Bölüm
13

METASTATİK YUMUŞAK DOKU SARKOMLARINDA SİSTEMİK TEDAVİ SEÇENEKLERİ

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GİRİŞ

Yumuşak doku sarkomları (YDS), tüm vücut bölgelerinde mezenkimal hücrelerden kaynaklanan, heterojen nadir bir tümör grubudur. Malign hücreler; kas, yağ, lifli, kıkırdak, sinir veya damar dokusu gibi bir veya birkaç kökenden farklılaşabilir. Bu tümörler en sık ekstremitelerde (özellikle alt ekstremite) görülür; ardından sırasıyla karın boşluğu / retroperiton; gövde / torasik bölge; baş ve boyun bölgesi olacak şekilde kliniğe yansır.

Bireysel tedavilere verilen yanıtına, prognozuna, YDS'nin 50'den fazla histolojik alt tipi vardır. Geçmişte bu tümörlerin tümü bir araya toplanmış ve benzer şekilde tedavi edilmiş olsa da, tedavi seçiminin özellikle de metastatik aşamada histolojiye dayalı olması gerektiği konusunda fikir birliğine varılmıştır.

Bu bölümde GİST ve uterusun sarkomları hariç metastatik yumuşak doku sarkomunun sistemik tedavisi gözden geçirilecektir.

GENEL TEDAVİ PRENSİPLERİ

Yayılma Paterni: Primer veya nüks sarkomlardan kaynaklanan lokal komplikasyonlar önemli morbidite ve zaman zaman mortaliteye neden olabilirken, sarkomların yaşamı tehdit edici yönü aslında hematojen yayılıma eğilimidir. Tümör yayılım şekli tümör tipine ve konumuna göre değişir:

- Ekstremite, göğüs duvarı veya baş ve boyundaki YDS'nin çoğu için primer metastaz bölgesi akciğerlerdir [1,2]. Ancak, istisnalar da var. Ekstrapulmoner metastazlar retroperiton, spinal ve paraspinal YDS de baskın tipi miksoid / yuvarlak hücreli liposarkomlarda gelişse de AC metastazları hemen hemen hepsinde gelişir [3].

[183]. Lynch sendromunun daha önce düşünülenden daha yaygın olduğu göz önüne alındığında, MSI-H / dMMR YDS›li tüm hastalar, aile öyküsünden bağımsız olarak Lynch sendromu için germline genetik değerlendirmesi için yönlendirilmelidir [184].

YENİ NESİL DİZİLENME

Metastatik YDS ve kemik sarkomunlu hastalarda yeni nesil dizilenmenin potansiyel etkisini aydınlatma için 56 farklı histolojiye sahip 5635 hastanın değerlendirmesi yapılmıştır. [185]. 2017 ASCO da sunulan ön raporda göre % 7 ila 16 hedefleyici ilaca ulaşılabileceği bildirildi. Bu nedenle tedavi yanıtsız hastalarda yeni nesil dizilenme yapılması için yönlnedirilmesi uygun olacaktır.[186]

NTRK füzyon geni ve larotrektinib:

Çok küçük bir YDS'li hasta grubunda neurotrophic tropomyosin receptor kinase (*NTRK*) geni saptanmıştır.[187-189] Oldukça seçici bir NTRK inhibitörü olan larotrektinib'in potansiyel etkinliği, üç çalışmada kayıtlı NTRK füzyon pozitif saptanan 55 hastanın kombine analizi ile gösterildi [190] Tüm kohortta, bağımsız gözden geçirme ile genel cevap oranı % 75 idi ve yanıt verenlerin % 86'sı halen tedavi altında ya da 9,4 ay ortanca izleminde küratif olması amaçlanan ameliyat geçirmişti. İnfantil fibrosarkomların 7 sinde objektif yanıt alındı ve NTRK füzyonlu 11 YDS'nin 10'unda objektif yanıt alındı. Tedavi iyi tolere edildi; yanıt veren hiçbir hasta, advers olay nedeniyle larotrektinib'i kesmedi. Güvenlik analizinde, en yaygın advers reaksiyonlar (≥% 20), transaminazlarda yükselme , yorgunluk, bulantı, kusma, baş dönmesi, ishal, kabızlık ve öksürüğü içeriyordu [191].

Kasım 2018'de, larotrektinib, bilinen bir direnç mutasyonu olmadan, metastatik olan veya cerrahi rezeksiyonun ciddi morbidite ile sonuçlanabileceği bilinen bir direnç mutasyonu olmadan NTRK gen füzyonu olan solid tümörlerde kullanım için FDA tarafından onaylandı. Önerilen dozlar yetişkinler için günde iki kez oral olarak 100 mg ve çocuklar için günde iki kez 100 mg / m2 (doz başına maksimum 100 mg) şeklindedir. FDA hepatotoksisite ve nörotoksisitenin izlenmesini önerir.

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