BÖLÜM 3

COVID-19 İMMÜNOPATOGENEZİ

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GİRİŞ

Aralık 2019'da Çin'in Wuhan şehrinde bilinmeyen bir nedene bağlı pnömoni vakaları bildirilmesi sonrası yeni bir betacoronavirus keşfedildi. Orta Doğu Solunum Sedromu coronavirüs (Middle East respiratory syndrome MERS CoV) ve akut respiratuar sendrom coronavirüs (Severe Acute Respiratory Syndrome-SARS-CoV)'den farklı olarak bu yeni tanımlanan coronavirüs (SARS-CoV2), coronavirus ailesinin yedinci üyesi olarak ortaya konuldu.

Coronavirusler zarflı, tek zincirli RNA virüsleri olup, insanlar, bazı diğer memeliler ve kuşlarda bulunabilmekte, respiratuar, enterik, hepatik ve nörolojik klinik tablolara neden olmaktadır[1]. Tüm genom analizleri ile SARS-CoV2 genomu ile yarasa orijinli coronavirüsler arasındaki %96 oranında benzerlik olması yarasanın rezervuar konak olabileceğini düşündürmüştür[2].

SARS-Coronavirüs-2019 (COVID-19) salgını tüm dünyayı etki altına almış, hızlı yayılımı ve mortalite hızı nedeniyle acil bir durum teşkil etmiştir. Yaklaşık bir yıl içinde (21 Aralık 2020 tarihine kadar) dünya'da 75.479.471 doğrulanmış COVID-19 vakası ve 1.686.267 ölüm bildirilmiştir[3]. Çoğu hasta hafif bulgular ve iyi prognoz sergilerken, bazı hastalarda ciddi pnömoni, pulmoner ödem, Akut Respiratuvar Sıkıntı Sendromu (ARDS) ve çoklu organ yetmezliği gelişebilir[4]. Şiddetli COVID-19'da görülen ARDS, nefes almada zorluk ve düşük kan oksijen seviyesi ile karakterizedir[5]. Bazı hastalar ikincil bakteri ve mantar enfeksiyonlarına yenik düşebilir[6]. Ölüm ile sonuçlanan COVID -19 vakalarının %70'inde ARSD'ye bağlı solunum yetmezliği etkendir[5]. Ayrıca COVID-19 sonucu mortal olan vakaların %28'inde viral enfeksiyonun neden olduğu hedef organ hasarı, salınan sitokinler sonucu çoklu organ yetmezliği ve sekonder enfeksiyonlara bağlı sepsis görülmüştür[5].

Bu bölümde, SARS-CoV2 enfeksiyonunun immünopatogenezine genel bir bakış yapacağız. SARS-CoV2'nin bağışıklık sistemi ile etkileşimini

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(NET)'tir. Histonlar ve platelet fosfolipidleri arasındaki elektrostatik ilişki, koagülasyon yolağını ve pulmoner megakaryositleri aktive edebilir. Küçük damar vaskülitlerinde de etyopatogenezde işaret edilen NET, COVID-19 patogenezinde enfeksiyon, inflamasyon ve trombozu ilişkilendirebilir[67,68].

COVID-19 ve immünolojik hastalıklar

Son zamanlarda ortaya çıkan "long COVID", yani uzamış COVID terimi, COVID-19 pozitif hastaların %10'unu etkileyen, heterojen bir fenomen olarak tanımlanmaktadır[69]. Hafif semptomlu COVID-19 hastaların kardiyovasküler, nörolojik ve respiratuar sistemi içeren bazı kalıcı semptomlar geliştirmesi, persistan immün aktivasyon veya inflamasyonun uzamış COVID-19'da rolü olabileceğine işaret eder. Uzamış COVID-19'da da birçok otoimmün hastalıkta olduğu gibi kadın predominansı gösterilmiştir. COVID-19 sonrası otoimmünite-ilişkili durumlar için mevsimsel human coronavirus (HCoV)-spesifik T hücrelerinin multipl skleroz hastalarında myelinle çapraz reaksiyon vermesine atıfta bulunularak moleküler benzerlik hipotezi öne sürülmüştür[43].

Kronik otoimmün hastalığı olan bireyler için viral enfeksiyonlar da dahil olmak üzere enfeksiyonlar için risk artışı bilinmektedir[70,71]. Benzer şekilde, kullanılan immün-supresör ilaçların da enfeksiyon yatkınlığına katkı sağlayabileceği, enfeksiyonların da altta yatan otoimmün hastalığı alevlendirebileceği düşünülmektedir. Bunlara rağmen otoimmün hastalığı olan bireylerde SARS-CoV-2 enfeksiyonu veya mortalite için genel popülasyona göre artmış risk bildirilmemiştir[72].

Sonuç

Birçok çalışma, şiddetli COVID-19 hastalığı için primer neden olarak viral sitopatik etkiden ziyade hiperinflamatuar yanıta işaret etmektedir. Çok-yönlü viral invazyona karşı sürdürülemeyen immün homeostaz sonucu sitokin fırtınası gelişebilir. Sitokin fırtınası, çoklu organ yetmezliği, ciddi lenfopeni ve sepsisle sonuçlanabilen, artmış sitokin seviyeleri ve anormal koagulasyon ile karakterize kritik bir dönemdir. İmmün yolakların daha iyi anlaşılması ile daha etkili tedavi seçenekleri ortaya konulacaktır.

Anahtar kelimeler: COVID-19, immünoloji, immünopatogenez

Akılda kalması gerekenler

- COVID-19'un normal immün yanıtı bozduğu ve kritik hastalarda kontrolsüz immün yanıta yol açtığı gösterilmiştir. Bu immünolojik etkiler, granülosit ve makrofaj anomalileri, artmış sitokin seviyeleri, lenfopeni, lenfosit aktivasyonu ve disfonksiyonu, IgG ve total antikor düzeylerinde yükselmelerdir.
- Ağır COVID-19 tablosu, Sistemik Lupus Eritematozus veya IFN regülasyon bozukluğu ile karakterize 'STING-associated vasculopathy with onset in infancy' (SAVI) gibi otoimmün/otoinflamatuar hastalıkları akla getirmektedir.
- Hastaların bir kısmı asemptomatik dönem sonrası ikinci faza geçer. Yaklaşık %20 hasta ise terminal faza ilerleyerek çoklu organ yetmezliği, ciddi lenfopeni ve sepsis geliştirebilir.
- İmmün etyopatogenezin daha net anlaşılması ile daha etkin tedavi seçenekleri ortaya konulacaktır.

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