Anti-GBM disease: A model for autoimmune kidney diseases

The renewed interest in anti-GBM disease is spurred by the detection of autoantibodies in other forms of glomerulonephritis and has led to an exciting development in studies on pathogenesis as well as diagnosis and management. The newly published review [1] by Professor Mårten Segelmark, gives a comprehensive update on Anti-GBM disease subgroups, pathogenesis and therapies. “A must read for all nephrologist”, explains Professor Denis Fouque, editor-in chief of Nephrology Dialysis and Transplantation (NDT), the journal in which the review was published.

For many years anti-GBM disease was thought to be the only kind of glomerulonephritis driven by autoantibodies. Now it has become evident that autoantibodies also play an important part in ANCA-associated nephritis, membranous nephropathy and IgA-nephritis. This has renewed the interest in anti-GBM as a model for autoimmune kidney diseases. The discovery of the B-cell epitopes led to the development of rapid immunoassays for the detection of circulating anti-GBM. This has enabled early diagnosis, which has had an impact on the prognosis.

A large percentage of patients with anti-GBM disease also have myeloperoxidase-ANCA (MPO-ANCA). As a group, double-positive patients are older, and they have more prodromal symptoms. This opens up a window of opportunity for early diagnosis, but it is questionable if double-positive patients have a better overall renal prognosis. The clinically most important aspect of double positivity is the increased relapse risk, making maintenance immunosuppressive therapy warranted for double-positive patients.

There are also several reports of overlap between membranous nephropathy and anti-GBM disease. Such patients usually have nephrotic-range proteinuria in combination with crescentic glomerulonephritis. It has been suggested that membranous nephropathy might trigger an autoimmune response against the cryptic anti-GBM epitopes. However, there are no cases described with simultaneous anti-PLA2R antibodies and antibodies to type IV collagen. An alternative explanation is that some anti-GBM antibodies
preferentially deposit on the subepithelial side of the GBM, thereby mimicking the immune complexes seen in membranous nephropathy.

Cyclophosphamide is today the standard therapy to stop the autoantibody production. Historical data indicate that cyclophosphamide substantially shortens the time circulating antibodies are present. This reduces the risk of flares with nephritis and pulmonary haemorrhage, and enables renal transplantation at an earlier time point. In ANCA-associated vasculitis it has been shown that targeting B-cells with rituximab leads to a more rapid decline of circulating antibodies. There are reports of the use of rituximab in anti-GBM disease, but no head-to-head comparison.

Plasma exchange is used to lower levels of circulating autoantibodies. However, each session only removes about one third of the IgG in the body. Thus it takes several days to reach non-toxic levels. Immunoabsorption techniques have been employed as an alternative. This leads to a more rapid decline of the antibodies, but it is not clear in how many patients this would make a difference in outcome.

“In conclusion, the detection of autoantibodies in other forms of glomerulonephritis, renewed the scientific interest in anti-GBM disease, which now serves as a model in the research of autoimmune kidney diseases”, explains Segelmark. Professor Denis Fouque, editor-in-chief of Nephrology Dialysis and Transplantation (NDT) adds: “The review is a ‘must read’ for all nephrologist!”

Press Contact:
ERA-EDTA PRESS OFFICE
Dr. Bettina Albers
Jakobstrasse 38
99423 Weimar
Germany
Tel. +49 3643/ 7764-23
Fax +49 3643/ 7764-52

About ERA-EDTA

With more than 11,000 members, the ERA-EDTA (“European Renal Association – European Dialysis and Transplant Association”) is one of the biggest nephrology associations worldwide and one of the most important and prestigious European Medical Associations. It supports basic and clinical research in the fields of clinical nephrology, dialysis, renal transplantation and related subjects. It also supports a number of studies as well as research groups and has founded a special "Fellowship Programme" for young investigators as well as grant programmes. In order to involve young nephrologists in all its activities, ERA-EDTA has created the "Young Nephrologists' Platform" (YNP), a very active committee whose board includes members who are 40 years old or younger. In addition, it has established various working groups to promote the collaboration of nephrologists with other medical disciplines (e.g. cardiology, immunology). Furthermore, a "European Renal Best Practice" (ERBP) advisory board was established by the ERA-EDTA to draw up and publish guidelines and position statements. Another important goal of the ERA-EDTA is education: The series of CME courses combined with the annual congress offer an attractive scientific programme to cover the need for continuous medical education for doctors working in the fields of nephrology, dialysis and transplantation. The association’s journals, NDT (Nephrology, Dialysis, Transplantation) and CKJ (Clinical Kidney Journal), are currently the leading nephrology journals in Europe; furthermore NDT-Educational is the Society's online educational journal, with free access for all users, as well as being a very important and useful feature of the NDT-Educational "Literature Review". The ERA-EDTA Registry is a large epidemiologic database comparing countries by assessing nephrology practices throughout Europe. ENP, the European Nephrology Portal, is the latest new initiative of ERA-EDTA, where all those interested in the activities of the Society can find everything that is happening, all in one place. Finally, ERA-EDTA is a member of the European Kidney Health Alliance (EKHA), a consortium of patients, nurses and foundations relating to renal issues that actively interacts with the European Parliament. For more information, please visit www.era-edta.org