Bölüm
42

Multiple Endokrin Neoplaziler

Prof. Dr. Havva Belma KOÇER
Doç. Dr. Volkan ÖTER

Ana Konular

- Giriş
- Multıple Endokrin Neoplazi Tip 1
- Multiple Endokrin Neoplazi Tip 2
- Multiple Endokrin Neoplazi Tip 4

GİRİŞ

Multiple endokrin neoplaziler (MEN) vücudun endokrin sistemini etkileyen bir grup bozukluk olup tek bir hastada iki veya daha fazla endokrin bezi tutan tümörler ile karakterizedir. Bu tümörler iyi huylu (benign) veya kötü huylu (malign) olabilirler. Bu bozukluk daha önce "çoklu endokrin bez adenopatisi" ve "pluriglandüler sendrom" olarak adlandırılmış olup günümüzde ise MEN isimlendirilmesi tercih edilmektedir.

Dört majör MEN tipi vardır: Tip 1 (MEN-1, Wermer sendromu) ve Tip 2 (TİP 2 A, MEN-2A, Sipple's sendromu), Tip 3 (MEN-2B veya diğer adıyla MEN Tip 2B) ve Tip 4 (MEN-4).

Her bir form, spesifik endokrin bezlerde tümör gelişimi ile karakterizedir. MEN sendromlarının klinik belirtileri, tümörlerin bölgeleri ve salgı ürünleri ile ilişkilidir. Her bir tümörün tanı ve yönetimi, MEN olmayan hastalardakine benzerdir. Tüm MEN tipleri genellikle otozomal dominant kalıtım gösterirler. MEN sendromunda her bir fenotipi dikte eden ve dolayısıyla bu bozukluklarla ilişkili çeşitli anormalliklere yol açan çoklu olası kodon değişiklikleri vardır.

MULTIPLE ENDOKRİN NEOPLAZİ TİP 1

Tanımı

MEN-1 otozomal dominant kalıtım gösteren bir bozukluktur ve 100.000'de 2–3'lük bir prevalansa sahiptir. Otopsi serilerinde görülme sıklığı %0.22-0.25 civarındadır. MEN-1'e neden olan gen, kromozom 11'in (11q13) uzun kolunda yer alır ve 10 eksondan (9 kodlama) oluşan supressör bir gendir. Sporadik veya ailesel formu vardır. MEN-1 sendromunun özelliklerine sahip, ancak aile öyküsü olmayan hastalar, MEN-1'in sporadik formunu oluşturur. MEN-1 olan hastalar belirli coğrafi bölgeye ait değildir. Irksal veya etnik yatkınlıkları yoktur. Oluşumunda rol alan herhangi bir risk faktörü bilinmemektedir.

MEN-1 sendromu ile ortaya çıkan 20'den fazla (endokrin sistem kaynaklı olan veya olmayan) tümör gelişimi görülebilmekte olup bunlardan sık görülenleri; anjiyofibromlar (%88), kolajenomlar (%72), adrenal kortikal tümörler (%35), tiroit adenomlar (%10) ve yüz epandimomlarıdır (<%5). MEN-1, tümör baskılayıcı geninin germline inaktive edici mutasyonları sonucunda paratiroid bezi (%95), pankreas (%40), hipofiz bezi tümörleri (%30) ile sonuçlanır (Tablo 1).

değişikliklere dayanan hastalığa sahiptir. Son zamanlarda, siklin-bağımlı kinaz (CDK) inhibitör geni CDKN1B'deki germline mutasyonlarının, hem insan MEN-1 hem de MEN-2 sendromlarının özelliklerine sahip farelerde bir MEN-X'e neden olmasından sorumlu olduğu belirlenmiştir. Daha sonra da, MEN-1 gen mutasyonu olmayan MEN-1 özellikli birçok hastada CDKN1B geninde mutasyon tarif edilmiştir. MEN-1 ile ilişkilendirilen tümörlerin %3'ünde CDNK1B mutasyonlarına sahip olduğu ortaya konulmuştur. Bugüne kadar, MEN-1 benzeri tümörler bulunan hastalarda 8 farklı heterozigot CDNK1B mutasyonu tanımlanmıştır ve bu durum insanlarda MEN-4' ün, sıçanlarda otozomal resesif olan MEN-X' in aksine, otozomal dominant bir bozukluk olduğunu göstermektedir .

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