18.
BÖLÜM

ANTİKANSER TEDAVİ SIRASINDA GELİŞEN AŞIRI DUYARLILIK REAKSİYONLARI VE YÖNETİMİ

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GİRİŞ

Kemoterapötiklere bağlı gelişen aşırı duyarlılık reaksiyonları, özellikle de potansiyel ölümcül etkileri, bu ajanların terapötik kullanım alanlarını sınırlamaktadır. Çoklu dozlarda hastalar ilaca karşı duyarlı hale gelir ve sonraki ilaç maruziyeti aşırı duyarlılık reaksiyonlarının gelişimine neden olur. Bu da daha etkin birinci basamak tedavilerin kesilmesini ve ikinci basamak tedavilere geçme zorunluluğunu doğurmaktadır.

Gell ve Coombs 1963 yılında, aşırı duyarlılık reaksiyonlarını doku hasarı mekanizmalarına göre Tip I(IgE aracılı ani gelişen reaksiyonlar), Tip II (Antikor bağımlı, IgM/IgG aracılı), Tip III (immün kompleks aracılı), Tip IV (Gecikmiş tip veya T hücre aracılı) olmak üzere 4 ayrı gruba ayırmıştır [1].

Klinikte ise tedavi sırasındaki başlangıç zamanına bağlı olarak ani ve gecikmiş tip aşırı duyarlılık reaksiyonları şeklinde ikiye ayrılır[2]. Ani reaksiyonlar IgE aracılı bir mekanizma tarafından indüklenir ve son ilaç uygulamasından 1-6 saat sonra ortaya çıkar[3]**.** Genellikle ürtiker, anjiyoödem, konjunktivit, rinit, bronkospazm, gastrointestinal semptomlar (bulantı, kusma, ishal, karın ağrısı), anafilaksi veya anafilaktik şok gibi izole semptomlar şeklinde ortaya çıkarlar. Bazı klavuzlarda, IgE'ye bağımlı olmayan ve anafilaksiyi taklit eden sistemik aşırı duyarlılık reaksiyonları 'anafilaktoid" reaksiyonlar olarak adlandırılır[4].

İnfüzyon reaksiyonlarının en yaygın olarak görüldüğü kemoterapötik ajanlar taksanlar, platin grubu ilaçlar, pegile lipozomal doksorubisin, asparaginaz, prokarbazin, etoposid, bleomisin, sitarabin ve iksabepilondur. Bunlar genel-

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lığı %13 iken plasebo ile % 9.8 saptanmış. Reaksiyonların çoğu hafif, %1'den azı grade 3/4 şeklindeymiş. Pertuzumab kolunda 4, plasebo kolunda 2 hastada anafilaksi gelişmiş.

Rutin premedikasyon endike değildir. FDA onaylı etiket bilgileri, hastaların ilk infüzyondan sonra 60 dakika ve sonraki infüzyonlardan sonra en az 30 dakika yakından izlenmesini önermektedir. İnfüzyonla ilişkili önemli bir reaksiyon meydana gelirse infüzyonu yavaşlatılması veya durdurması ve uygun tıbbi tedavilerin uygulanması gerekir. Şiddetli infüzyon reaksiyonları olan hastalarda tedaviyi kalıcı olarak kesmek önerilmektedir.

Margetuximab: Faz III SOPHIA çalışmasında, margetuximab kemoterapi kombinasyonu ile tedavi edilen hastaların % 13'ünde infüzyonla ilişkili hipersensitivite reaksiyonları meydana gelmiş. Grade 3 reaksiyonlar %1.5' unda görülmüş ve çoğu tedavinin ilk siklusu sırasında oluşmuş[83].

Rutin premedikasyon endike değildir. FDA onaylı etiket bilgileri, ilacın şiddetli veya yaşamı tehdit eden infüzyonla ilişkili reaksiyonlar nedeniyle kalıcı olarak kesilmesini ve hafif veya orta derecede infüzyonla ilişkili reaksiyonlar yaşayan hastalarda sonraki sikluslar için premedikasyon (antihistaminler, glukokortikoidler, antipiretikler) yapılmasını önermektedir.

SONUÇ

Antikanser ajanların klinik kullanımının artmasıyla birlikte bu ilaçlara karşı gelişen hipersensitivite reaksiyonları sık görülmektedir. Bazen öngörülemeyen ciddi, yaşamı tehdit edici bir komplikasyon şeklinde ortaya çıkabilir. Etiyopatogenezde genellikle multipl hipersensitivite mekanizmaları rol oynar. Hastaların da bu konuda bilinçlendirilmesi önemlidir. Hipersensitivite reaksiyonunu takiben ilacın hastaya yararlı olduğu kanıtlanmışsa, aynı ilacı uygulamaya devam edip etmeme konusunda her zaman ikilem vardır. Premedikasyon, desensitizasyon protokolleri, daha yavaş infüzyon hızı, deri testleri ve aralarında çapraz reaksiyon yoksa ilacın aynı kategoriden farklı bir ajan ile ikame edilmesini içerebilir. Ancak anafilaksi gelişti ise desensitizasyon kontrendikedir.

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