BÖLÜM
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HEREDİTER PRİMER HİPERPARATİROİDİ

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Giriş

Primer hiperparatiroidi (PHPT) 6. dekadta pik yapan, %90 sporadik olarak tespit edilen ve sık rastlanan endokrin hastalıklardandır. Vakaların yaklaşık %80'inde neden, soliter benign paratiroid adenomudur. PHPT'li vakaların %10'ununda ise, genetik ve herediter özellikler saptanır. Bu vakalarda sıklıkla paratiroid bezlerin tümünün etkilenmesi söz konusudur. Daha genç yaşta olan bu vakaların genelinde aile hikayesi mevcuttur. Ancak aile hikayesinin varlığı için detaylı bir sorgulama ve araştırma yapılmış olması gerekmektedir (1).

Sık görülen herediter formlarda [Multipl endokrin neoplazi (MEN) Tip 1, MEN 2A, MEN 4, hiperparatiroidizm - çene tümörü sendromu (HPT-ÇT)] PHPT' nin yanı sıra diğer endokrin ve endokrin dışı neoplaziler de görülebilmektedir. Daha nadir olarak herhangi bir sendromla ilişkili olmadan da [ailesel izole hiperparatiroidizm (AİHPT), ailesel hipokalsiürik hiperkalsemi (AHH), neonatal ciddi hiperparatiroidizm (NCHPT) ve otozomal dominant ılımlı hiperparatiroidizm (ODIHPT)] görülebilir (2).

Son yıllarda, çok sayıda spesifik gen mutasyonlarının çeşitli kalıtsal PHPT tiplerinden sorumlu olduğu tespit edilmiştir (Tablo-1). Bugüne kadar, kalıtsal PHPT'ye yol açan 11 farklı patojenik gen tanımlanmıştır. Hastalık genellikle otozomal dominant geçişe bağlı olarak meydana gelir. Ancak tanımlanmamış genetik nedenler ve tanımlanmış genlerin penetransının ve ekspresyonunun çeşitliliği hakkındaki bilgilerin tam olmamasından dolayı bu hastalığın gerçek sıklığı bilinmemektedir [1,2].

Tümör baskılayıcı genlerin inaktivasyonu (MEN 1, MEN 4, AİHPT, HPT-ÇT) ya da hücre çoğalmasını sağlayan onkogenlerin aktivasyonu (MEN 2A) veya parathormonun (PTH) sekresyonunu kontrol eden mekanizmadaki eşik değerin bozulması (AHH, ODIHPT, NCHPT) sonucunda gelişen PHPT'nin herediter formları aşırı ve uygun olmayan PTH sekresyonuna neden olur. Herediter primer hiperparatiroidinin (HPHPT) teşhisi uygun genetik testlerin uygulanması ile

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yaşamı tehdit eden hiperkalsemiye yol açabileceğinden intavenöz izotonik ve bifosfonat ile tedavi edilmelidir. Ardından total paratiroidektomi acilen planlamalıdır. Tipik olarak patolojide ağır hiperplastik paratiroid bezleri saptanır. Yakın zamanda NCHPT vakalarının bazılarında kalsimimetik tedavi denenmektedir (42).

Otozomal Dominant Ilımlı Hiperparatiroidizm

ODIHPT, herediter PHPT'nin sendromik olmayan bir varyantıdır. AİHPT ile benzerlik gösterir. CASR'ün intrastoplasmik kısmında izole inaktivasyon mevcuttur. Ancak fenotipte rölatif hipokalsiüri, hipomagnezemi ve nefrolitiasiz yoktur. Tedavisi paratiroidektomidir (43).

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