Bölüm **3**

Amiloidoz, Patogenez, Klinik ve Yeni Tedavi Yaklaşımları

Özlem Yayar

• GİRİŞ

Amiloidoz, öncü çözünebilir bir proteinden oluşan çözünmez fibrillerin hücre dışında birikmesi ile oluşan bir protein katlanma hastalığıdır. Bu sert ve dallanmamış fibriller, yaklaşık 10 nm çapındadır. Genellikle anti-paralel yapıda düzenlenen moleküler bir beta-plated (kırmalı) tabaka yapısına sahiptirler. Fibriller bu yapısı nedeniyle çözünmez, proteolize karşı dirençlidir ve polarize ışık altında bakıldığında Kongo kırmızısı ile çift kırılım özelliği gösterirler.

• PATOLOJİ

"Amiloid" terimi ilk defa 1838 yılında Schleiden tarafından bitki nişastasını tanımlamak için kullanılmıştır. 1854 yılında Rudolf Virchow, iyotla selüloza benzer bir şekilde boyanan doku birikimlerini tanımlamakta kullanmıştır. Kongo kırmızısı, 1883'te Paul Bottinger tarafından geliştirilmiş; daha sonra, amiloidin daha iyi gösterilmesi için 1920'lerde Bennhold tarafından kullanılmıştır.

İlk kez 1959›da yapılan elektron mikroskobik incelemede, amiloidin genellikle 8 ila 10 nm çapında düz ve dallanmayan fibriller gösterdiği tesbit edilmiştir. Birçok durumda, amiloid fibril çeşidi, immüno-histoloji veya immüno-elektron mikroskobu ile daha da detaylı tanımlanabilir.

kin-6 reseptör antagonisti) da dahil olmak üzere kullanılan biyolojik ajanların da, AA amiloidoz semptomlarını azalttığı gösterilmiştir.

Tüm sistemik amiloidozlar (AA, AL ve kalıtsal formlar dahil) için yaygın olan normal bir plazma proteini olan serum amiloid P bileşeninin hedeflenmesi, amiloidin doku birikimlerinin azaltılması veya uzaklaştırılması için etkili olabilir. SAP' ı plazmadan tamamen, dokulardan ise kısmen temizleyen bir ilaç olan (R)-1-[(R)-2-carboxy-pyrrolidin-1-yl]-6-oxo-hexanoyl] pyrrolidine-2-karboksilik asit (CPHPC), ile aralıklı tedavi sonrası anti-SAP antikorlarının verilmesiyle amiloid birikimlerinin karaciğer, böbrek ve diğer organlarda azaldığı bazı hayvan deneyleri ve erken faz insan deneylerinde gösterilmiştir.

• HASTALIK İZLEMİ

Tedavinin etkisinin takibi sistemik amiloidoz gibi hastalıkların takibi için önemlidir. Tekrarlanan ölçümler, tedavinin etkisini (veya etkisizliğini) izlemek için kullanışlıdır. İki farklı süreç izlenmelidir. İlk işlem, sırasıyla AA, AL ve ATTR amiloidozunda öncü protein SAA, serbest kappa veya lambda hafif zincir ve (mutasyona uğramış) TTR üretiminin düşmesidir.

Başarılı bir tedaviden sonra, SAA seviyeleri sürekli olarak 3 mg/L'nin altına düşmeli ve aynı kalmalı, serbest kappa ve lambda seviyeleri ve kappa/lambda oranı referans aralıklarında olmalı ve mutant TTR artık kanda tespit edilmemelidir.

İkinci işlem, klinik amiloid yükü olarak adlandırılan amiloid birikimidir. Serum albumin, alkalen fosfataz, bilirubin, NT proBNP, troponin, kreatinin klerensi, proteinüri, ventriküler duvar kalınlığı, ejeksiyon fraksiyonu, iletkenlik ve ritim, kalp hızı değişkenliği ve karaciğer, dalak ve böbrekler gibi genişlemiş organların boyutları, klinik amiloid yükünü izlemek için kullanılabilir.

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