Bölüm
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KANSERDE İMMUN SİSTEMDEN KAÇIŞ MEKANİZMALARI

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GİRİŞ

İmmun sistem tümörün yokedilmesi işlevinin yanında daha tümör gelişmeden bazı infeksiyöz hastalıklar (hepatit C vb.) ve Barrett özofajiti gibi kronik inflamatuar hastalıklara yanıtta ve tümör gelişmesinde de rol oynayabileceği bilinmektedir. Tümör gelişiminde en çok suçlanan immun sistem hücreleri doğal immunitenin hücreleridir. Doğal immun sistem elemanları anjiogenezisin ve doku remodelliğinin sağlanması başta olmak üzere salgıladıkları serbest oksijen radikalleri ile DNA hasarı, tümör baskılayıcı gen ve onkogenlerde mutasyonlara sebep olabilmektedirler. Bunun yanında T hücrelerinin Th2 ve regülatuar T hücre yönünde farklılaşması da tümör progresyonunda etkili olduğu bildirilmektedir[1].

Gelişmekte olan tümörün genetik ve biyokimyasal özellikleri tümör gelişimini önleyen ve destekleyen "immün-düzenleme" ile kontrol edilmekte olup, tümörün ilerleyişi "eleminasyon", "denge" ve "kaçış" süreçleriyle sağlamaktadır[2]. Tümör gelişminin erken basamaklarında doğal immunitenin elemanlarından özellikle doğal öldürücü (NK) hücreler, tümörle ilişkili makrofajlar ve nötrofiller, miyeloid baskılayıcı hücreler kanser hücrelerine karşı yanıtta ve eleminasyon fazında önemli roller üstlenmektedirler[3]. Tümör eleminasyonu ve gelişimi arasında bir denge oluştuktan sonra kanser hücrelerinin immün sistem tanımasından kaçtığı ve immunsüpresif bir çevre oluşturduğu kaçış fazı gerçekleşir[4,5]. Tümörlerin immunojenitelerini azaltma, immunsupresif bir çevre oluşturma, immun kontrol noktaları gibi bazı meleküllerin kullanımı gibi özellikleri sayesinde yeterli düzeyde adaptif immun yanıt oluşturmadıkları bilinmektedir[6,7].

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tümör dokusu ve lenf nodlarında yüksek düzeylerde Treg saptanmıştır[87]. Yakın zamanda yayınlanmış bir çalışmada, insan mesane dokusundaki Treg düzeyi hem TAM'lerle hem de IL-6-pozitif kanser hücre sayısı ile anlamlı derecede korelasyon göstermiştir[88]. Tümörü infiltre eden CD4 + FOXP3 + T hücreleri, uyaran sonrasında bile IL-2 veya IFN-γ üretmediği ve CD4 + efektör T hücrelerini baskıladığı ve fonksiyonel olarak Treg gibi davrandığı bildirilmektedir. Melanom ve over kanseri dahil olmak üzere diğer solid tümörler için benzer fonksiyonel bulgular bildirilmiştir[87].

Sonuç

Tümör hücrelerinin immun sistemden kaçması üç aşamada gerçekleşmekte olup son basamak olan "kaçış" aşamasında immun kontrol noktaları, yüzey ekspresyon değişiklikleri ve tümörün mikroçevresindeki değişiklikler tümör gelişimi ve yayılmasında ana rolü üstlenmektedir. Son yıllarda immun kontrol noktaları üzerine yapılan başarılı immunoterapiler uygun ortam sağlanması durumunda kanserin gelişimini engellemede immun sistemin ne kadar etkili olabileceğini gösterir niteliktedir.

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