Bölüm 2

FOLİKÜLER LENFOMA'DA GÜNCEL TEDAVİ

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GİRİŞ

Foliküler lenfoma (FL) en sık görülen ikinci B hücreli non-Hodgkin lenfoma (NHL) ve en sık görülen indolent B hücreli NHL'dır (1). Genel olarak foliküler lenfoma indolent bir seyir izler, hastaların büyük çoğunluğu ileri evrede (Ann Arbor sınıflama sistemine göre evre III ve IV) tanı alırlar ve çoğu hasta yaygın hastalığa rağmen asemptomatiktir (2). Doğası gereği indolent seyirli olmasına rağmen ve genellikle başlangıç tedavisine iyi yanıt veren ileri evre FL, sık nükslerle karakterize ve halen kür sağlanamayan bir malignitedir (3). Hastalık ilerledikçe, sonraki relapslar aşamalı olarak daha agresif ve dirençli hale gelebilir ve bazı olgular agresif lenfomaya dönüşebilir (2,3). FL yönetiminde son yıllarda birçok gelişmeye rağmen, hastalığın tekrarlayan doğası, klinisyenlerin tedavinin etkinliği ile yaşam kalitesi arasında dengeyi sağlamaya çalışması gibi sorunlar içerir. Yeni ajanların sayıları giderek artmakta, optimal tedavi konusunda yönetim stratejileri veya uygun sıralama tedavisi açısından tartışmalar devam etmekte ancak bugüne kadar evrensel olarak kabul edilmiş bir tedavi yaklaşımı standartı yoktur.

RİSK SINIFLAMASI VE PROGNOSTİK SİSTEM

FL'li hastalar arasında, hem hastalığın tanısında hem de tedaviye yanıtı değerlendirme de heterojenite olması sebebi ile tedavi öncesinde prognozun değerlendirilmesine yardımcı olmak için çeşitli modeller geliştirilmiştir. Hastaları klinik özellikleri ile prognostik açıdan ayıran, genel sağkalımla yada progresyonsuz sağkalım ile korele olarak düşük, intermitant ve yüksek riskli gruplar olarak ayıran ve yaygın olarak kullanılan Foliküler Lenfoma Uluslararası Prognostik İndeks (FLIPI) (4,5) ve daha sonra FLIPI2 (6) prognostik sistemleri kullanılmaktadır. (Tablo 1). FLIPI ve FLIPI2, hangi hastaların tedaviye ihtiyaç duyduklarını, hangi tedavinin seçileceğini veya tedaviye yanıtı öngörmede kullanışlı değildir (9,10). Yeni geliştirilen m7-FLIPI skoru, ECOG performans durumunu, FL'de yaygın olarak etkilenen yedi genin (EZH2, ARID1A, MEF2B, EP300, FOX01,

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CAR T Hücre Tedavisi

Relaps-refrakter NHL da, kimerik antijen reseptör T hücre (CAR-T) tedavisi özellikle ilgi çekici bir alandır. B hücresi lenfomalarına ilişkin veriler sınırlı olmasına rağmen, B hücresi kanserlerinde CD19'u hedef alan kimerik antijen reseptörü (CAR) tarafından modifiye edilen T hücrelerinin kullanımı ile yüksek yanıt oranları bildirilmiştir. Genetiği değiştirilmiş otolog T hücresini kullanan CAR-T tedavisi pan-B hücreli antijen olan CD-19'u eksprese eder. Çeşitli B hücreli malignitelerde devam eden çalışmalar da son derece etkili ve kalıcı cevaplar görülmüştür (64-65). Şu anda, CAR-T tedavisi, öncesinde en az iki sıra tedavi alan ve yanıtsız olan diffüz büyük b hücreli hastalar için FDA tarafından onaylanmış bir tedavidir. Relaps-refrakter FL'li hastalarda yapılan bir çalışmada CAR-T tedavisi ile 14 hastadan 10'unda (%71) tam remisyon elde eilmiştir ve ortanca remisyon süresi 29 ay olarak tespit edilmiştir (64). Bu çalışmaların sonuçları heyecan verici olmasına rağmen, CAR-T tedavisinin kendine özgü ve potansiyel olarak yaşamı tehdit eden toksisiteleri mevcuttur, özellikle sitokin salınım sendromu (CRS) ve nörotoksisite bunlardan en önemlileridir (64-65). CAR-T'ye yanıtı ve CRS gelişme riskini öngören biyobelirteçleri belirleme çalışmaları halen devam ediyor (66-67).

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