Drusen Composition

Histologically, drusen are composed of granular ground substance, degenerating lipid and protein particles, crystalline deposits of calcium and amino acids, residual bodies, and partially digested photoreceptor outer segment discs.

Components of the complement system, including C3 complement fragments, C5, and the membrane-attack complex (C5b-9), have been shown to be present in drusen. Dysregulation of complement leads to overactive complement activity that can cause immune-mediated damage. A polymorphism in complement factor H, a key regulator of complement activation, has been identified as a major risk factor for the development of AMD (see Chapter 1).

Drusen formation shares similarities with amyloid diseases, such as Alzheimer’s disease and Parkinson’s disease. Although amyloid proteins, such as the Aβ peptide, transthyretin, immunoglobulin light chains, and amyloid A, are found in drusen and sub-RPE deposits, nonfibrillar oligomers, rather than amyloid fibrils, appear to be the primary toxic agents present centrally within drusen and in close proximity to the inner collagenous layer of Bruch’s membrane. Antigen-presenting dendritic cells are present in and around drusen and may facilitate the clearance of amyloid oligomers.

Figure 2-7. (A) Periodic acid-Schiff staining of hard drusen (white asterisk) in the retina of a 76-year-old man with AMD (original magnification ×20). (B) Periodic acid-Schiff staining of hard drusen (white asterisk) seen in association with BLamD (white arrow) and BLinD (black arrow) deposits in Bruch’s membrane in the retina of a 76-year-old man with AMD (original magnification ×10). (C) Hematoxylin-eosin staining and (D) periodic acid-Schiff staining of hard drusen (white asterisks) in the retina of an 86-year-old woman with early AMD (original magnification ×20).