Bölüm
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NÖROENDOKRİN TÜMÖRLER İLE AİLESEL SENDROMLAR VE GENETİK POLİMORFİZM İLİŞKİSİ

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GİRİŞ

Gastroenteropankreatik nöroendokrin tümörler (GEP-NET), nöroendokrin enterokromafin hücrelerden köken alan ve farklı biyolojik davranışlar gösteren epitelyal neoplazmlardır. Gastrointestinal sistemde özellikle pankreas ve ince barsaktan köken alırken; akciğer ve timüs gibi organlar da nöroendokrin tümörlerin tespit edildiği diğer yerlerdir. Nöroendokrin tümörler (NET) daha önceki yıllarda nadir görülürken, son yıllarda tanı yöntemlerindeki ilerlemelerle (endoskopi ve kesitsel görüntüleme yöntemlerinin yaygın kullanımı ile) sıklığı giderek artmaktadır. Obendorfer, 1907'de nöroendokrin neoplazmları, gastrointestinal sistem karsinomlarından ayırarak literatüre 'karsinoid' terimini kazandırmış ve bu tümörler uzun süre karsinoid olarak anılmıştır. NET'lerin farklı organlarda gelişimi tedavi ve prognoz açısından büyük fark yarattığından klinisyenler bu tümörleri herkesçe kabul edilen sınıflandırmalar içine koymakta zorlanmaktadırlar. Günümüzde NET'ler pankreatik NET'ler ve diğer NET'ler (genellikle karsinoid) olarak ikiye ayrılır. NET'ler çoğunlukla benign olmakla birlikte, agresif seyirli de olabilecek tümörlerdir.

Nöroendokrin tümörleri oluşturan en büyük grup GEP-NET'lerdir (>%50) (1). GEP-NET'ler gastrointestinal sistem (GİS) tümörlerinin %2'sini oluşturur (2). Bütün neoplazmlar arasında yaklaşık %5'lik insidanslarıyla nadir tümörler oldukları düşünülse de, son yıllarda insidansları artmaktadır (3,24/100.000 Kuzey Avrupa, 5,25/100.000 ABD) (3). NET insidansı 1973-2004 yılları arasında 5 kat artmıştır (4). NET'ler diğer kanserlerle (over, meme, özofagus, endometrium gibi) birlikte bulunabilen tümörlerdir. NET'lerin üçte ikisi GİS'de, dörtte biri akciğerlerde, geri kalanı ise diğer endokrin dokularda görülür. GİS'de en sık

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endokrin hücre hiperplazisi ve tümör ilerlemesinde yer alan yolaklar hakkında bazı bilgiler edinmeye başlamıştır. Ana işlemler, transkripsiyon faktörleri ile gen regülasyonu, p53 yolu boyunca strese tepki, DNA replikasyonunun regülasyonu ve onarımı içerir. Spesifik genleri ve daha da önemlisi, endokrin tümör başlangıcında rol oynayan genlerin temel fonksiyonlarını bulmak zor olmaya devam etmektedir. Ailesel endokrin tümör sendromlarını tanımak, yalnızca genetik yatkınlığı değil aynı zamanda tümör patogenezini anlamak için önemli bir yoldur ve hem biyolojik araştırma hem de farmasötik hedeflerin tanımlanması için çok sayıda hayvan modeli mevcuttur. Son 15 yılda, endokrin tümörlere yatkın olan sendromların çoğu kapsamlı bir şekilde tanımlanmış ve incelenmiştir, bu nedenle klinisyenlere MEN hastalıklarının ayırıcı tanısı için önemli araçlar ve klinik takip ve tedavi için kılavuzlar sağlamıştır (61,62).

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