Bölüm
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SANTRAL SİNİR SİSTEMİ TÜMÖRLERİNDE İMMUNOTERAPİNİN YERİ

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GİRİŞ

Glioma en sık görülen primer malign beyin tümörüdür, yetişkinlerde vakaların yaklaşık % 80'ini oluşturmaktadır. Glial kaynaklı tümörler, glial fibril asidik protein pozitif (GFAPC) astrositik tümörler, oligodendrogliomalar, ependimomlar ve alt tiplerin bir karışımını içeren histolojik alt tipe göre sınıflandırılır[1]. Bunlardan, GBM olarak adlandırılan astrositik glioma derece IV, tanı sonrası ortalama 14,6 ay sağkalıma sahip olup ortalama 5 yıllık hayatta kalma oranı % 5'in altında olan en yaygın ve en ölümcül alt tiptir[2,3]. Rezeksiyon, radyoterapi ve kemoterapiyi birleştiren mevcut tedaviler istilacı sınırlardan / inoperabl cerrahi yataktan kaynaklanan rezidüel hastalığa dayalı tümör nüksünü önleyememektedir. Gen tedavisi gibi yeni yaklaşımlara, hedefleyici kemoterapötiklere ve / veya radyoterapötik yöntemlere rağmen yeni tanı konulan GBM hastalarının tedavisinde daha iyi tedavi seçeneklerine duyulan ihtiyaç son 10 yılda değişmeden kalmıştır. Ayrıca, tekrarlayan GBM'li hastalar için standart bir tedavi yoktur. SSS'de metastatik tümörlerin prevalansı GBM vakalarının sayısını fazlasıyla aşmaktadır, ancak genel sağkalım (GS) benzer şekilde düşüktür. Bu makalede, SSS'deki agresif tümörleri kalıcı olarak kontrol etmek için aşılama, immun kontrol noktası blokajı, adoptive T hücre transfer gibi yeni ve / veya genişletilmiş yaklaşımlar ve bunların etkinliği incelenecektir.

SSS TÜMÖRLERİ VE İMMÜNOSUPRESYON

Santral sinir sistemi'nin (SSS) başlangıçta, subkutan veya intramüsküler büyümeye kıyasla beyine intrakranal olarak enjekte edilen sıçan osteosarkom hücreleri-

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gu olarak, ikili PD-L1 ve CTLA-4 blokajına karşı dirençli olan uzun süreli klinik öncesi melanomlar, farelerin yaklaşık %33'ünde aşılamayla ortadan kalkmıştır; ancak aşılama anti-PD-L1 ile kombine edildiğinde bu oran farelerde %80'e çıkmaktadır.[21] Subkütanöz tümörlere yönelik bir klinik öncesi bağımsız çalışmada, PD-(L)1 ve CTLA-4 inhibisyonuyla kombine edilen aşılama, ikili ve monoterapötik tedaviyle kıyaslandığında farelerde tümör rejeksiyonu ve sağkalımı iyileştirmiştir.[94] Geçmişteki çalışmaların çoğunluğu SSS dışı tümör modelleri üzerinde gerçekleştirildiğinden dolayı, gelecekteki klinik öncesi ve klinik çalışmaların bu tedavi yaklaşımlarını GBM hastalarında değerlendirmesine ihtiyaç duyulmaktadır.

SONUÇ

GBM anatomik lokalizasyonu nedeniyle tedavisi zor olan aynı zamanda geleneksel tedavilere dirençli olan oldukça fazla immunsüoresif bir tümördür. Beyinin metastaik tümörleri GBM' e kıyasla 20 kat daha sık görülür. Beyin tümörleri için geçmiş immünoterapötik çabalar ağırlıklı olarak ümit verici bağışıklık aktivitesi ve klinik tepkiler elde etmiş olan terapötik aşılamaya odaklanmıştır. Gen tedavisi de dahil olmak üzere mevcut umut vaat eden yaklaşımları daha da fazla test etme ihtiyacı yeni nesil terapötikler (yani, IDO inhibitörleri / STING agonistleri), ve yeni immünoterapötik kombinasyonları test etmeyi geliştirir. Antitümör immün yanıtları inflamasyon bağlamında gerçekleştiğinden, tümör ve tedaviye bağlı inflamasyonun ilave etkisi/sinerjisi beyin ödemine ve nörolojik tehlikeye neden olma olasılığı tanınmalıdır. Deksametazon rutin olarak beyin ödemini önlemek için kullanılmasına rağmen, immünoterapötik çalışmalarda kullanımı da aşırı derecede immünsüpresif olduğu için düşük dozlarla sınırlıdır. Yeni nesil CNS immünoterapileri, eğer daha etkiliyse, beyin ödemi ve nörolojik tehlike için daha da yüksek bir risk taşıyabilir, bu nedenle immünosüpresif olmayan anti-enflamatuar yaklaşımların belirlenmesi önemlidir. VEGF inhibitörü bir antikor olan bevacizumab'ı kullanmak sekonder enflamasyonu azaltan, şu anda GBM immünoterapisi ile kombinasyon halinde araştırılan bu yaklaşımlardan biridir. (NCT02336165, NCT01814813). Gelecekteki çalışmalar, hastalara sürekli gelişen seçenekleri sunmaya odaklanmalı, ayrıca CNS malignitelerinin özel olarak hedeflenmesi gereken benzersiz immünosüpresif fenotiplere sahip olduğunu kabul etmelidir.

Anahtar Kelimeler: Gliom, immünoterapi, aşılama,SSS,

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