4. Bölüm

COVID-19 ENFEKSİYONU İMMÜNOPATOLOJİSİ

Didem AKAL TAŞCIOĞLU [1]

GİRİŞ

2019 yılı Aralık ayında Çin'in Wuhan Eyaletinde ortaya çıkan koronavirüs (SARS-CoV-2) enfeksiyonu, dünya çapında yayılarak morbidite ve mortalite oranları oldukça yüksek bir salgına sebep olmuş ve Dünya Sağlık Örgütü (WHO) tarafından Mart 2020'de küresel salgın (pandemi) olarak kabul edilmiştir. Coronaviridae ailesine ait olan koronavirüsler zarflı, segmentsiz, tek sarmallı pozitif uçlu RNA virüsleridir[1]. Filogenetik genomik çalışmalar; SARS-CoV-2'nin nükleotid benzerliğinin yarasa koronavirüsü (BatCoV) ile %96 ve SARS-CoV ile %79,6 olduğunu bildirmektedir[2–4]. Benzer şekilde, genomik çalışmalar, yarasaların yeni tanımlanan SARS-CoV-2 için doğal konakçı olduğunu ve Çin'in Vuhan kentindeki canlı hayvan pazarında bulunan çok miktarda yarasa ve kontamine yarasa atıklarının insanlara bulaşmaya neden olarak enfeksiyonun başlangıcında etken olabileceği fikrini ortaya koymuştur.[5]

SARS-CoV-2'nin vücuda girişi ACE-2 reseptörleri aracılığıyla gerçekleştirilir. SARS-CoV-2 enfeksiyonu hem doğuştan gelen hem de adaptif bağışıklık tepkilerini birlikte aktive eder. SARS-CoV-2, tipik bir IgM/IgG modeliyle antikor üretimini uyarmasına rağmen, hücresel bağışıklık da bozulur. Şiddetli vakalarda, düşük CD4+ ve CD8+ T hücre sayıları, bozulmuş bağışıklık fonksiyonları ile ilişkilidir ve düşük lenfosit alt gruplarına eşlik eden yüksek nötrofil/lenfosit oranları gösterilmiştir. Son zamanlarda, koronavirüs enfeksiyonu-19'da (COVID-19) bozulmuş T hücre cevabları ile birlikte yüksek IFN -α/γ oranları ve artmış IL-1, IL-6, TNF-α, MCP-1, IP-10, IL-4, IL-10 düzeyleri bildirilmiştir. Şiddetli COVID-19 hastalarında artan proinflamatuvar sitokinler ve kemokinler; CD4+, CD8+ ve düzenleyici T hücrelerinin baskılanmasına neden olarak, aşırı inflamatuvar yanıtlara, doku ve organ hasarı ile ölümcül sitokin fırtınasına neden olabilmektedir. Sonuç olarak, sitokinlerin (IL-6, IL-1, IFN), reseptörlerinin veya sinyal yollarının bloke edilmesini içeren, konakçı bağışıklık sistemine karşı geliştirilecek yeni tedavilerin umut vaat edici olabileceği düşünülmektedir.

KORONAVİRÜSÜN KONAK HÜCRELERE GİRİŞİNİ DÜZENLEYEN ARACILAR

SARS-CoV-2'nin konak hücrelere girişi, virüs zarfına ait, transmembran tip I glikoprotein yapısında olan anjiyotensin dönüştürücü enzim- 2 (ACE-2) reseptörleri, tarafından gerçekleştirilir. [6,7](Şekil 1)[8].

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kortikosteroidler ile birlikte, sitokin inhibitörlerinin (IL-6 veya IL-1 inhibitörleri) kullanılması evre III enfeksiyonda organ yetmezliği gelişmeden sistemik inflamasyonu azaltmak için önerilir. İntravenöz immünoglobulin uygulaması, anormal inflamatuvar durumda immün sistemin modülasyonunda başka bir alternatif olarak önerilmiştir.[75] Ancak antiinflamatuvar tedavi kullanımında hasta seçimi, antiinflamatuvar tedaviye başlama zamanı ve süresi hastaların prognozu açısından önemlidir. İmmünosupresanlar, inflamatuar sitokin antagonistleri, JAK inhibitörleri üzerinde tartışılan tedavi seçenekleridir.

SARS-COV2 ENFEKSİYONUNUN KLİNİK BULGULARI

COVID-19 enfeksiyonu klinik bulguları, asemptomatik vakalardan, öksürük, ateş gibi semptomların görüldüğü hafif-orta dereceli olgulara ve ciddi olgularda ortaya çıkan tüketim koagülopatisi, bilateral pnömoni, akut solunum sıkıntısı (ARDS), sepsis gibi ağır klinik bulgulara kadar değişkenlik gösterir.[19,76] Ancak viral bulaş, presemptomatik ve asemptomatik vakalarda da mevcuttur.[77] Çeşitli çalışmalarla, hastalık ciddiyetinin, ileri yaş ve bireyin altta yatan hastalıkları ile ilişkili olduğu gösterilmiştir. Ancak ciddi olgular sadece bu risk grupları ile sınırlı olmayıp genç hastalarda da hastalık ağır seyredebilmektedir.[78]Aynı zamanda hastalığın ileri yaş gruplarında ve erkeklerde kadınlara göre daha fazla görülmesi; bireyler ve kadın-erkek arasındaki immün fonksiyonlardaki farklılara dikkati çekmektedir.[79]

SONUÇ

Bugüne kadar, COVID-19'a yönelik bir antiviral ilaç tasarlanmamıştır. MAS patogenezinde belirli sitokinlerin rolüne ilişkin veriler hala yetersiz olsa da, proinflamatuvar sitokinler ve kemokinler yeni terapötikler için çekici bir hedef olmaya devam etmektedir. Bununla birlikte, bu çalışmalarda en önemli kısıtlayıcı faktör, doğuştan gelen bağışıklık tepkisinde ve bağışıklık sistemindeki duyarlılıklarda bireysel farklılıkların olmasıdır.

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