Bölüm
7

MEME KANSERİNDE PROGNOSTİK VE PREDİKTİF FAKTÖRLER

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GİRİŞ

Meme kanseri farklı histolojik alt tiplerden oluşan heterojen bir kanserdir. Bu değişkenlikten altta yatan farklı moleküler ve genetik yapı sorumlu olup buda farklı klinik tablolara neden olmaktadır. Meme kanserinde nüks ve metastataz riski yüksek olan hastalara uygulanan tedaviler ile meme kanserinden ölüm oranını azalmıştır (1-4). Meme kanserinde teşhis sırasında tedaviden bağımsız olarak klinik sonuç hakkında bilgi sağlayan faktörler prognostik faktörlerdir. Nüks veya metastaz riski yüksek olan hastaları seçmeye yardımcı olabilecek güvenilir prognostik faktörler hastanın sağkalımı için çok değerlidir [5,6]. Buna karşılık belirli bir tedavi yöntemine cevap verme olasılığı hakkında bilgi sağlayan faktörler ise prediktif faktörlerdir.Klinik olarak uygulanabilir prediktif faktörler, adjuvan tedavinin kişiselleştirilmesinde, hangi tedavilerin hastalara fayda sağlayacağının belirlenmesinde ve potansiyel olarak toksik ve pahalı tedavilere gereksiz maruz kalma durumundan koruma sağlamaktadırlar. Prognostik ve prediktif faktörler ayrı ayrı sınıflandırılmalarına rağmen aslında birçok faktör hem prognostik hemde prediktif faktör özelliğindedir (örn, İnsan epidermal büyüme faktörü reseptörünün 2 [HER2] aşırı ekspresyonu varlığı). Genetik şifrelerin çözülmeye başlandığı günümüzde yeni nesil gen dizi analizleri ve biyoteknolojik gelişmeler moleküler onkolojide yeni ufuklar açmış, onkolojik anlayışımızda büyük gelişmeler sağlamıştır.

Meme kanserinde prognozu belirleyen faktörler; hastaya ,tümöre ve tedaviye bağlı olarak üç temel başlıkta ele alınabilir.

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limeraz (PARP) oral inhibitörlerinin (olaparib ve talazoparib) etkin olduğu faz 3 çalışmalarda gösterilmiştir.

6. Yeni Nesil Sekanslama (NGS)

Kanserin progresyonunda ve metastazında rol oynayan moleküler driverlerin anlaşılması, bireyselleştirilmiş kanser tedavisine neden olabilecek spesifik genomik anormalliklerin belirlenmesi amaçlayan araştırma alanıdır. Muhtemel prognostik bilgi sağlamanın yanı sıra, spesifik mutasyona dayalı tedavi için adayları belirlemek ve tahmin etmek için yeni nesil sekanslamanın (NGS) değeri umut verici olmakla birlikte, rutin klinik kullanım için henüz hazır değildir. Şimdiye kadar en sık gözlenen somatik mutasyonlar p53 geninde ve fosfatidilinositol-4,5-bisfosfat 3-kinaz, katalitik alt ünite alfa (PIK3CA) genindeydi. Mutasyona uğramış p53, ağırlıklı olarak bazal benzeri meme kanserlerinde ve HER-2 ile zenginleştirilmiş alt tipte daha sık bulunduğu tespit edilmiştir.

Mutasyona uğramış bir PIK3CA geni, genel olarak ER-pozitif Luminal alt tipte daha sık olarak gözlenmekte olup ER-pozitif HER-2-negatif metastatik meme kanserinde alfa spesifik bir PIK3CA inhibitörünün (alpelisib) fulvestrant ile kombine edilmesinin etkinliği artırdığı gözlenmiştir.

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