Bölüm
29

KEMİK METASTAZLARINDA YENİ SİSTEMİK TEDAVİLER

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GİRİŞ

Meme kanseri kadınlarda en sık görülen kanser olup, en sık metastaz yeri kemiktir. Kemiğe metastaz sonucunda ağrı, patolojik kırık, hiperkalsemi, spinal kord basısı gibi iskelet ilişkili olaylar gelişebilmektedir. Bu durum kanser hastalarında önemli morbidite ve morbidite nedeni olup, yaşam kalitesini olumsuz etkilemektedir. Kemik metastazlarına yaklaşım, ağrı kontrolü, iskelet ilişkili olayların önlenmesi ya da minimalize edilmesi ve tümör kontrolünün sağlanmasını içermektedir. Bu amaçla analjezikler, cerrahi, radyoterapi, kemiğe yönelik radyonüklit tedaviler ve termal ablasyon yöntemleri uygulanabilmektedir. Sistemik tedavide ise bisfosfonatlar (zoledronik asid, ibandronik asid, pamidronad, vs), RANK ligand inhibitörü (denosumab), Src inhibitörleri (dasatinib, bosutinib, saracatinib), cathepsin-K, kemokin reseptör tip-K ve GPNMB inhibitörleri kullanılmaktadır. Bu bölümde kemik metastazı olan meme kanserinde uygulanan sistemik tedavilerden bahsedilecektir.

Kemik metastazları özellikle akciğer, meme ve prostat kanserlerinde en sık görülen uzak metastaz bölgesidir (1). Osteoklastik ve osteoblastik aktivite artışına bağlı kemik yapım ve yıkımı artmakta ve iskelet ilişkili olaylarla sonuçlanabilmektedir (2, 3).

Evre 4 meme kanseri olan hastaların %65-75'inde kemik metastazları gelişmektedir. Kemik metastazı geliştikten sonra medyan sağkalım 19-25 aydır (4, 5). Kemikte kanser hücreleri kemik formasyonu ve rezorpsiyonunu bozan osteolitik, osteoblastik ve/veya mikst kemik lezyonlarına yol açmaktadırlar.

Kemik metastazlarına yaklaşım hasta ve metastaz ile ilişkili faktörlere dayanmaktadır. Hastalığın yaygınlığı, metastazın yaşam kalitesi üzerine etkisi, hasta-

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viye eklenen klodronat, çalışma girişinde 50 yaşından büyük kadınlarda iskelet ve iskelet dışı metastazsız sağkalımı iyileştirmiştir (her iki durumda da $p<0.05$). 36 klinik denemeden 22.982 hastayı içeren büyük bir meta-analizde, adjuvan bisfosfonatların menopoz sonrası kadınlarda uzak nüksü önemli ölçüde azalttığını tespit etmiştir (% 18.4'e karşılık % 21.9) (74).

Denosumabın adjuvan kullanımı ile ilgili yapılan D-CARE çalışmasında ise, 67 aylık medyan izlemede, kemik metastazsız sağkalım (HR 0.97,% 95 CI 0.82-1.14, p = 0.70), hastalıksız sağkalım (HR 1.04, % 95 CI 0.91-1.19, p = 0.57) ve genel sağkalım (HR 1.03,% 95 CI 0.85-1.25) avantajı sağlamadığı görülmüştür (75).

Kuzey Amerika ve Avrupa'da orta-yüksek nüks riski olan meme kanseri hastalarında bisfosfonatların (zoledronat, klodronat veya ibandronat) adjuvan kullanımı önerilmektedir.

SONUÇ

Kemik metastazı olan meme kanseri hastalarında amacımız yeterli ağrı kontrolünü düzenlemek, kemik hasarını azaltmak ve işlevi korumak, iskelet ile ilişkili olay riskini en aza indirmek, ve lokal tümör kontrolünü sağlamaktır. Tedavi seçimi hastadaki spesifik semptomlara, metastazın ortaya çıkış şekline, tümörün histolojik tipine, hastanın performans statüsü ve tedavi seçimine göre şekillenmelidir. Yaşam beklentisi düşük olan, patolojik kırık ve/veya spinal kord basısı gibi iskelet ilişkili olayları olmayan hastalarda yalnızca takip yapılabilmektedir. İzole, semptomatik tek kemik metastazlarında lokal tedaviler düşünülmelidir. Litik metastazlarda sistemik tedavide antirezorptif ajanlar bisfosfonatlar ve denosumab kullanılmalıdır. Strontium-89, Samarium-153 ve Radyum 223 ağrı kontrolünde etkinlikleri gösterilmiş ajanlardır.

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