Bölüm
5

MYELOMADA GENETİK VE EPİGENETİK DEĞİŞİKLİKLER

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Myelomada genetik değişiklikler, diagnostik özelliğin yanı sıra tedaviyi de etkilediği için oldukça yoğun çalışılmıştır. Myelomanın genetik alt tipini belirlemek riski daha net olarak öngörmede ve daha uygun tedavi seçeneklerini belirlemede önemlidir (1). Myelomada hem genetik hem de çevresel faktörler hastalık etyolojisinde rol oynarlar. Klonal heterojenite hem solid tümörlerde hem de hematolojik malignensilerde olduğu gibi myelomada da belirgin bir özelliktir (2). Bu nedenle myelomadaki değişiklikleri; kromozomal, DNA düzeyi mutasyonlar ve epigenetik değişiklikler olarak ayrı ayrı değerlendirmek gerekir.

KROMOZOMAL DEĞİŞİKLİKLER

Myelomalı hastaların yaklaşık yarısında karyotip analizinde değişiklikler görülmektedir (3). Bu hastalarda sayısal kromozomal anomaliler görüldüğü gibi dengeli veya dengesiz olabilen yapısal kromozomal anomalileri de görülebilmektedir.

Myeloma, hiperdiploid olan ve olmayan (non-hiperdiploid) olarak ikiye ayrılabilir (1,4). Hiperdiploidi, yani diploid (2n) olması gereken kromozom sayısının artışı, yeni tanı alan hastaların ortalama %55'inde görülmekte iken (2,4), hipodiploidi de daha az olmakla beraber yine sıklıkla karşımıza çıkmaktadır (3). Hiperdiploidide görülen kromozomal artışlar rastgele değildir ve bazı kromozomlarda (3, 5, 7, 9, 11, 13, 15, 19 ve 21. kromozomlar) daha fazla gözlenmektedir (5-10). Hiperdiploidi genel olarak iyi prognoz göstermesi yani progresyonsuz sağ kalım

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kop altında göz ile görülemeyecek kromozomal anomalileri uygun FISH probları kullanarak görmek mümkündür. Ayrıca interfaz FISH ile duyarlılık artmakta, daha az sayıdaki mutasyonlu hücreyi yakalamak mümkün hale gelmektedir (3). Genom analizi, gen ekspresyon çalışmaları ile pek çok yeni bilgi edinilmiş olsa da myeloma analizlerinde rutin uygulamada altın standart sitogenetik çalışmalar ve FISH'tir (16).

Sonuç

Yapılan çok sayıda araştırmalar ile myelomanın oldukça heterojen olan alt yapısı ile ilgili geniş bilgiler edinilmiş ve subklonal heterojenitenin de etkili olduğu ortaya konmuştur. Ancak moleküler genetik alanındaki gelişmeler ve gündelik klinik uygulamalarda gittikçe artan kullanım alanı bulan yeni nesil dizilime gibi yeni teknolojilere rağmen halen myelomaya özgü gerek etiyopatogenezde gerekse tedaviye yön vermede tek bir sorumlu genetik varyasyon saptanamamış; subklonlarda sürücü olabilecek çok sayıda mutasyonun birlikte görülebileceği ve rol alabileceği öne sürülmüştür. Ancak sadece genomik değil transkriptomik ve proteomik çalışmaların da artmasıyla hastalık hakkındaki bilgi birikimin artması ve ilişkili olabilecek biyomarkırların tesbiti ile hedeflenmiş tedavi seçeneklerinden gen ve hücre tedavilerinin geliştirilmesine kadar birçok alanda yol gösterici bilgiler elde edilecektir.

Anahtar Kelimeler: Myeloma, sitogenetik, moleküler genetik, epigenetik

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