Are the cytoplasmic microstructures within GBM pathologically significant?

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The current issue of CEN features the so-called podocytic infolding glomerulopathy, which is characterized by the emergence of spherical or tubular cytoplasmic microstructures in association with cytoplasmic projections of podocytes within the thickened glomerular basement membrane (GBM) in electron micrographs as well as nonargyrophilic holes in the GBM at light microscopic levels [1]. This type of glomerular change has been recently proposed as a possible new pathological entity in Japan. The three original articles and 15 case reports in this issue are the first survey of the cases with this type of glomerular pathology.

The GBM and other basement membranes are made up by self-assembly of constituent molecules, such as collagen type IV and laminin, which are secreted by the adjacent parenchymal cells. The established basement membranes are thought to be a stable structure, providing a mechanical support and constant milieu for the parenchymal cells. Reflecting the structural and functional stability of basement membranes, cytoplasmic microstructures and cellular projections have been only rarely reported within the basement membranes. One of those rare observations includes the basement membranes of the proximal convoluted tubule, which contains occasional cytoplasmic vesicles at the concavity of the tubular bend [2]. These vesicles are thought to be torn off from the basal cytoplasm of the proximal tubular cells due to higher mechanical stress at this location, and preserved within the basement membranes which shield the vesicles from disposal by

interstitial cells. In this issue, Fujigaki et al. [3] showed clearly that the microstructures in the GBM are connected with the cellular processes of podocytes by three dimensional analysis.

Another example of heterogeneity of the basement membrane was found around the ductal epithelium of excretory glands, including the liver, pancreas, lacrimal glands and salivary glands [4, 5], where the cellular projections of ductal epithelial cells were associated multilaminar basement membranes and fine collagen fibrils. The multilaminar lamina densa together with fine collagen fibrils were thought to be produced by the epithelial cells. The functional significance of cellular projection of ductal epithelial cells are unknown, but may be correlated the extremely high mechanical demand of this epithelium.

The 25 cases reported in this issue revealed clearly that the podocyte infolding glomerulopathy represents not solitary unreproducible observations, but constantly reproducible ones, although the incidence is extremely low. The unique microscopic appearance suggests the common pathological process of these cases, but the etiology is obviously diverse. In this issue, Masuda et al. [6] reported a different type of glomerulopathy with cytoplasmic microstructures within GBM, and suggested that they represented cellular debris trapped during the remodeling of the GBM.

What does the morphology of podocyte infolding glomerulopathy indicate? It would be to some extent rationalized to suppose that the podocytes in this condition are surrendered to more mechanical demand to produce more GBM materials and make basal projections which are torn off to deliver cytoplasmic microstructures to be remained for considerable period in GBM. The paucity of the cases and the diversity of the etiology at present prevent further analysis of the pathology.

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