Bölüm
8

KRONİK LENFOSİTİK LÖSEMİ'DE MİNİMAL REZİDÜEL HASTALIK

Nazlı DEMİR[1]

Kronik lenfositik lösemi(KLL) tedavisinde son yıllarda yaşanan gelişmeler ile tedavi yanıt oranlarında belirgin iyileşmeler meydana gelmiştir. Tek ajan tedavi protokollerinden kombinasyon tedavilerine geçilmiş, ardından hedefe yönelik tedaviler ve yeni ajanlar ile yanıt oranları belirgin olarak artırılmıştır. Monoklonal antikorların kemoterapi ile kombinasyonu, progresyonsuz sağkalım(PFS) ve genel sağkalım(OS) sürelerini uzatmıştır(1-6). İbrutinib, İdelalisib ve Venetoclax gibi hedefe yönelik tedavilerin ilk sırada ve relaps refrakter hastalık hallerinde, monoterapi ve kombinasyonda kullanımı yaşam sürelerini uzatmıştır(7-14). KLL tedavisindeki nihai amaç rezidüel hastalığı saptanamayacak düzeye indirip kür elde etmek olmuştur.

Klinik çalışmalarda tedavinin faydasını göstermek için kullanılan altın standart sonlanım noktası genel sağkalımdır(OS). Ancak yeni tedaviler ile yaşam sürelerinin uzaması, OS ölçümü için geçen takip sürelerini de giderek uzatmıştır. Yeni ilaçların kullanıma girmesini hızlandırmak amacıyla çalışmalarda farklı sonlanım noktaları da kullanılmaya başlanmıştır. Progresyonsuz sağkalım(PFS) bunlar arasında en sık kullanılandır. Ancak etkin tedaviler ile PFS süreleri de uzamıştır. Bu nedenle klinik çalışma sürelerini kısaltmak ve yeni ajanlara ulaşımı kolaylaştırmak için yeni bir sonlanım noktası olarak minimal rezidüel hastalığın(MRD) kullanımı gündemdedir.

MİNİMAL REZİDÜEL HASTALIK NEDİR?

Tedavi sonrası klinik, morfolojik ve radyolojik incelemeler ile saptanamayan ancak daha spesifik yöntemler ile gösterilebilen kalıntı KLL hücreleri nüksün sorumlusudur. Nüksün zamanı, kalıntı hastalığın miktarı ve lösemik hücrelerin çoğalma hızı ile ilişkilidir(15).

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ghput sekanslama(HTS) yöntemi ile hasta plazmasındaki serbest tümör DNA'sı saptanarak rezidü hastalık taraması yapılabilir(15,55)

Sonuç

MRD'nin KLL'de kullanımı, prognozu tahmin etmek ve tedavi süreci ile stratejisine karar vermede yol göstericidir ve bireyselleştirilmiş tedavi yaklaşımlarının önünü açabileceği düşünülmektedir(15). Çalışmalarda elde edilen olumlu veriler nedeniyle MRD'nin bir sonlanım noktası olarak kullanılması gündemdedir. Çalışmalar, tedavi sonunda periferik kanda MRD negatifliğinin, tam yanıt varlığından bağımsız olarak tedavi etkinliğinin bir belirteci olduğunu göstermektedir.

MRD negatifliğini elde etmek ve idame tedavisi almaksızın uzun süreli remisyonda kalmak hastaları idame ve ardışık tedavilerden kaynaklanan toksisiteden koruyacak, hastalar ve toplum üzerindeki tedavi maliyetini azaltacak ve pahalı tedavilerin kullanımını geciktirecektir(15).

Erken dönemde MRD negatifliği elde edilen hastalarda toksisiteden kaçınmak amaçlı tedavinin azaltılması veya kesilmesi, MRD negatifliği sağlanamayan hastalarda ise çapraz direnç olmayan ajanlarla erken dönemde farklı tedaviler gündemdedir(38).

Standart bir yöntem belirlenmemiş olması ve her yöntemin farklı avantaj ve dezavantajlarının olması sorunların başında gelmektedir.

Klinik çalışmalarda elde edilen olumlu veriler nedeniyle MRD'nin bir sonlanım noktası olarak kullanılması gündemdedir ancak bu konuda literatür verilerinin artması gerekmektedir.

Anahtar Kelimeler: Minimal rezidüel hastalık, kronik lenfositik lösemi, akım sitometrisi, polimeraz zincir reaksiyonu

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