Bölüm
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KANALOPATİLERİN KLİNİĞİ VE GENETİĞİ

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GİRİŞ

Kalbin elektriksel aktivitesini kontrol eden transmembran iyon kanallarındaki anormallikler aksiyon potansiyelini bozar ve miyokardın disritmiye açık olmasını sağlar (1). Konjenital aritmi sendromları veya ani aritmik ölüm (SCD) sendromları olarak da adlandırılan bu grup hastalık çoğunlukla genç ve sağlıklı insanları etkiler (2,3). Tür spesifik elektrokardiyografik (EKG) anormallikleri ve T dalga değişiklikleri, farklı klinik ve tetikleyici faktörler, senkop, hızlı, genellikle polimorfik ventriküler taşikardi (VT) veya ventriküler fibrilasyonun (VF) ile karakterize hastalıklardır. SCD nedeni olduklarından tanı ve tedavileri önem kazanır (2,3).

UZUN QT SENDROMU

Uzun QT sendromu (LQTS), EKG'de QT uzaması/T-dalga değişiklikleri ve klinik olarak çarpıntı, senkop ve SCD ile karakterizedir. Siyah Afrikalılar ve Afrikalı-Amerikalılar arasında daha az, Kafkasyalılar arasında daha sık görülmekle birlikte tüm dünyada prevalansın 1:2000–2500 aralığında olduğu tahmin edilmektedir (4).

Patofizyoloji ve genetik

LQTS aksiyon potansiyelinden sorumlu Na ve K kanalarını kodlayan genlerdeki mutasyonlarla ilişkilidir (4)(tablo1). Transmembran içeri doğru depolarize edici akımlar büyük oranda Na ve Ca kanalları, dışa doğru repolarize edici akımlar ise büyük oranda K kanallarıyla oluşur. LQT1 ve LQT2, sırasıyla net K akımını azaltan ve repolarizasyonu geciktiren yavaş (Iks) ve hızlı (Ikr) iyon kanallarındaki ;LQTS3 ise içe

NA kanalındaki (INa) fonksiyon kazancına neden olan mutasyonlardan kaynaklanır. Aksiyon potansiyelinde uzama QT intervalinde ve T dalgasında değişikliklere yol açar (4).

LQTS tipik olarak değişken penetrasyonlu otozomal dominant kalıtım gösterir ve nadiren sensorinöral sağırlık ile ilişkili resesif bir geçiş gösteren Jervell and Lange Nielsen sendromu tanımlanmıştır (5). Mutasyonların çoğu aileye özgüdür veya çok nadirdir. LQTS lu ailerin yaklaşık %25'i henüz tanımlanmış genetik lokusa sahip değildir. Mutasyonu taşıyan kişilerin klinik olarak etkilenme oranı %25 olarak belirtilmiş (5).

Klinik ve riskin belirlenmesi

Uzun QTS'unda klinik değişkendir. LQTS3'de ilk klinik sunum SCD olabilirken, LQTS1 ve LQTS2'de SCD öncesi senkop görülür (17). Klinik belirtiler daha çok yaşamın ilk yıllarında ortaya çıksada, 40 yaşın üzerinde devam eden kardiyak olay riski vardır. LQTS1, daha kısa QTc, düşük kardiyak olay oranı ile ilişkilidir (6). LQTS1 de 5-15 yaşlarındaki erkekler özellikle yüzme gibi egzersiz sırasında en yüksek risk altında iken LQTS2 li kadınlar puberte döneminden sonra daha yüksek risk altındadır (5). LQTS2'de işitsel veya emosyonel stimulasyunlar, nokturnal olaylar yaygındır. LQTS1'de cinsiyetin riske katkısı yok-

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Tedavi

Asemptomatik ER EKG paterninin klinik etkileri açık değildir. SCD öyküsü olan tanılı hastalarda ICD implantasyonu önerilmektedir (3). İki veya daha fazla inferior/lateral derivasyonlarda 1mm'lik ST segment yükselmesi ve senkop öyküsü, güçlü bir aile öyküsü (açıklanamayan SCD vakası), yüksek riskli bir ER EKG paterni gösteren veya patojenik mutasyon saptanan asemptomatik bireylerde ICD düşünülebilir. İzole ER EKG paternli asemptomatik hastalarda ICD implantasyonu önerilmez (3).

İzoproterenol infüzyonu, elektrik fırtınasını bastırmada yararlı olabilir. ICD'ye ek kinidin VF'nin sekonder önlenmesinde kullanılabilinir. Fosfodiesteraz III inhibitörü olan silostazolün ERS' unda kinidin tedavisine dirençli VF 'yi başarıyla sonlandırdığı da bildirilmiştir (3,69).

SONUÇ

Kanalopatiler kalbin elektriksel aktivitesini kontrol eden transmembran iyon kanallarını kodlayan genlerdeki veya ilgili proteinlerdeki mutasyonlardan kaynaklanır. İyon kanallarındaki bu işlevsel değişiklikler aksiyon potansiyelinin zamanlamasını ve şeklini bozar ve aritmilerin oluşmasını sağlar. Çoğunlukla genç, yapısal kalp hastalığı olmayan sağlıklı insanları etkiler. Ani kardiyak ölüm nedenlerinden biri olarak kabul edildiklerinden tanı ve tedavileri önem kazanır.

Anahtar Kelimeler: Konjenital aritmi sendromu, ani kardiyak ölüm, genetik aritmiler, iyon kanalları

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