BÖLÜM
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Radyoaktif İyot Dirençli Diferansiye Tiroid Kanseri: Tanı ve Tedavi Yaklaşımı

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Özet

Diferansiye tiroid kanserli hastalarda yaşam beklentisinin kısaldığı ve tiroid kanserine bağlı ölümlerin en sık görüldüğü grup RAI dirençli (RAID) hastalardır. RAID hastalar genel olarak 4 kategoride toplanır; (1) Başlangıçta RAI tutulumu olmayan metastatik DTK hastaları, (2) Takipte RAI direnci gelişen DTK hastaları, (3) Bazı lezyonlarda RAI tutulumu varken bazılarında RAI tutulumu gözlenmeyen hastalar, ve (4) RAI tutulumu olmasına rağmen progresyon gösteren metastazlı hastalar. Boyun ultrasonografi (USG), bazal toraks bilgisayarlı tomografi (BT), abdomen BT, spinal manyetik rezonans (MR) gibi anatomik görüntülemeler yanında ^{18}F-FDG PET/BT; alternatif tedavilere rehberlik de ederek RAID hastaların takibinde prognostik değere sahiptir. RAID hastada serum Tg ve anatomik/fonksiyonel metastaz takibi yapılarak progresyon hızına göre tedavi yönetimi önerilir; TSH supresyonu ile yakın takip, lokal tedavi, sistemik tedavi, radyonüklid tedavi gibi. Tedavi seçeneklerinin yıllarca kısıtlı kaldığı bu hasta grubunda tirozin kinaz inhibitörlerinin (TKİ) kulanımı umut vaat edici olmuştur. Ayrıca rediferansiyasyon amaçlı kullanılan BRAF ve MEK inhibitörleri ve immünoterapi ajanları alternatif tedavi şansı sağlamaktadır. Son yıllarda hız kazanan moleküler ve genetik araştırmalar sayesinde yakın gelecekte sistemik tedavide yenilikler de mümkün olacaktır.

VB-111, anjiyogenez geçiren endotelyal hücrelere sınırlı etkilerle, hem doku hem de duruma özel, terapötik olarak vasküler hedefleyici bir gendir. Sistemik uygulama, tümör vaskülaritesinin seçici yıkımını sağlar. Kemoterapi ile birleştirildiğinde sinerjik antitümör aktivitesi görülebilir. VB-111'in ileri evre solid tümörlü hastalarda Faz I klinik bir çalışmada güvenli ve iyi tolere edildiği bulunmuştur. İleri progresif RAID 'lı 29 hastayı kapsayan Faz II doz artırıcı bir denemede, iki ayda bir, bir doz 1013 viral partikül alan hastaların %35'i (6/17) 6 aylık bir PFS göstermiştir (98).

Sonuç

Moleküler tıptaki son gelişmeler RAID 'lı hastaların tanı ve tedavisinde büyük ilerlemeye yol açmıştır. Bu ilerlemenin önemli kısmı onkogenik hedeflere yönelik yeni ajanlarla tedaviler ve RAI direncini kırmaya yönelik kombinasyon rejimleridir. Sistemik tedavilerin klinik çalışmalarında uzun süreli PFS bildirilmiş olmasına rağmen, OS açısından bir iyileşme gösterilememiştir ve dahası ilaca bağlı toksisite ve direnç başlıca problemler olarak görünmektedir. Ayrıca, tiroid dokusu en yüksek immünojenik tepkiler veren dokular arasındadır ve böylece antitümör etkinliği arttırmak için yüksek fırsatlar sunar. İmmün hücreler, tiroid kanser hücreleri veya endotel hücrelerini hedefleyen kombinasyon stratejileri içeren akılcı tasarımlı klinik çalışmalar ilerlemiş tiroid kanseri hastaları için en büyük yararı sağlayacaktır. Gelecekteki araştırmalar ayrıca daha iyi moleküler karakterizasyona, farklılaşma sürecine ve sistemik tedavide yeniliğe odaklanabilir.

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