Bölüm 2

EPİGENETİK MEKANİZMALAR İLE PARKİNSON HASTALIĞI ARASINDAKİ İLİŞKİNİN KLİNİK AÇIDAN ÖNEMİ

Orçun AVŞAR[1]

1.GİRİŞ

Parkinson hastalığı (PH), yaşla birlikte ilerleyen, çeşitli motor ve motor olmayan semptomlar içeren ve semptomların zamanla artış gösterdiği yaygın bir nörodejeneratif hastalıktır. Parkinson hastalığı, Alzheimer hastalığından sonra en sık görülen ikinci nörodejeneratif hastalıktır ve 65 yaş üstü nüfusun %1-2'sini etkilemektedir [1]. PH, motor semptomlar olan bradikinezi, tremor, rijidite, postural instabilite ve motor olmayan semptomlar olan koku alma disfonksiyonu, depresyon, kabızlık, REM uyku davranış bozukluğu ile karakterizedir. Bu semptomlar, ilk kez 1817'de James Parkinson tarafından tanımlanmıştır [2]. Patolojik açıdan, Substantia Nigra pars compacta (SNpc)'da dopaminerjik nöronların ölümü ve etkilenen beyin bölgelerindeki nöronlarda Lewy cisimlerinin meydana gelmesi şeklinde ifade edilmektedir. Lewy cisimleri, büyük oranda α-synuclein içerirken daha az oranlarda ubiquitin ve başka proteinlerden oluşmaktadır [3]. Parkinson hastalarındaki sıvı hareketlerinin giderek azalması, Substantia Nigra pars compacta'da dopamin sentezinin azalmasından ve özellikle dorsal striatuma iletilme sorunundan kaynaklanmaktadır [4].

PH vakalarının büyük çoğunluğu (>%90) ailesel değildir ve sporadik ya da idiyopatik olarak kabul edilmektedir. Ailesel PH vakaları ise yaklaşık %5-10 oranında görülmektedir ve *PARK2, SNCA*, *LRRK2*, *PINK1*, *GBA* genlerinde görülen nadir mutasyonlar Mendel kalıtımı ile etki göstermektedir. Ancak, sporadik Parkinson hastalığında altta yatan nedenler hala gizemini korumaktadır [1, 5]. Bu bağlamda, tek bir neden değil bireysel farklılığın altında yatan mekanizmalar karşımıza çıkmaktadır. Ailesel Parkinson hastalığının düşük prevalansı; çevresel faktörlerin, patojenlerin, yaşam boyu hem nükleer hem de mitokondriyal DNA'da meydana gelen mutasyonların Parkinson hastalığının ortaya çıkmasında önemli rolü olduğunu göstermektedir [6]. Yaşlanma, PH için en önemli risk faktörüdür

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