Bölüm

9

Hipertansiyonda Kompleman Sistem ve Uç Organ Hasarı

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GİRİŞ

Yapılan çalışmalar hipertansiyon ve hipertansif uç organ hasarında sadece hemodinamik faktörlerin değil aynı zamanda inflamasyonun da önemli bir rol oynadığını göstermektedir. Kompleman sistemi, mikroorganizmalara karşı savunmada ve antikor aracılı doku hasarında rol oynayan, çözünür ve hücre zarında yer alan bir grup proteinden oluşur. Doğuştan gelen bağışıklık sisteminin önemli bir bileşeni ve antikor aracılı yanıtların bir tamamlayıcısıdır. Son deneysel veriler, arteriyel hipertansiyonun tüm aşamalarında kompleman sistemin rolünü kuvvetle desteklemektedir. Bu nedenle kompleman aktivasyonu, hipertansiyon patolojisini, damar sistemi üzerindeki doğrudan etkilerinin yanı sıra, doğuştan ve adaptif immün yanıtlar üzerindeki etkileriyle de yönlendirebilir. Bu bölümde temel olarak, hipertansiyon ve uç organ hasarında kompleman sistemin rolünü gözden geçireceğiz.

KOMPLEMAN SİSTEM VE HİPERTANSİYON

Çözünür ve zara bağlı proteinlerden oluşan kompleman sistem, esas olarak doğuştan gelen bağışıklık fonksiyonlarına hizmet eden karmaşık bir ağ olmakla birlikte, kompleman işlevlerinin doğuştan gelen bağışıklığın ötesine geçtiğini gösteren çok sayıda kanıt bulunmaktadır [(1)]. Kompleman sistemin kontrolsüz aktivasyonu, otoimmüniteye, doku inflamasyonuna ve yaralanmalara neden olabilir. Kompleman sistem pıhtılaşma sistemleri, doğuştan ve adaptif bağışıklık ile birlikte hasardan sonra mikrobiyal invazyona karşı korur ve bariyer işlevlerini sürdürmeye yardımcı olur. Kompleman aktivasyonunun renal, kardiyovasküler, nörolojik, alerjik ve enfeksiyöz bozukluklar dahil olmak üzere birçok patolojik durumda ortaya çıktığı gösterilmiştir.

Kompleman aktivasyonu için üç ana yol kabul edilmiştir: klasik, alternatif ve lektin yolları. Bu yollardan C3, üç yolun tamamının işlevi için önemlidir ve C3

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kompleman sistemin hipertansif beyin hasarı, malign nefroskleroz veya endotel disfonksiyonu gibi diğer hipertansiyonla ilişkili komplikasyonlar üzerindeki etkileri henüz tam olarak tanımlanmamıştır.

Kompleman sistem kan basıncının düşürülmesi için önemliyken, hipertansif uç organ hasarına eşlik eden lokal inflamasyonun önlenmesindeki rolü de dikkate alınmalıdır. Kompleman sistem proinflamatuar ve antiinflamatuar fonksiyonlara sahip olduğundan, kompleman kaskadının tam inhibisyonu, arteriyel hipertansiyonda istenmeyen etkilere neden olabilir. Bu nedenle, kompleman sistem, hipertansiyon, böbrek ve kardiyovasküler hastalıklarla mücadele için yeni terapötik yaklaşımların tasarımında kullanmak istenirse komplemanların bu hastalık patolojilerine uzaysal, zamansal ve hücresel katkılarının tam olarak aydınlatılması gerekmektedir. Farklı kompleman yolaklarını hedefleyen ve hali hazırda diğer endikasyonlar için faz II ve III denemelerinde değerlendirilmekte olan birkaç ilaç adayı bulunmaktadır ve bunların hipertansiyon tedavisinde de kullanım potansiyeli vardır. Bu hastalardaki genetik kompleman varyasyonları hakkında büyük veri analizlerini, hücre içi ve hücre dışı komplemanların fonksiyonel problanmasını ve diğer (doğuştan gelen) bağışıklık sensörleriyle çapraz etkileşimini entegre eden bütünsel bir yaklaşım gerektirmektedir.

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