Why Is Electron Microscopy Crucial in the Diagnosis of Light Chain-LC ("Myeloma") Cast Nephropathy?

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Abstract

Renal disease is a common cause of morbidity and mortality in patients with plasma cell dyscrasias. The serum free light chain assay is used in patients, mostly older, with unexplained acute kidney injury to screen for potential myeloma cast nephropathy. The presentation will use 2 cases that clearly illustrate the value of electron microscopy and in addition discuss findings in a series of these cases reported in a recent article published in Ultrastructural Pathology (48(5): 422-437; 2024). The morphological features of tubular casts in patients with multiple myeloma have not been systematically analyzed.

This presentation addresses the morphology of these casts, with emphasis on ultrastructural features, in a series of 23 patients with light chain ("myeloma") cast nephropathy compared them with those in 10 patients with a variety of renal diseases. The immunofluorescence data was correlated with morphological findings to provide diagnostic assessments and guidelines.

The ultrastructural features identified as diagnostic of tubular casts with underlying myeloma included: amyloid and crystals in the casts, multiple well-defined fracture planes forming a complex jigsaw puzzle arrangement of cast contents, indicative of the fragility of the immunoglobulin LCs, and reactive tubular cells lining the cast-containing tubules. These findings were absent in non-myeloma casts.

Myeloma casts failed to exhibit LC monoclonality in 33% of MCN and often did not stain for IgA or IgM. The majority of non-myeloma casts stained for both kappa and lambda LCs, lgA and lgM, and showed uniform finely to coarsely granular electron density and cellular debris.