Bölüm
25

KASTRASYONA DİRENÇLİ METASTATİK PROSTAT KANSERİNDE SİSTEMİK TEDAVİ

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GİRİŞ

Tanı ve tedavide ilerleme kaydedilmesine rağmen prostat adenokarsinoma erkek Batı popülasyonunda yüksek oranda kalmaya devam etmektedir ve kansere bağlı ölümlerin yaklaşık % 20'sinden sorumludur [1]. Çok sayıda çalışma, prostat kanserinin, nükleer reseptör ailesine ait ligand bağımlı bir transkripsiyon faktörü olan androjen reseptörü (AR) tarafından yönlendirildiğini göstermektedir [2 , 3]. Ligandın yokluğunda, AR, chaperone proteinleri ile komplekslenmiş hücre sitoplazmasında bulunur. Ligand bağlanmasından sonra, nükleusa translokasyon yapar ve DNA-bağlama alanında (DBD) ve ligand bağlama alanında (LBD) bulunan özel motiflerin etkileşimini takiben bir homodimer oluşturur. Hücre çekirdeğinde dimerleşmiş AR, androjen hedef genlerinin proksimal veya daha distal intra ve intergenik bölgelerinde bulunan düzenleyici bölgelerdeki bilişsel DNA yanıt elemanlarını tanır [4 , 5]. Daha sonra, transkripsiyonel olarak aktif bir kompleks oluşturur ve aşağı akış gen ekspresyonunu uyarır [2 ,3]. Fosforilasyon, asetilasyon ve ubikikasyon gibi translasyon sonrası modifikasyonlar AR fonksiyonunu daha da ince ayarlar [7 , 8]. Bazı liganddan bağımsız aktivite gösteren birkaç AR ek varyantı da mevcuttur. Vakaların yaklaşık% 90'ında, prostat kanseri hala organla sınırlıdır veya tanıda yalnızca lokal olarak ilerlemektedir [3]. Klinik evre ve prostat spesifik antijen (PSA) seviyelerini içeren birden fazla parametreye bağlı olarak, aktif sürveyans, lokal radyoterapi veya prostatektomi tercih edilip edilmeyeceğine karar verilir [10]. Hastalık prostat dışına yayıldıktan sonra dolaşımdaki testosteron düzeylerini azaltmak için cerrahi veya kimyasal kastrasyon yoluyla androjen yoksunluk tedavisi (ADT) sıklıkla kullanılır [2 , 3]. Ne yazık ki, yanıt sadece geçicidir ve çoğu hasta ADT'ye direnç geliştirir ve 18 ila 36 ay sonra kastrasyon dirençli prostat kanserine (KDPK) doğru ilerler [3 , 9 ,11]. AR

- Potansiyel seçenekler arasında tümör büyümesinin androjenik stimülasyonu etkileyen ilaçlar (abirateron, enzalutamid), sipuleucel-T ile hücresel immünoterapi, taksan kemoterapisi (dosetaksel, kabazitaksel) ve kemik hedefleyen ve bir radyoizotop olan radyum-223 bulunur.

Seçilmiş vakalarda bir rolü olabilecek daha eski yaklaşımlar arasında antiandrojenler, antiandrojen yoksunluğu, adrenal steroidojenezin ketokonazol veya steroidlerle baskılanması, östrojenler ve progesteronlar bulunur.

- Aksiyal iskeletteki osteoblastik lezyonlar, vakaların çoğunda baskın metastaz bölgesidir.

Kemik metastazı olan erkekler için, bir osteoklast inhibitörünün kullanılması, iskelet komplikasyonları riskini azaltmak için sistemik tedaviye ek bir yardımcıdır (patolojik kırık, epidural omurilik sıkışması). Ek olarak, eksternal radyoterapi veya radyofarmasötikler kemik metastazlarından dolayı bir veya daha fazla bölgede şiddetli ağrı çeken erkekler için önemli semptom hafiflemesi sağlayabilir.

- Büyük bilimsel gelişmeler, son yıllarda gelişmiş prostat kanserini tedavi etmek için mevcut olan ilaçların cephaneliğini arttırmıştır. Bu bileşiklerin hastalığın erken evrelerinde etkinliğini araştırmak ve ayrıca bunları hastalarda sırayla birleştirmek ve kullanmak için çalışmalar devam etmektedir. Bu gelişmelere rağmen, ek terapi seçeneklerine hala yüksek bir tıbbi ihtiyaç vardır.

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