BÖLÜM 20

Pankreas Kanserleri ve Tedavisi

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Giriş

Pankreas kanserleri tüm kanserlere bağlı ölümlerin en sık dördüncü sebebidir ve eğer eğilim mevcut şekilde devam ederse 2030 yılında ikinci sıraya yükselmesi beklenmektedir (1, 2).

Pankreas kanserlerinin %90'ı pankreatik duktal adenokarsinomlardır (PDAC). En önemli risk faktörleri gen mutasyonlarına bağlı ailesel risk, kronik pankreatit, pankreatik kistler ve diabetes mellitustur (3, 4). Diğer risk faktörleri sigara, alkol, obezite, metabolik sendrom ve yaşlılıktır (5).

Hastaların önemli bir kısmına lokal ileri evre ya da metastatik safhada tanı konulur. Bu durumun en önemli sebebi hastalığın lokalizasyonuna bağlı olarak geç semptom vermesidir (6). Pankreas kanserlerinde 5 yıllık sağkalım beklentisi ne yazık ki %10'un altındadır (7). Hatta erken tanı alan ve rezeke edilen hastalarda 5 yıllık sağkalım %31'in altındadır (8). Hastalığın derin lokalizasyonu, agresifliği, tarama testlerinin yetersizliği yüksek mortalitenin en önemli sebepleridir.

Pankreas kanserinin tanısı görüntüleme yöntemleri ile konur (transabdominal ultrasonografi, bilgisayarlı tomografi, manyetik rezonans görüntüleme (MRI), pozitron emisyon tomografisi (PET), Endoskopik Retrograd Kolanjiyo Pankreatografi (ERCP) ve endoskopik ultrasonografi) (9). Bu yöntemlerin bazı kısıtlamaları vardır. Örneğin erken evre pankreas kanserinin tespiti, küçük metastazların tespiti veya peritoneal lezyonların tespiti güç olabilir (10). Karsinoembriyonik antijen (CEA) ve kanser antijeni 19-9 (CA19-9) gibi serum tümör belirteçleri klinik tanıda sıklıkla kullanılır. Ancak bu belirteçlerin pankreas kanseri için sensitivite ve spesifiteleri düşüktür (11). Kodlamayan bir RNA (non-coding RNA, ncRNA), bazı genetik belirteçler (Kirsten fare sarkoma virüs (KRAS), tümör protein 53 (TP53), SMAD4 (small mother against decapentaplegic4) ve sikline bağımlı kinaz inhibitörü 2A (CDKN2A)), dolaşımdaki tümör DNA'sı (ctDNA), dolaşımdaki tümör hücreleri (CTC) ve eksozomlar tümör belirteçleri olarak çalışılmaktadır. Bu belirteçlerin yakın

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İmmünoterapiler

İmmün kontrol noktası (checkpoint) inhibitörleri özellikle yüksek tümör mutasyon yüküne (Tumor Mutational Burden, TMB) sahip hastalarda faydalıdır (64). Ancak bu ilaçların metastatik pankreas kanserindeki çalışmaları hayal kırıklığı yaratmıştır. Yanlış eşleşme onarım (mismatch repair, MMR) eksikliği pankreas kanserlerinde çok nadir izlenir (%1) (65). Pembrolizumab, MMR mutasyonu olan tüm solid tümörlerde FDA tarafından onaylanmıştır. Ancak pankreas kanserlerinin mikroçevresinde sitotoksik T hücre sayısı azdır bu sebeple immün checkpoint inhibitörleri başarılı sonuçlar vermemektedir (66). İmmünomodulatuar ajanlarla immun checkpoint inhibitörleri kombinasyonu çalışmaları devam etmektedir.

Aşılar

Günümüze kadar ileri evre pankreas kanseri tedavisinde çalışması olan iki aşı vardır; GVAXve CRS207 (66). Ancak bu aşıların kullanıldığı ilk çalışmalar olumlu sonuçlar vermemiştir. Bu aşıların immun checkpoint inhibitörleri ile kombine kullanımları konusundaki çalışmalar devam etmektedir.

Sonuç

Pankreas kanserlerinin görülme sıklığı ve mortalitesi son yıllardaki tanı ve tedavi alanındaki gelişmelere rağmen hala oldukça yüksektir. Hastalığın erken evrede yakalanma ihtimali düşüktür. Tek kür şansı cerrahidir ancak başarısı sınırlı olduğu için her hastaya adjuvan kemoterapi verilmelidir. Hastalık başlangıçta potansiyel olarak cerrahi şansına sahipse neoadjuvan tedavi düşünülebilir. Gemsitabin hakimiyetinde geçen uzun yıllar sonrası yeni kombinasyon rejimleri metastatik hastalıkta yer bulmuşlardır. Yeni tedaviler ümit vericidir ancak henüz tedavi standartlarını değiştirememişlerdir. Her kanserde olduğu gibi multidisipliner yaklaşım son derece önemlidir.

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