26. Bölüm

Metastatik Tiroid Kanseri Sistemik Tedavisi

Dr. Celal ALANDAĞ[1]

Diferansiye tiroid kanseri bir çok solid tümör ile karşılaştırıldığında mortalitesi daha yüksektir. Genellikle lokal veya lokal-ileri evrede tanı konulmaktadır. Erken evrelerde cerrahi tedavi ile remisyon sağlanabilmektedir. Metastatik evrede geçmişte tek seçenek kemoterapi idi, fakat bu hastalıkta kemoterapinin etkinliği düşüktür. Son yıllarda diferansiye tiroid kanserinde hedefe yönelik ilaçlar ile tedavide başarı oranları artmıştır. Medüller tiroid kanserinde erken evrede cerrahi yeterli olmaktadır. İleri evrelerde sistemik tedavi olarak hedefe yönelik tedaviler daha ön plandadır. Anaplastik tiroid kanseri çok agresif bir tümördür. İnoperabl olan hastalarda beklenen yaşam süresi çok kısadır. Kemoterapi ve hedefe yönelik tedavi seçenekleri kısıtlıdır. Son yıllarda tiroid kanseri tedavisinde immünoterapi gibi yeni tedavi seçenekleri üzerinde çalışmalar devam etmektedir.

DİFERANSİYE TİROİD KANSERİ

Giriş

Diferansiye tiroid kanseri (DTK) tiroide sınırlı ise tedavisi tiroidektomidir. Bölgesel lenf nodu yayılımı olan hastalarda tiroidektomiye ilave olarak boyun lenf nodu diseksiyonu uygulanmaktadır. Metastatik DTK tedavisinde seçilmiş hastalarda tiroidektomi, boyun lenf nodu diseksiyonu ve metastazektomi cerrahisi yapılmaktadır. Metastazektomiye uygun değil ise sistemik tedavi yapılmaktadır. Cerrahi sonrasında risk faktörleri bulunan hastalarda adjuvan radyoaktif iyot (RAİ) tedavisi yapılmaktadır. Radyoaktif iyot tedavisi metastatik DTK tedavisinde de sıkça kullanılmaktadır. Fakat hastaların küçük bir bölümünde tek başına hastalık kontrolünde yeterli olabilmektedir. Tiroid stimülan hormon (TSH) tümörün büyümesini arttırdığı için DTK hastalarında TSH baskılanma tedavisi kullanılmaktadır. Ekzojen tiroid hormonu verilerek negatif geri baskılama yolu ile hipofizden TSH salınımı baskılanmaktadır. Radyoterapi bir diğer tedavi modalitesidir, tiroid kanserinde tümör kitlelerine radyoterapi uygulanmasıyla hastalık kontrol altında tutulabilmektedir. Cerrahi, RAİ, TSH supresyon tedavisi ve radyoterapi ile kontrol edilemeyen metastatik DTK'inde tedavi seçenekleri; kinaz inhibitörleri, immünoterapi ve geleneksel sitotoksik kemoterapidir.

KİNAZ İNHİBİTÖRLERİ

Tümörogenezisde proliferasyon, anjiogenezis, invazyon, metastaz ve apoptozdan kaçış önemli aşamalardır. Büyüme faktörleri hücre üzerinde reseptörlerine bağlandıktan sonra hücre içinde birçok kinaz aktive olmaktadır. Kinaz mutasyonları, kinazların büyüme faktörü uyarısı olmaksızın aşırı çalışmasına bu da tümörogenezise neden olmaktadır. Diferansiye tiroid kanserinde serin kinaz olan BRAF, tirozin kinaz olan RET ve RAS ki-

[1] Dr., Sivas Numune Hastanesi dralandag@hotmail.com

bir doksorubisin/adriamisin diğer tedavi seçenekleridir. Performansı iyi olmayan hastalarda adriamisin veya haftalık paklitaksel gibi tek ajan tedavileri tercih edilebilmektedir (50).

Hedefe Yönelik Tedaviler

Bir faz 2 çalışmada, BRAF V600E mutasyonu bulunan ATK tanılı 16 hastaya dabrafenib günde 2 kez 150 mg ve trametinib 2 mg günde bir kez verilmiştir. Objektif cevap oranları %69 bulunmuş ve 7 hastanın cevabı halen devam ettiği belirtilmektedir. Median GSK ve PSK sürelerine halen ulaşılamamıştır fakat 12 aylık tahmini olarak sırasıyla %80 ve %79 olduğu bildirilmektedir. En sık görülen yan etkiler: halsizlik, ateş ve bulantıdır (51). Diğer bir hedeflenebilir mutasyon NTRK muasyonudur. Faz 1 çalışmada NTRK mutasyonu olan solid tüm tümörler dahil edilmiş, bu hastalardan 7 kişide tiroid kanseri mevcuttur (bir kişi ATK tanılıdır), tüm hastalara NTRK inhibitörü olan larotrektinib verilmiştir, tüm grupta objektif cevap oranı %80, tiroid kanser tanılı hastalarda objektif cevap oranı %100, 1 hastada tam cevap bildirilmiştir. Grad 3-4 yan etki oranı %5'tir. Bu çalışmadan sonra NTAK mutasyonu olan tüm solid tümörlerde larotrektinib FDA onayı almıştır (52). Multikinaz inhibitörlerinden lenvatinib ile ilgili küçük çalışmalar yapılmıştır etkinlik bildirilmektedir fakat kılavuzlara girmemiştir (53).

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