Bölüm **4**

Fabry Hastalığı, Patogenez, Klinik ve Tanı, Nefrolog Kimi, Nasıl Tedavi Etmeli?

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• GİRİŞ

Fabry hastalığı (Anderson-Fabry hastalığı) en sık görülen lizozomal depo hastalığıdır. Glikosifingolipid metabolik yolunun X'e bağlı konjenital bozukluğu olup, çeşitli hücrelerde lizozomal globotriaçilseramid (Gb3) birikimi ile sonuçlanır, böylece hastalığın geniş yelpazedeki bulgularına yol açar. Hidrofilik deaçile türev olan globotriaçilsfingozinin (lysoGb3) sitotoksik, proinflamatuar ve profibrotik etkileri olduğu düşünülmektedir. Klasik Fabry hastalığının prevalansı tüm etnik kökenler düşünüldüğünde 1:8454 ile 1:117.000 arasında değişmektedir.

• PATOGENEZ

Fabry hastalığındaki metabolik kusur, terminal galaktozun globotriaçilseramid (Gb3) terminalinden hidrolitik bölünmesini katalizleyen lizozomal alfa-galaktosidaz A (alfa-Gal A) enziminin eksikliğidir. Klinik olarak anlamlı Fabry hastalığının meydana geldiği alfa-Gal A aktivitesinin eşik seviyesinin, normal kontrolün % 30 ila 35'i olduğu düşünülmektedir. Klasik Fabry hastalığı formuna sahip erkekler çoğu zaman ortalamanın % 1'inden az alfa-GalA aktivitesine sahiptir. Daha yüksek alfa-Gal A aktivitesi en sık kadınlarda ve atipik varyantlarda görülür. Kesin olmasa da, enzim aktivitesi ile hastalık semptomları arasında bir ilişki vardır. Enzim aktivitesi, Fabry ile ilişkili komplikasyonların ortaya çıkma olasılığının temel belirleyicisidir.

KBH Evre 4 Fabry nefropatili hastalarda veya glomerüloskleroz oranı >% 50 veya proteinüri > 1 gr/gün olanlarda, ERT'ye rağmen böbrek fonksiyonunun bozulmaya devam ettiği gösterilmiştir. Ancak bu veriler de küçük ölçeklidir ve kontrol grubu olarak retrospektif verileri kullanmıştır. Kadın Fabry nefropatili hastalarda yapılan çalışmalarda da sonuç benzerdir.

Renal replasman tedavisi (RRT) altında olan Fabry nefropatili hastalarda 3 yıllık hasta sağ kalımı % 60-63 oranında bildirilmiştir. Bu durumda hastalara ERT tedavisi non-renal nedenlere bağlı olarak verilebilir, küçük ölçekli çalışmalarda hastaların yaşam kalitesini arttırdığını göstermiştir. Tedavinin diyaliz tedavisi esnasında verilmesi önerilmektedir.

ACE-i ve ARB kullanımının diğer proteinürik böbrek hastalıklarında olduğu gibi Fabry nefropatisinde de nefroprotektif olduğu gösterilmiştir.

D vitamininin Fabry nefropatisi üzerindeki faydalı etkisinin kesin bir kanıtı bulunmasa da, KDIGO kılavuzları, KBH Evre 3-5 olan hastalarda, D vitamini eksikliğinin düzeltilmesini önermektedir. Aynı faydalı etkinin Fabry nefropatisine sekonder KBH'da da söz konusu olabileceği düşünülmektedir.

Özetle bu çalışmalar, Fabry nefropatili hastalarda ERT'nin renal fonksiyonun bozulmasından veya aşikar proteinüri başlangıcından önce KBH Evre 1 veya 2'de etkili olduğunu, çünkü proteinüriyi azaltmadığını göstermiştir. Proteinüri (> 1 g / gün) veya KBH Evre 3 (eGFH<60 mL/dak /1.73 m^2) geliştiğinde, ERT'nin potansiyel koruyucu etkisini destekleyen veri yoktur. Bu durumlar ve tedavinin yüksek maliyeti (> 200 000 Euro / yıl) özellikle dikkate alınmalıdır.

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