Bölüm
19

MULTİPLE MYELOM TEDAVİSİNDE HEDEFE YÖNELİK MONOKLONAL ANTİKOR DIŞI YENİ AJANLAR

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GİRİŞ

Multiple myeloma (MM) klonal plazma hücrelerinin neoplastik proliferasyonu ile karakterize bir hematolojik malignitedir. Klonal plazma hücreleri kemik iliğinde prolifere olur ve iskelet sisteminde osteolitik lezyonlar, osteopeni ve patolojik fraktürler beklenir. Diğer hastalık ilişkili komplikasyonlar hiperkalsemi, renal yetmezlik, anemi ve enfeksiyonlardır.

Günümüzde, standart tedavi yaklaşımları ile MM kür elde edilemeyen bir hastalıktır, bu nedenle relaps ve refrakter hastalık büyük bir sorun olmaya devam etmektedir. MM hastalığının temelinde yatan genetik heterojenite ve kemik iliği mikroçevresinin hastalık ilerlemesi üzerindeki etkisi de hastalığın iyileştirilmesini zorlaştırmaktadır (1,2). İmmünolojik temelli tedaviler, aşılar, immünomodulatuvar antikorlar ve özellikle hücresel tedavilerin her biri kendine özel etki mekanizmasına sahiptir, bu tedaviler ile; ilaç direncinin üstesinden gelinebilir, daha uzun süreli hastalıksız sağ kalım ve tümör kontrolü sağlanabilir (3). Multiple myelomun prekürsör gelişim süreçlerinde, altta klonal bir süreç ve TP53, CDKN2C, K-/N-RAS ve FAM46C mutasyonları, c-MAF, siklin D1/D2, IRF4 ve c-MYC'te bozulmaya yol açan kompleks genetik anomaliler vardır ve bu mutasyonların-genetik anomalilerin anlamı bilinmeyen monoklonal gamopati (MGUS) ve smoldering multiple myelomada (SMM) da var olduğu gösterilmiştir (4). Tümör hücrelerinin immün sistemden kaçışına ve ilaç direnci gelişimine yol açan; IL-6, IGF-1, SDF-1 alfa, B hücre aktivasyon faktörü (BAFF) ve proliferasyon indükleyen ligand (APRIL) gibi büyüme faktörleri/ ligandlar kemik iliği mikroçevresinde salgılanır. IL 6; Bcl-xL ve Mcl-1 upregulasyonunu da içeren birçok yolla, plazma hücre sağkalımı ve plazma hücre apopitozunda önemli rol oynamaktadır. Th1 hücreleri, sitotoksik

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cevaplanmamış önemli bir soru, maliyet etkinlikleridir ve özellikle bu tedavilerle eklenen maliyetin klinik sonuçlarıdır (84).

Sonuç

Günümüzde, standart tedavi yaklaşımları ile MM kür elde edilemeyen bir hastalıktır, bu nedenle relaps ve refrakter hastalık büyük bir sorun olmaya devam etmektedir. MM hastalığının temelinde yatan genetik heterojenite ve kemik iliği mikroçevresinin hastalık ilerlemesi üzerindeki etkisi de hastalığın iyileştirilmesini zorlaştırmaktadır. Uygun hastalarda; immünolojik temelli tedaviler, aşılar, immünomodulatuvar antikorlar ve özellikle hücresel tedavilerin her biri kendine özel etki mekanizmasına sahiptir, bu tedaviler ile; ilaç direncinin üstesinden gelinebilir, daha uzun süreli hastalıksız sağ kalım ve tümör kontrolü sağlanabilir.

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