Bölüm 14

PARKİNSON HASTALIĞINDA PATOGENEZ VE TEDAVİ YAKLAŞIMI

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GİRİŞ

Parkinson hastalığı (PH), dopamin eksikliği nedeniyle hem motor, hem de non-motor bulguları olan karmaşık bir nörodejeneratif hastalıktır (1,2). Yaşam şekli, ileri yaş, çevresel ve genetik faktörler PH etiyolojisinde suçlanan faktörlerdir (3). Alfa-sinüklein patolojisinin ve genetik mutasyonların tespit edilmesi ile PH patogenezini araştıran çalışmalar hız kazanmıştır (4,5). PH ile ilgili günümüzde patogenezde mitokondriyal disfonksiyon, oksidatif stres, protein agregasyonu, bozulmuş otofaji ve nöroinflamasyon dahil olmak üzere spesifik birçok mekanizma suçlanmaktadır (6). PH'nda semptomatik tedavinin yanı sıra PH hastalarının patofizyolojik olarak tanımlanmış alt tiplerinin açıklanması ile yeni hedefe yönelik tedavi seçenekleri üzerinde yoğunlaşılmıştır (7).

PARKİNSON HASTALIĞI KLİNİĞİ VE EPİDEMİYOLOJİSİ

İngiliz hekim ve bilim insanı James Parkinson tarafından 1817 yılında "Titremeli Felç Üzerine Bir Deneme" adlı kitabında ilk olarak tanımlanan bu sinir sistemi hastalığı, Alzheimer hastalığından sonra görülen en sık ikinci nörodejeneratif hastalıktır (8-10). Hastalığın başlıca motor bulguları istirahat tremoru, bradikinezi, rijidite ve postural instabilitedir (11). Ayrıca motor bulguların başlamasından yıllar öncesine kadar uzanan prodromal dönemde, hastalarda kognitif bozukluklar, anhedoni, apati, otonomik semptomlar, uyku bozuklukları gibi birçok non-motor belirtiler de görülmektedir (12,13). Parkinson hastalığı prevalansı özellikle yaşla birlikte artış gösterir (2). Tüm dünyada yaşam boyu görülme riski erkeklerde %2 iken, kadınlarda %1.3'tür (14).

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SONUÇ

PH patofizyolojisi tam olarak açıklanamamış olan kompleks nörodejeneratif bir hastalıktır. Hastalık etyolojisinde genetik yatkınlık, çevresel toksinler ve yaşlanmanın önemli bir rol oynadığı ve patogenezde multifaktöriyel nedenlerin sorumlu olduğu düşünülmektedir. Nigral dejenerasyonun esas patolojisinde; fibriller alfa-sinükleinlerin monomerik yapılarının bozulması ve hücre içinde birikimi yer almaktadır. Mitokondriyal disfonksiyon, artmış oksidatif stres, otozom-lizozom sistemlerinin çalışmaması ve nöroinflamasyon da patogenezde sorumlu diğer patolojik mekanizmalardır. PH'da genetik çalışmaların hız kazanması ve patogenetik mekanizmaların daha iyi anlaşılması; PH'da semptomatik tedavinin yanısıra nöromodülasyon ve nöroprotektif tedavi seçeneklerini de gündeme getirmiştir.

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