

Bölüm 31

YUMUŞAK DOKU SARKOMLARINDA İMMUNOTERAPİNİN YERİ

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GİRİŞ

Yumuşak doku sarkomları (YDS), yetişkinlerdeki tüm solid tümörlerin yaklaşık % 1'ini oluşturur.¹ Yumuşak doku sarkomları kas, yağ, kan damarı ve sinir de dahil olmak üzere mezenkimal kök hücrelerinden kaynaklanır. 50'den fazla histolojik tip tanımlanmıştır. YDS vücudun herhangi bir yerinde ortaya çıkabilir, ancak en yaygın anatomik bölgeler ekstremiteler (% 60-70), karın ve retroperitonumdur (% 20). Çoğu hasta lokalize hastalık ile başvurur. Cerrahi olarak tümörün rezeksiyonu tedavinin temelini oluşturur. Bununla birlikte, yüksek histolojik dereceli olan ve 5 cm'den büyük lokalize tümörler, % 50'den fazla nüks riski taşır. Yüksek riskli lokalize tümörleri olan hastalar genellikle cerrahi, radyoterapi ve / veya kemoterapi kombinasyonlarıyla tedavi edilir. Optimal tedaviye rağmen, YDS' li hastalarının büyük bir kısmında lokal rekürrens veya uzak metastaz (tipik olarak akciğerlere) veya her ikisi de ilerleyen zamanlarda gelişecektir. Bu yaklaşımlar genel sağkalımı önemli ölçüde iyileştirememiştir. İlâveten metastatik hastalıkta da uygulanan kemoterapi, metastatik yumuşak doku sarkomu olan hastaların sonuçlarını önemli ölçüde etkilememiştir. Bu hastaların prognozu çok kötüdür. Ortanca genel sağkalım 8 ila 12 aydır.²

İmmünoterapi, refrakter kanserlerin tedavisinde çekici bir yaklaşım olmuştur. Sarkom, immünoterapinin etkili bir şekilde uygulandığı ilk kanser olarak kabul edilir. Eşzamanlı streptokok enfeksiyonu olan hastalarda tümör gerilemelerinin gözlemlerine dayanarak, Coley, 19. yüzyılın sonlarında şiddetli erizipel ataklarına sekonder sarkomların tam bir gerilemesini tanımlamış, ancak diğer hastalarda bu sonuçları yeniden oluşturamamıştır.³ Bundan sonra Amerikan Gıda ve İlaç İdare-

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yüksek ekspresyonunun, kontrol noktası inhibisyonundan yararlanacak sarkom hastalarını ayırt edebildiği henüz kanıtlanmamıştır.⁷⁹

Sarkomlarda kontrol noktası inhibisyonunun geleceği muhtemelen PD-1 / PD-L1 eksenini inhibisyonu artıran kemoterapi ve / veya radyoterapi kombinasyon çalışmalarında olacaktır. Bu, klasik kanser tedavilerinin neden olduğu nekroza bağlı olası antijen salınımına dayanmaktadır. Halen birinci basamak sarkom tedavisi için doksorubisine pembrolizumab ilavesinin değerlendirildiği bir Faz II çalışması devam etmektedir. Aynı doğrultuda, radyoterapiyi arttıran antijen salınımı ile PD-1 inhibisyonu sonuçlarını artırma potansiyeli,⁸⁰ Sarkom Araştırma Birliği aracılığıyla değerlendirilmesi planlanan bir yaklaşımdır. Kontrol noktası inhibitörlerinin tirozin kinaz inhibitörleri (TKİ) ile kombinasyonu, TKİ'lerin bağışıklık sistemi ve tümör mikroçevresi üzerindeki etkisine dayanan aktif bir araştırma hattıdır.^{81,82}

Son olarak, adoptif hücre transfer terapisi, NY-ESO-1-pozitif sarkomlarda az sayıda ümit vaat etmektedir. CAR T hücre tedavisi, hematolojik malignitelerde olağanüstü başarıdan sonra sarkomda da bozulmuştur. Ara analizdeki geçici sonuçlar, HER-2 pozitif sarkomlar için umut vermektedir. Bugüne kadar, aşılarda kontrol noktası inhibisyonu veya spesifik TCR/CAR ile transdüksiyonlu T hücreleri dahil olmak üzere farklı immünoterapi yaklaşımlarının hepsi sarkom hastaları için yeni terapötik seçenekler oluşturmak için uygun adaylardır. Bu tedavilerin kombinasyonu mümkündür ve ileriye giden yolu temsil edebilir. Özetle, bağışıklık sisteminin anlaşılmasında hızla artan bilgi, sarkomlarda immünoterapilerin gelişimine kapı açmıştır ancak bu konuda alınması gereken çok uzun bir yol vardır.

Anahtar kelimeler: Sarkom, immünoterapi, aşılama, adoptive hücre tedavi

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