Bölüm 10

PARANEOPLASTİK NÖROLOJİK SENDROMLAR

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GİRİŞ

Paraneoplastik nörolojik sendromlar (PNS) sinir sistemini etkileyen nadir bir hastalık grubudur. Altta yatan eşlikçi tümörün uzak etkisiyle oluşur; bası, metastaz, metabolik ve nutrisyonel eksiklik, enfeksiyon, koagülopati ya da kanser tedavisinin yan etkileri gibi mekanizmalar ile değil,otoimmün kökenli mekanizmalar ile gelişir (Graus & Dalmau, 2007, Honorat & Antonie, 2007).Sinir sisteminin serebral korteksten spinal kord, nöromusküler kavşak ve kasa kadar herhangi bir kısmını etkileyebilir. Bu alanlardan birini ya da birkaçını aynı anda tutabilir. Herhangi bir tipte tümör ile birlikte görülebilmesine rağmen küçük hücreli akciğer kanseri (KHAK) ilk sırada olmak üzere en sıkover kanseri, meme kanseri, nöroendokrin tümörler, timoma ve lenfoma seyrinde görülür(Darnell & Posner, 2006). PNS görülme sıklığı nörolojik sendrom ve altta yatan tümöre göre değişir. KHAK'li hastalarda sıklığı %9'a çıkabilirken (Gozzard& ark., 2015), solid tümörlerde genel sıklığı %1'den azdır(Pelosof & Gerber, 2010). Vakaların %80'inde tümör klinik olarak aşikar olmadan önce PNS bulgu ve belirtileri ortaya çıkar (Honorat & Antonie, 2007). PNS'ler nadir görülmesine rağmen erken tanınması, PNS tipine göre erken müdahale ile semptomların stabillenmesi veya iyileştirilmesi, ve altta yatan tümöre erken müdahale edilebilmesi açısından önemlidir (Vedeler& ark., 2006).

PARANEOPLASTİK NÖROLOJİK SENDROMLARIN İMMÜNOLOJİK MEKANİZMASI

PNS'lerin patogenezi tam net olmamakla birlikte, genel anlamda immün aracılıklı oldukları kabul edilir. Sistemik tümör hücreleri, kan-beyin bariyeri sayesinde bağışıklık sisteminden muaf tutulan 'nöronlara has antijenleri' eksprese edebilirler. Ektopik olarak eksprese edilen bu ortak antijenler,'anti- nöronal antikorların' üretimine yol açabilmektedir. Bu antikorların varlığı nörolojik sendromun paraneoplastik kaynaklı olduğunun göstergesidir.

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Dermatomiyozit

Dermatomiyozit inflamatuvar bir miyopatidir. 40- 50 yaşta en sık görülmekle birlikte her yaşta hastayı etkileyebilir. Subakut başlangıçlı, proksimal kas zaafı en önemli klinik belirtisidir. Serum kreatin kinaz seviyesi 10 kat ve üzeri artmıştır. Başta gottron papüleri ve heliotropik erupsiyonlar olmak üzere tipik cilt bulguları izlenebilir (Callen, 2010). Kas histopatolojisinde perifasiküler atrofi ve fibrozis, perimisial inflamasyon, kompleman aracılı mikroanjiopati dikkat çeker (Amato& Barohn, 2009) .

Dermatomiyozitte malignansi sıklığı %20-25 arası raporlanmıştır (Callen & Wortmann, 2006). Dermatomiyozit için tipik bir paraneoplastik antikor tanımlanmamıştır (Titulaer & ark., 2011). En sık over, akciğer, pankreas, mide, kolorektal kanserler ve lenfomalar ile görülür (Callen, 2001). Lenfoma riskinin dermatomiyozit tanısı sonrası ilk 1 yıl artmış olduğu, diğer kanser türlerinin riskinin de ilk bir yıl en yüksek olup sonrasında azaldığı, over, pankreas ve akciğer kanseri riskinin 5 yıl sonunda bile ortalamanın üzerinde kaldığı gösterilmiştir (Callen, 2001). Çocuk hastalarda splenomegali ya da lenfadenopatiye özellikle dikkat edilmelidir (Morris & Dare, 2010). Erişkin tüm hastalarda detaylı tarama yapılmalıdır. Kadın hastalarda pelvik USG, mamografi, toraks ve abdomen BT, erkek hastalarda toraks ve abdomen BT,50 yaş altı olanlarda testis USG yapılmalıdır. 50 yaş üstü tüm hastalarda kolonoskopi önerilmektedir. Tarama ilk 3 yıl, yılda 1 defa tekrarlanmalıdır. Sonrasında eğer yeni bir semptom ya da uyarıcı bulgu gelişirse tekrarlanmalıdır (Callen, 2006, Callen, 2001, Titulaer & ark. 2011).

İlk taramaları negatif olan PNS hastalarında tarama tekrarı:

Güncel öneri PNS ve paraneoplastik antikoru olan hastalarda, ilk incelemelerden 3-6 ay sonra taramaların tekrarlanması, sonrası ise 4 yıla kadar her 6 ayda 1 düzenli taramaların tekrar edilmesidir. Akciğer grafisi ya da tümör belirteçleri ile tarama önerilmemektedir (Vedeler & ark., 2006, Titulaer & ark., 2011)

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