Pathology of C3 Glomerulopathy: an Update and Review with Focus on Ultrastructural Evaluation

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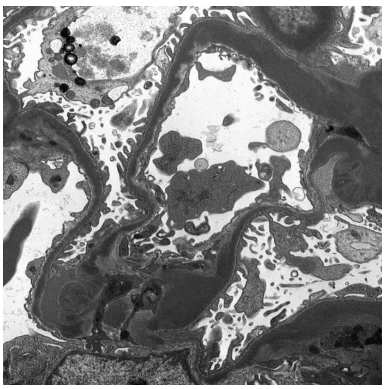
Abstract

C3 glomerulopathy (C3G) is an ultra rare disorder and encompasses a heterogenous group of diseases driven by dysregulation of the alternative pathway (AP) complement cascade and shared kidney biopsy findings of C3 dominant immunofluorescence staining. Dysregulation of the AP complement cascade occurs through autoantibodies, genetic mutations, and often unknown mechanisms. They may occur spontaneously or be triggered by infections, autoimmune disease, or monoclonal proteins. Light microscopic findings are heterogeneous but often show a membranoproliferative glomerulonephritis pattern of injury. Immunofluorescence microscopy is required for diagnosis, and it is recognized that a subset of cases may overlap with immune complex mediated glomerulonephritis. Electron microscopy is necessary for subclassification of C3G into C3 glomerulonephritis and dense deposit disease variants and can be helpful in identifying superimposed processes such as microangiopathic injury. Electron microscopy findings may also help favor a complement driven process in cases of immunoglobulin mediated membranoproliferative glomerulonephritis. Making a diagnosis of C3G requires clinical exclusions of infection related glomerulonephritis as well as the possibility of masked monoclonal deposits via paraffin immunofluorescence.



The ultrastructure of dense deposit disease.

References

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