are extruded (neutrophil extracellular traps [NETs]).[5] As a result of NETs, endothelial damage occurs and antigens are presented to dendritic cells, resulting in the activation of both classic and alternative complement pathways.[6]

Smoking directly affects complement activation. Kew et al[7] reported that tobacco smoke extracts modify C3 in vitro, activating the alternative complement pathway.

Under physiological conditions, complement activation may assist in the clearance of apoptotic cells and cellular debris to prevent local necrosis and associated damage to the vascular system. In pathological settings, complement activation

Correspondence to:
Giovanni Maria Rossi, MD, Nefrologia, Azienda Ospedaliero-Universitaria di Parma, Via Gramsci 14, 43126 Parma, Italy, phone: +390521702126, email: giovannimariarossi463@gmail.com
Received: October 12, 2023.
Accepted: October 13, 2023.
Published online: October 26, 2023.
Pol Arch Intern Med. 2023; 133 (10): 16592
doi:10.20452/pamw.16592

may enhance inflammation and influence adaptive immune response.[8]

It is reasonable to hypothesize that smoking may have a greater effect on the activation of complement pathways in genetically predisposed individuals, while other patients may be protected from the effects of smoking as a result of wide diversity of the genetic environment, namely mutations and genetic variants of complement regulatory proteins.

The study by Patel et al[1] adds valuable information on the role of smoking in terms of the disease activity and mortality. In addition, the data suggest that smokers are more likely to require renal replacement therapy, which is a proxy for more severe renal involvement, suggesting that smoking cessation interventions are important in AAV, and should be considered a part of routine clinical management for patients with vasculitis.

ARTICLE INFORMATION

DISCLAIMER The opinions expressed by the author(s) are not necessarily those of the journal editors, Polish Society of Internal Medicine, or publisher.

CONFLICT OF INTEREST None declared.

HOW TO CITE Gentile M, Rossi GM. The role of smoking in antineutrophil cytoplasmic antibody–associated vasculitis: time to highlight the importance of smoking cessation interventions. Pol Arch Intern Med. 2023; 133: 16592. doi: 10.20452/pamw.16592

REFERENCES

1 Patel A, Masiak A, Joshi S, et al. Influence of smoking on disease activity and prognosis of antineutrophil cytoplasmic antibody–associated vasculitis: a retrospective cohort study. Pol Arch Intern Med. 2023; 133: 16478.

2 Haubitz M, Woywodt A, de Groot K, et al. Smoking habits in patients diagnosed with ANCA-associated small vessel vasculitis. Ann Rheum Dis. 2005; 64: 1500-1502.

3 Maritati F, Peyronel F, Fenaroli P, et al. Occupational exposures and smoking in eosinophilic granulomatosis with polyangiitis: a case-control study. Arthritis Rheumatol. 2021; 73: 1694-1702.

4 Hoovestol RA, Mikuls TR. Environmental exposures and rheumatoid arthritis risk. Curr Rheumatol Rep. 2011; 13: 431-439.

5 Lee J, Taneja V, Vassallo R. Cigarette smoking and inflammation: cellular and molecular mechanisms. J Dent Res. 2012; 91: 142-149.

6 Geetha D, Jefferson JA. ANCA-associated vasculitis: core curriculum 2020. Am J Kidney Dis. 2020; 75: 124-137.

7 Kew RR, Ghebrehiwet B, Janoff A. Cigarette smoke can activate the alternative pathway of complement in vitro by modifying the third component of complement. J Clin Invest. 1985; 75: 1000-1007.

8 Yin W, Ghebrehiwet B, Weksler B, Peerschke EI. Regulated complement deposition on the surface of human endothelial cells: effect of tobacco smoke and shear stress. Thromb Res. 2008; 122: 221-228.