MİDE KANSERİNDE HİPERTERMİK İNTRAPERİTONEAL KEMOTERAPİNİN YERİ

41 BÖLÜM

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ÖZET

Küresel olarak, 2018 yılında bir milyondan fazla yeni mide kanseri teşhis edildi ve mide kanseri dünyada en sık görülen 5. kanser türü oldu. Dünya genelinde 2018 yılı içinde mide kanserine bağlı görülen ölümlerin 783.000 olduğu tahmin edilmektedir. Mide kanseri en ölümcül kanser türü sıralamasında 3. sırada yer almaktadır. Agresif seyirli bir hastalık olan mide kanserinde, tanı sırasında hastaların %40'ı metastatik hastalığa sahiptir. Periton en sık tutulan bölgedir. Senkron tutulum oranı %14'tür. Hastaların %9'unda periton tek tutulum bölgesidir. Periton tutulumu olan hastaların prognozu kötü olup, medyan sağkalım süresi 3 ile 4 ay arasındadır.

Serbest kanser hücrleri primer tümörden ayrıldıktan sonra peritoneal yüzeye tutunur ve subperitoneal alana ilerleyerek tümöral nodülleri oluşturur. Serbest tümör hücrelerinin karın içinde yayılmasında etkili olan diğer yol ise primer tümör cerrahisi sırasında, lenfatik ve kan damarlarından, dokudan hücrelerin iatrojenik olarak yayılmasıdır.

Multimodal tedavi seçeneklerindeki ilerlemelere rağmen peritoneal metastazın eşlik ettiği mide kanserinde, mevcut NCCN klavuzu sistemik kemoterapi ya da destek tedavisi önermektedir. Ancak peritonun kan damarlarından fakir olması nedeniyle sistemik olarak uygulanan kemoterapötikler tümör depozitlerine çok düşük konsantrasyonlarda ulaşır. Tümör depozitlerinde yeterli konsantrasyonlara ulaşılabilmesi için hasta tarafından tolere edilemeyebilecek yüksek dozların sistemik olarak uygulanması gerekir. İntraperitoneal uygulamada, tümör hücrelerine kemoterapötiklerin direkt temasının sağlanması, sistemik ilaç düzeyinin tolere edilebilecek seviyelerde olması, ısının ve kemoterapötik ajanın sinerjistik etkisi, peritona sınırlı evre IV mide adenokarsinomlu hastalarda hipertermik intraperitoneal kemoterapi uygulanmasının avantajlarıdır.

İntraperitoneal kemoterapi, lokal-ileri mide kanserinde cerrahi sonrasında peritoneal metastaz gelişiminin engellenmesi için profilaktik, var olan peritoneal hastalık durumunda tedavi edici ve son olarak da yaygın peritoneal tutulum olan hastalarda palyatif olarak kullanılabilir.

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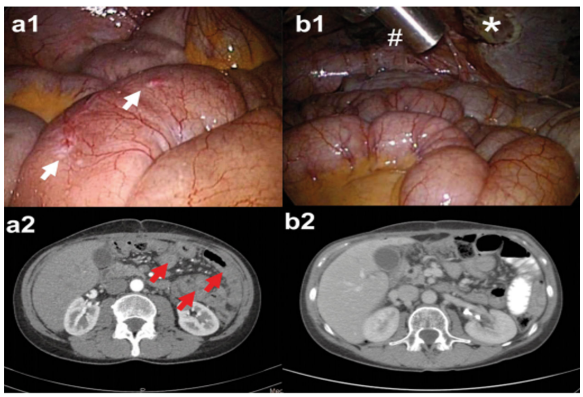

Resim 4: Laparoskopi (a1,a2) ve biligisayarlı tomografi (b1,b2) görüntüleri.İlk PIPAC seansında a1'de beyaz oklar ince barsakta çoklu tutulumu, a2'de ise kırmızı oklar ince barsak duvarındaki yaygın kalınlık artışını göstermektedir. Dördüncü PIPAC seansında aynı hastaya ait tam makroskopik yanıtın laparoskopi görüntüsü b1, radyolojik görüntüsü b2 ile gösterilmiştir (Adapte edilmiştir (58)).

Mide Kanserinde İntraperitoneal Olarak Kullanılan Kemoterapötikler

İntraperitoneal kemoterapide kullanılacak olan ideal bir ilaçtan beklenilen ilk özellik, spesifik kanser türü üzerine in vitro ve in vivo olarak etkinliğinin gösterilmiş olmasıdır. Biyodağılımı, farmakokinetik özellikleri ideal ve doku penatrasyonu yeterli olmalıdır. İlacın moleküler ağırlığı plasma periton bariyerden difüzyonunu engelleyecek büyüklükte olmalı ki peritoneal kavite içindeki ilaç konsantrasyonu yüsek olması sağlanırken eş zamanlı plasma konsantrasyonu sistemik toksisiteye yol açmayacak düzeylerde kalması sağlanır. Lokal toksisitesi düşük, kullanımı sağlık personeli için güvenli olmalıdır ve hipertermi ile sinerjistik etkileşim göstermelidir (63).

Mide kanserinin tedavisinde kullanılan çeşitli intraperitoneal kemoterapatikler mevcut olup, hangisinin en etkili olduğu ya da en etkili kombinasyonun hangisi olduğuna dair henüz bir fikir birliği oluşmamıştır.

Mitomisin-c, kolorektal kanser peritoneal metastazları ve psödomiksoma peritoneiden elde edilen tecrübeyle ilk kullanılan ilaçtır (14). Sıklıkla 15mg/m^2 dozunda , 42 derecede, 90 dk sürede uygulanır. Ancak süre ve doz konusunda farklılıklar mevcuttur (14,21,22).

Sisplatin, mitomisin-c ile birlikte 50 ile 200 mg/m^2 arasındaki dozlarda, 60 ile 90 dk arasında değişen perfüzyon süreleri ile kullanılır (64). Oksaliplatin, 460 mg/m^2 dozunda 30 ile 60 dk arasında değişen sürelerde uygulanır (23). Oksaliplatin ile 5-FU'nun sinerjistik etki göstermeleri nedeniyle 5-FU ve leucovorin, intraperitoneal kemoterapi sırasında ya da hemen öncesinde oksaliplatinin sitoksisitesini arttırmak için uygulanır. Hem sisplatinin hem de oksaliplatinin kabul edilebilir hematolojik toksisitesi mevcuttur. Ancak sisplatinin nefrotoksisitesi daha fazladır. Oksaliplatinin sodyum bazlı solüsyonlarda degrade olması nedeniyle 5% dekstroz içinde verilir. Ancak bu da elektrolit bozukluklarına neden olabilir (65,66). Hiperterminin sinerjistik etkisi hem oksaliplatinde (67) hem de siplatinde (68) gösterilmiştir.

Antrasiklinler içinde intraperitoneal kemoterapide en çok çalışılan doksorubisin olup farmakokinetik özellikleri istenilen düzeylerdedir (69,70). İn vitro şartlarda hipertermi sitotoksik etkiyi orta derecede arttırır (67). Doksorubisin intraperitoneal olarak 15mg/m^2 dozunda kullanılır. Yüksek dozlarda (30 mg/m^2) peritoneal enflamasyon, fibrozis ve obstrüksiyonla sonuçlanır (71).

Catumaxomab, monklonal antikor olup EpCAM-pozitif hücereler üzerine sitotoksik etkilidir. Mide kanser hücreleri %85 - %100 oranında EpCAM pozitifir (72). Malign asitli hastalarda yapılan çalışmada (73) intraperitoneal catumaxomab kullanımı parasentez ihityacında azalmaya yol açmıştır.

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