6.
BÖLÜM

KANSER HASTALARINDA TAŞİARİTMİLER

Aysel YAĞMUR [1]

Kardiyak disritmiler kanser hastalarında yaygındır. Disitmilerin tanınması ve tedavisi, kanser popülasyonunda görülen yaygın etiyolojilerin anlaşılmasını gerektirir. Bunlar, miyokardın kanserle tutulması veya kemoterapi, radyasyon ve cerrahi dahil olmak üzere çeşitli kanser tedavilerini içerebilir. Önceden var olan kardiyovasküler hastalık, elektrolit düzensizlikleri veya hormonal anormallikler gibi diğer altta yatan komorbiditelerden de kaynaklanabilir. Asemptomatik bir hastada tesadüfen ortaya çıkabildiklerinden, disritmilerin klinik olarak tanınması zor olabilir. Semptomatik olduğunda hastalar çarpıntı, baş dönmesi, senkop veya kalp durması ile gelebilir. Teşhis genellikle 12 derivasyonlu EKG, Holter monitör veya yatak başı kardiyak monitörde ritim yorumlamasıyla yapılır.

Miyokardda tümör invazyonu olduğunda, kardiyak iletimin uyarılması ventriküler ve supraventriküler ektopiye yol açabilir [1,2]. Taşiaritmiler sıklıkla miksomalar, rabdomiyomlar ve fibromlarda görülür ve miyokardiyumun veya ileti sisteminin uyarılmasından kaynaklanabilir [3]. Şu anda, kanser tedavilerinde kullanılan Gıda ve İlaç İdaresi (FDA) onaylı kemoterapi kategorileri arasında alkilleyici ajanlar, antimetabolitler, antimikrotübül ajanları, histon deasetilaz (HDAC) inhibitörleri, tümör nekroz faktörü alfa (TNF α) olabilir. Kardiyovasküler toksisitelerin geliştiği mekanizmalar kemoterapiler arasında büyük farklılıklar gösterir.

ANTRASİKLİNLER

Bu iyi çalışılmış kemoterapötik ajanların kullanımı, kardiyotoksisite ile sınırlandırılmıştır. Yaygın endikasyonlar arasında meme kanseri, sarkomlar ve çeşitli pediatrik maligniteler bulunur.

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lerde QT uzamasının% 16–18 ve yüksek dereceli uzamanın% 3. 7–12 insidansı ile ilişkilidir [99]. Çeşitli faz 1-3 denemeleri benzer oranlarda QT uzaması göstermiştir [100-102]. Klinik olaylar nadir olmakla birlikte, bu ilacın QT uzaması için bir Kara Kutu Uyarısı vardır ve ilacı reçete etmek için özel eğitim gerektirir [99,103]. Nilotinib, BCR-ABL füzyon proteini, c-kit ve PDGFR reseptörlerini hedefleyen Philadelphia kromozom pozitif kronik miyelojenöz löseminin (CML) birinci veya ikinci basamak tedavisi için TKI onaylıdır. Nilotinibe maruz kalan sağlıklı gönüllülerde, maksimum QT aralığı değişikliği 18 ms idi ve 500 ms'den büyük mutlak QT aralıkları deneklerin% 1'inden daha azında meydana geldi [103,104]. İlk denemeler, TdP riskinde artış olmaksızın 5-15 ms'lik QT uzaması gösterdi [105]. Nilotinib ile tedavi edilen hastaların% 0. 3'ünde ani kardiyak ölüm (SCD) bildirilmiştir, ancak öncesinde QT uzaması ve TdP açıkça belgelenmemiştir. Bununla birlikte nilotinib, QT uzaması için bir Kara Kutu Uyarısı aldı [89,104]. VEGFR, c-kit ve PDGFR'yi hedefleyen Sunitinib, metastatik renal hücreli karsinom ve gastrointestinal stromal tümörlerin tedavisinde etkilidir. İlaçla tedavi edilen hastalarda (Fridericia formülü kullanılarak) QTc'deki ortalama artış 15. 4 ms'dir. 500 ms'den fazla QT uzaması% 2,3'ten daha azında görüldü ve TdP hastaların% 0,1'inden azında görüldü [6,38,66].

Histon deasetilaz inhibitörleri (HDI'ler), nihai apoptoza yol açan proteinlerin transkripsiyon sonrası aktivitesini hedefler. Bu ajanlar ayrıca QT prolongasyonu ile ilişkilendirilmiştir. HDI'ler, moleküler benzerliklerinin bir sonucu olarak HERG kanalını etkileyebilir ve böylece repolarizasyon anormalliklerine yol açabilir [106]. Kutanöz T hücreli lenfoma tedavisinde kullanılan bir HDI olan vorinostat ile yapılan bir faz 2 çalışmasında, klinik sekel kanıtı olmaksızın üç hastada QT uzaması gözlenmiştir [107]. Çeşitli hematolojik malignitelerde kullanılan başka bir HDI olan romidepsin, QT uzamasına neden olabilir. Romidepsinle ani kardiyak ölüm raporları vardır, ancak tetikleyici olay iyi belirlenmediğinden QT uzaması bildirilmiştir [103,108]. Bu verilere dayanarak, HDI'ler QT uzaması ile ilişkilidir, ancak yüksek TdP riski belirsizliğini korumaktadır.

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