# BÖLÜM 50

# NÖROFİBROMATOZİS

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## GİRİŞ

Nörofibromatozis (NF); başta santral sinir sistemi ve periferik sinir sistemi olmak üzere kemik, göz, kas-iskelet sistemi, gastrointestinal ve endokrin sistemi de etkileyebilen multisistemik bir nörokütanöz hastalıktır.[1] Nörofibromatozisin klinik ve genetik olarak farklı formları bulunmaktadır. Nörofibromatozis tip 1 (NF1), Nörofibromatozis Tip 2 (NF2), Schwannomatoz ve Legius en sık bilinenleridir.[2] Deride sütlü kahverengi (cafe-au-lait) lekeler ve nörofibromlar ayırt edici özellikleridir. 1982 yılında, 7 tip ve 'başka türlü sınıflandırılamayan' olgular için sekiz kategoriden oluşan nörofibromatoz sınıflaması önerilirken; son yapılan çalışmalarda, 'gastrointestinal tip' Tip 8 ve 'Nörofibromatozis/Noonan' Tip 9 olarak kategoriye eklenmiştir.[3] Nörofibromatozisler, klinik bulguların heterojenitesine bağlı olarak, 9 farklı forma ayrılmıştır.[3,4]

## NÖROFİBROMATOZİS TİP 1

Nörofibromatozis tip 1 (NF1; OMIM#162200); 19.yüzyılda tanımlanan ve VonRecklinghausen hastalığı veya periferal nörofibromatoz olarak bilinen nörokütanöz hastalıktır.[5] İnsidansı her canlı doğumda 1/2600 ile 1/3000 arasında değişir.[6] Otozomal dominant kalıtılır.[6] NF1, tüm nörofibromatozis olgularının %96'sını oluşturmaktadır.[7] Olgular arasında etnik ve cinsiyet açısından herhangi bir fark yoktur.[2]

## GENETİK

NF1,17q11.2 kromozomunda bulunan NF1 genindeki kalıtsal veya herhangi bir ailevi geçmişi olmaksızın yeni mutasyonlar (denovo) nedeniyle oluşmaktadır.[8] Hastaların yüzde ellisinde kalıtsal mutasyon, diğer yarısında spontan mutasyon vardır.[7] NF1 genindeki mutasyonlar, aynı aile üyeleri arasında bile farklılık gösterebilmektedir.[9] Nükleotid değişiklikleri, nokta mutasyonlar, insersiyon veya mikrodelesyon, splice bölge mutasyonları dahil olmak üzere hemen hemen her türlü mutasyon ve hatta tüm gen delesyonları bile görülebilir.[10] Somatik mutasyonlar da, NF1'in mozaik şekline neden olabilir. Mozaik mutasyonlar daha az şiddetli olmaktadır ve genellikle daha lokalize, tek taraflı lezyonlara neden olmaktadır.[11]Hastalık şüphesi olan bireylerin %95'inde mutasyonları tespit eden genetik test mevcuttur.[12] Genetik testler, özellikle sporadik olarak etkilenen küçük çocuklarda teşhis için faydalıdır.[12]

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Legius sendromu tanısı tanı kriterleri ve genetik testler ile doğrulanmış olguların takibinde beyin ve spinal MRG tetkiki ile izlemde göz muayenesinin rutin olarak yapılması önerilmemektedir.[20]

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