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Infectious immunity and pneumococcal vaccine responses in multiple myeloma and related disorders

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av

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Avhandlingen baseras på följande delarbeten

I. Karlsson J, Andréasson B, Kondori N, Erman E, Riesbeck K, Hogevik H, Wennerås C. Comparative study of immune status to infectious agents in elderly patients with multiple myeloma, Waldenstrom's macroglobulinemia, and monoclonal gammopathy of undetermined significance.
Clin Vaccine Immunol 2011;18(6):969-977.

II. Karlsson J, Hogevik H, Andersson K, Roshani L, Andréasson B, Wennerås C. Pneumococcal vaccine responses in elderly patients with multiple myeloma, Waldenstrom's macroglobulinemia, and monoclonal gammopathy of undetermined significance.
Trials Vaccinol 2013;2:31-38.

III. Karlsson J, Roalfe L, Hogevik H, Zancolli M, Andréasson B, Goldblatt D, Wennerås C. Poor correlation between pneumococcal IgG and IgM titers and opsonophagocytic activity in vaccinated patients with multiple myeloma and Waldenstrom's macroglobulinemia.
Clin Vaccine Immunol 2016; 23(4):379-385.

IV. Karlsson J, Blimark C, Hogevik H, Wennerås C, Andréasson B. Respiratory viruses in multiple myeloma: A single-center epidemiological study.
In manuscript.

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Infectious immunity and pneumococcal vaccine responses in multiple myeloma and related disorders

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ABSTRACT

Multiple myeloma (MM), Waldenstrom's macroglobulinemia (WM), and monoclonal gammopathy of undetermined significance (MGUS) are B cell conditions associated with suppressed immune functions and susceptibility to infection. Severe pneumococcal disease is common not least in MM patients and vaccination is considered important, although the protective efficacy is debated. The aims of the first two studies of this thesis were to investigate humoral immunity to a spectrum of prevalent pathogens, and responses to pneumococcal vaccination with either a 23-valent polysaccharide vaccine or a 7-valent conjugated vaccine in elderly patients with MM, WM, and MGUS. We further compared two methods for evaluation of pneumococcal vaccine responses, serotype-specific ELISA and opsonophagocytosis (OPA) in the same groups of patients, and retrospectively examined the prevalence of respiratory viruses in MM. Background antibody levels to pathogens were the most depressed in MM but low antibody levels were also seen in WM and MGUS compared to age-matched controls. Pneumococci, *Staphylococcus aureus*, varicella zoster virus, and fungi (Candida, Aspergillus) were identified as risk pathogens, while immunity to *Haemophilus influenzae* and most viruses was retained in all study groups. Likewise, responses to pneumococcal vaccination were suppressed in all three patient categories. No differences between the vaccine types given as single doses were found. Pneumococcal antibody titers as measured by ELISA and OPA correlated very poorly in MM and WM patients, and our data indicate that ELISA measurements may overestimate anti-pneumococcal immunity in these patients. Rhinovirus, influenza virus and respiratory syncytial virus were the most commonly detected respiratory viruses in the investigated MM cohort. Patients with virus-positive tests were younger and had shorter disease duration than patients with negative analyses. In summary, patients with MM, WM and MGUS have a suppressed humoral immunity to many common pathogens, foremost bacteria. Reduced responses to pneumococcal vaccination can be expected in these patients. The use of an OPA method should be preferred for evaluating pneumococcal vaccine responses in B cell malignancies.

Keywords: Multiple myeloma, Waldenstrom's macroglobulinemia, MGUS, elderly, immunity, infection, pneumococcal vaccination, ELISA, opsonophagocytosis

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