BÖLÜM 18

Hepatoselüler Kanser ve İmmünoterapi

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1. Hepatoselüler Karsinom'a Genel Bakış

Karaciğer kanseri; 2020 yılında dünya çapında yaklaşık 900.000 yeni vaka ile erkeklerde en sık görülen 5. kanser olup kadınlarda ise 9. sırada yer almaktadır (1). Küresel olarak kansere bağlı ölümlerin dördüncü önde gelen nedenidir ve insidansı 2025'te bir milyon yeni vaka öngörüsü ile beraber artmaktadır (2).

Hepatoselüler karsinom (HSK), primer karaciğer kanserlerinin büyük çoğunluğunu oluşturur (2). En sık olarak kronik viral hepatit, alkol tüketimi, alkole bağlı olmayan yağlı karaciğer hastalığı (Non-alcoholic fatty liver disease=NAFLD) ve alkole bağlı olmayan steatohepatit (Non-alcoholic steatohepatit=-NASH) gibi altta yatan bir karaciğer hastalığı zemininde ortaya çıkar. Özellikle NAFLD ile ilişkili HSK insidansının ve prevalansının özellikle Amerika Birleşik Devletleri'nde artması beklenmektedir ve NAFLD'nin önümüzdeki yıllarda en sık görülen neden olması kuvvetle muhtemeldir (3).

HSK'li hastaların yönetiminde "Barselona Klinik Karaciğer Kanseri Evreleme Sistemini (BCLC)" benimsenmiştir. Erken evre HSK için standart tedavi; karaciğer rezeksiyonu, karaciğer transplantasyonu ve ablasyon tedavisidir. Orta evre hastalığı olan ise transarteriyel kemoembolizasyon (TAKE) ve transarteriyel radyoembolizasyon (TARE) için değerlendirilir (4). Erken tanı ve tedavi önemli olmakla birlikte hastaların çoğuna ileri evrede tanı konmaktadır. Ayrıca, erken evre HSK için lokal tedavi alan hastalar yüksek rekürrens riski altındadır (5).

HSK'nin önemli tümör heterojenitesi göstermesi, farklı karaciğer hasarı etiyolojileri ve farklı derecelerde karaciğer fonksiyon bozukluğu ile ilgili olarak farklı bir mikro çevreden ortaya çıkması nedeniyle, farmakolojik tedavisi zordur (6). Makrovasküler invazyon veya

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üzere vasküler endotelyal sistemi hedef alan ilaçları içeren ilaç kombinasyonlarına dayanmaktadır. Birinci basamakta atezolizumab ve bevasizumab kombinasyonunu ile sorafenibi karşılaştıran IMbrave150 çalışmasının sonuçları, deney kolunda PFS ve medyan OS'de önemli katkılar göstermiştir. Kombinasyon, 2020'de FDA tarafından onaylanmış ve sonuçlar, birinci basamakta çığır açarak paradigma değişikliği ile altın standart haline gelmiştir. Lokalize HSK'de lokal tedavilerle kombinasyon halinde ve rezektabl hastalıkta neoadjuvan veya adjuvan tedavi olarak ICI'ların sonuçları beklenmektedir. Öngörücü biyobelirteçler için araştırma, bu tedavi yönteminin daha da geliştirilmesi için oldukça önemlidir. Birkaç istisna dışında, ICI çalışmaları Child-Pugh A'lı hastalarda yapılmıştır. Nivolumabı araştıran CheckMate 040 çalışmasının Child-Pugh B (7 + 8) kohortunun ön sonuçları, Child-Pugh A hastaları için yaklaşık yarı oranında bir RR (%10) göstermiştir. ChechMate 040'taki Child Pugh A ve B hastaları için toksisite yönetilebilir ve ilacı bırakma oranı benzer olsa da, bu bulgular ICI'nın, Child-Pugh evre B'ye sahip seçilmemiş hastalarda kullanılmaması gerektiğini göstermektedir.

ICI'ları tek başına veya diğer ajanlarla kombinasyon halinde araştıran çalışmaların umut verici sonuçlarına rağmen, ilerlemiş HSK hastalarının prognozunu optimize etmek için hala cevap bekleyen sorular vardır. Yanıtı tahmin etmek ve böylece klinisyenlerin tedaviyi kişiselleştirmeye yardımcı olmak için biyobelirteçler tanımlanmalıdır. Sirozlu ve karaciğer fonksiyon bozukluğu olan hasta popülasyonunda ICI'ların güvenliğine ilişkin uzun vadeli veriler olgunlaştırılmalıdır.

Sonuç olarak; günlük pratik ortamında, ICI tabanlı rejimlerin daha çok hastaya etkin bir şekilde kullanılıyor olabilmesi için tedavi stratejilerini optimize etmek üzere daha fazla çalışmalara ihtiyaç vardır.

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