

BÖLÜM 26

DENEYSEL ALZHEİMER HASTALIĞI MODELLERİ

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Alzheimer hastalığı (AH), günlük yaşamsal aktivitelerde azalma ve bilişsel yeteneklerin bozulması ile karakterize, nöropsikiyatrik semptomların ve davranış değişikliklerinin eşlik ettiği nörodejenaratif bir hastalıktır (1). Yaşlı popülasyonda görülen nörodejenaratif demansların en sık nedenidir. Dünyada 20 milyondan fazla Alzheimer hastası vardır ve yaklaşık 300 bini ülkemizde olan bu hastaların sayısı gün geçtikçe artmaktadır. Yapılan araştırmalarda 65 yaşın üstündeki ortalama her 15 kişiden birinde, 80-85 yaşın üzerindeki her iki kişiden birinde AH'nın görüldüğü belirtilmiştir (1,2).

1. Alzheimer Hastalığının Patogenezi

AH patogenezi için yapılan epidemiyolojik araştırmalar AH'nın tek bir faktöre bağlı olmadığına işaret etmektedir. Hastalığın oluşumunda yaşlanmaya bağlı olarak hücre dışı amiloid beta (A β) protein birikimi sonucu senil plak oluşumu, hücre içi tau proteinlerinin anormal fosforilasyonu sonucu nörofibriler yumak (NFY) oluşumu, kolinerjik iletide bozulma, nöroinflamasyon artışı, mitokondriyal fonksiyon kaybı ve sinaptik fonksiyon kaybı ile karakterizedir (1-3).

AH patogenezinden biri ve önemli bir etkeni olan hücre dışında senil plakların birikimidir. AH'deki senil plakların ana bileşeni A β proteindir. A β proteini, bir ucu hücre içinde diğeri hücre dışında olmak üzere hücre zarını enlemesine geçen amiloid prekürsör protein (APP)'nin çözünür olmayan parçalarıdır. A β proteini

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sürekli ve uzun süreli bellek, mekânsal algı, motor davranış değişiklikleri, genel lokomotor aktivitesi ve anksiyete gibi farklı davranış değişiklikleri araştırılabilir.

Sonuç

Halen kullanılmakta olan deneysel AH modellerinin hiçbirisi insanda gözlenen klinik tabloyu tam olarak taklit edememektedir. Ancak, oluşturulan bu modeller günümüzde AH ile ilişkili bilimsel çalışmalara önemli ölçüde katkı sağlamakta ve gerek hastalığın etkisini anlamaya yönelik, gerekse daha etkin ve özgün tedavi stratejileri ortaya koyabilmek için tedavi amaçlı kullanımlarının önemini tartışılmaz bir boyuta getirmektedir.

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