BÖLÜM 4

MEME KANSERİ GENETİĞİNE BAKIŞ

Nazan ERAS[1]

Giriş

Genom, sürekli olarak DNA hasarına ve genomik instabiliteye yol açan dış ve iç faktörlere maruz kalır. Bu hasarlar, bir DNA molekülünün bir veya iki sarmalının bütünlüğünü etkileyerek, DNA'da tek zincir veya çift zincir kırıklarına neden olurlar (1). DNA çift zincir kırıkları, aşırı ve yıkıcı mutasyonlar oluşturabilen çok ciddi ve zararlı hasarlar olarak kabul edilir (2). DNA onarım yollarını, hücre siklusunun durmasını ve apoptozisi içeren hücresel olaylar dizisi; DNA hasarını düzeltmesi, kontrolsüz hücre bölünmesi ve onarılmamış DNA hasarlarının sonraki nesillere aktarılmasının önlenmesinde önemlidir. Bu yolaklarda yer alan genlerde mutasyona sahip kişiler radyasyona daha duyarlıdırlar ve DNA'ya zarar veren ajanlara maruz kaldıktan sonra bozulmuş bir proliferatif kapasiteye sahip olduklarından, normal bir popülasyona kıyasla kanser gelişimi açısından daha yüksek risk altındadırlar (1).

Her yıl dünya çapında 1,6 milyon yeni vakanın meydana geldiği tahmin edilen meme kanseri önemli bir halk sağlığı sorunudur (3, 4). Kadınlar arasında en yaygın görülen kanser olan meme kanseri tüm kadın kanserlerinin yaklaşık %25'ini meydana getirmektedir (5). Meme kanseri, en çok kansere bağlı ölüm görülen hastalık olarak da bilinmektedir (6). Son yıllardaki tarama, erken teşhis ve tedavideki iyileştirmeler ile mortalite oranı azalmıştır, ancak yine de önemli bir ölüm nedeni olmaya devam etmektedir (3, 4). Hastalığın ortaya çıkmasına yol açan etkenleri ortadan kaldırmaya yönelik yapılan girişimleri kapsayan birincil korunma, meme kanseri yükünü azaltmada en etkili, ancak henüz yeterince kullanılmamış stratejilerden biri olmaya devam etmektedir (3, 7). Meme kanserindeki birincil korunma önlemleri; sağlıklı beslenerek obeziteden kaçınma, fiziksel aktivitenin artırılması, erken doğum yapma ve emzirmenin teşviki, sigara ve alkol kullanımının engellenmesi gibi uygulamaları içerir (7). Etkin bir birincil korunma için hastalığın ortaya çıkmasına yol açan etkenlerini tanımak ve korunma yollarını bilmek önemli olacaktır. Meme kanseri ile ilişkili birçok risk faktörü tanımlanmıştır.

Meme kanseri gelişiminde etkili olan risk faktörleri

Parks ve ark. (8); kadın cinsiyet olma, ileri yaş, meme kanseri öyküsünün bulunması, yüksek patolojik riske sahip olma ve daha önce radyasyona

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dirmenin gerekliliği vurgulanmıştır (69).

Kansere yatkınlık genleri, belirli bir kanser türü için rölatif risklerine göre kategorize edilebilir. Yüksek penetranslı genler, 5'ten daha yüksek bir kanser rölatif riski ile ilişkilidir. Düşük penetranslı genler, rölatif olarak 1,5 civarında risk taşırken, orta-penetranslı genler 1,5 ile 5 arasında rölatif kanser riskleri taşırlar. BRCA1, BRCA2, TP53, PTEN, STK11 ve CDH1 genleri yüksek penetranslı genler iken; CHEK2, PALB2, ATM, BRIP1, RAD51C, XRCC2, NBS1, RAD50, MRE11, BARD1, ABRAXAS ve RAD51D genleri orta penetranslı genlerdir. MAP3K1, FGFR2, LSP1, TNRC19 ve H19 genleri ise düşük penetranslı genlerdir (80).

Sonuç

Bir hastanın meme kanserine karşı genetik yatkınlığının bilgisi, uygun şekilde klinik yönetimi yönlendirebilir. Bu bilgiler; meme kanseri izleme seçeneklerinin ve ilk tarama yaşının modifiye edilmesine, spesifik risk azaltma önlemlerinin önerilmesine, gene özgü kanser ilişkilerine dayalı olarak ailesel kanser risklerinin netleştirilmesine, tedavi rehberliği sunulmasına, risk altındaki diğer aile üyelerinin belirlenmesine, özelleştirilmiş ve gene özgü tedavi seçeneklerinin önerilmesine olanak sağlar.

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