4. BÖLÜM

Mesane Tümörlerinin Sınıflandırılması

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Mesane kanseri dünya çapında yedinci en sık kanserdir, erkeklerde kadınlardan 3-4 kat daha fazla görülür (1). Primer ürotelyal tümörlerin sınıflandırılması ve derecelendirilmesi uzun zamandır tartışma konusudur (2). Birçok derecelendirme sistemi vardır, klinik davranışları en iyi yansıtan patolojik sınıflamaları geliştirme çabalarına rağmen, deneyimli patologlar arasında bile, gözlemciler arası değişkenlik yüksektir ve çoğu olgu ara kategoriye düşer (39-50). Mesane tümörleri için en sık kullanılan derecelendirme sistemleri Dünya Sağlık Örgütü (WHO) tarafından önerilenlerdir. 1973 yılında WHO sistemi tümörleri benign ürotelyal papillom ve 3 farklı derecede (derece 1,2 ve3) karsinom olarak sınıflamayı önermiştir (3). WHO 1973 derecelendirme sisteminin en önemli kısıtlılığı derecelerin net olmayan tanımlarıdır ve spesifik histolojik kriterler içermezler. Aralık 1998'de, WHO ve Uluslararası Ürolojik Patologlar Topluluğu (ISUP) üyeleri mesanenin ürotelyal neoplazilerinin WHO/ISUP konsensus klasifikasyonunu yayınlamışlardır (4). 2004'te WHO ürotelyal tümörler için sınıflamasını yeniden gözden geçirmiş ve WHO/ISUP sistemini benimsemiş, ürotelyal tümörler için yeni birleşik bir derecelendirme sistemi doğmuştur (5). Dünya Sağlık Örgütünün (WHO) ürotelyal sistem tümörleri sınıflamasının 2016 yılındaki dördüncü baskısı, 2004 sınıflandırmasında daha fazla gelişme sunmaktadır, ancak daha fazla veri elde edilene kadar, Avrupa Üroloji Birliği şu anda hem WHO 1973 hem de WHO 2004/2016 sınıflandırmalarının kullanılmasını önermektedir (1, 6, 7).

Son WHO 2016 Sınıflandırması, ürotelyal neoplazmların morfolojisi, farklı diferansiasyon sergilemedeki benzersiz yetenekleri, çok sayıda morfolojik varyantları ve farklı genomik yolaklarının modern bir revizyonudur (Tablo 1) (1).

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genomik instabilite (kararsızlık), tümör derecesinde ve evresinde artış ile ilişkiliydi. İnvaziv ürotelyal karsinomda çok sayıda-multiple tümör baskılayıcı-supresor genler ve onkogenler tanımlanmıştır, ancak kanser gelişimi için bunların gerekli olup olmadığını belirlemek genellikle zordur (45).

Tekrarlayan mutasyonlar TP53, FGFR3, PIK3CA, RB1, TSC-1, APC ve HRAS gibi genlerde meydana gelir; TERT promoter mutasyonları ile birlikte TP53 ve FGFR3, en yaygın olanıdır (46, 47). TERT mutasyonları, mesane neoplazmalarının % 79'unda mevcut olmasına rağmen, klinik sonuçlarla hiçbir ilişkisi yoktur; bununla birlikte, histolojisi örtüşen diğer tümörlerde bu mutasyonun göreceli nadirliği göz önüne alındığında, varlığı büyük tanısal fayda sağlayabilir. Yeni nesil sıralama (sequencing) çalışmaları, ürotelyal tümörlerin mutasyonel manzarasının, tümör başına 300'den fazla mutasyon, 200'den fazla kopya numarası değişikliği ve 20'den fazla yeniden düzenleme-(rearrangement) ile oldukça karmaşık olduğunu göstermiştir (48, 49). Mesane kanserinde en sık değiştirilen yollar arasında rapamisin yolunun PI3K/AKT/memeli hedefi (50-52), FGFR3/RAF/RAS yolu (53), TP53/RB1 yolu (54), immün yanıt kontrol noktası modülatörleri (55, 56) ve kromatin düzenleyen ve yeniden şekillenen genler (57, 58) bulunur. Bu yolları hedef alan yeni terapötik ajanlar geliştirildikçe, terapide gelişmeler olacaktır. Ek olarak, ortaya çıkan veriler, immün modüle edici ajanların ilerlemiş ürotelyal karsinomun tedavisinde umut verici bir role sahip olabileceğini göstermektedir (59).

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