BÖLÜM 82

SEREBROTENDİNÖZ KSANTOMATOZİS

Pembe SOYLU ÜSTKOYUNCU [1]

GİRİŞ

Serebrotendinöz ksantomatozis (CTX); otozomal resesif geçişli, safra asit sentezi metabolizması bozukluğu olup, kanda kolestanol, dokularda özellikle santral sinir sistemi, tendonlar, akciğer, kemik, cilt ve gözde kolesterol ve kolestanolunun birikimi ile karakterize, lipid depo hastalığır. [1-4]

İlk kez 1937 yılında tanımlanmıştır.[5] Ortalama tanı yaşı 35 yaş olup genellikle erişkin dönemde tanı konulan, pediatrik hastalık olarak tanımlanmıştır.[1]

CYP27A1 genindeki homozigot veya compound heterozigot mutasyonlar sonucunda ortaya çıkar. Sterol 27-hidroksilaz enzimini kodlayan gen, 2q33'te yerleşmiştir.[6] Günümüzde çok sayıda mutasyon tanımlanmıştır. [2,7] Genotip fenotip ilişkisi yoktur. Aynı mutasyona sahip aile bireyleri arasında bile farklı fenotipik varyasyonlar bildirilmiştir. Özellikle santral sinir sistemi beyaz cevherini tuttuğu için nörolojik bozukluklar arasında lökodistrofiler başlığı altında yer almaktadır.[1-4]

Kesin olarak bilinmemekle birlikte dünya genelinde prevelansının 5/100000'den az olduğu tahmin edilmektedir. [2,7,8,9] Kızlarda erkeklere göre daha sık görülür. İnsidansının Amerika'da 1:72000-1:150000 olduğu şeklinde yayınlar.[10,11] mevcuttur. En yüksek insidans yaklaşık olarak 1/108'dir. [12-14] ve Fas kökenli Yahudilerde, aktif genetik tarama programlarının bulunduğu İsrail'de bildirilmiştir.

Etiyoloji ve Patogenez

CTX sterol 27-hidroksilaz genindeki anormallikten kaynaklanır. [15] Enzim defekti sonucunda kolik asit ve kenodeoksikolik asit sentezlenemez. 5β-kolestan-3α, 7α, 12α-triol, C27 konumunda hidroksile edilemez ve karaciğerde birikir. Bu metabolit C25 pozisyonunda endoplazmik retikulumda alternatif bir yolla metabolize edilir. İleri hidroksilasyonlar, C22 veya C23 pozisyonunda, idrarda glukuronidler olarak bulunan karakteristik safra alkollerinin senteziyle sonuçlanır. 5β-kolestan-3α, 7α, 12α-triol dışındaki safra asidi öncülleri birikir. Safra asit öncülü olan 7α - hidroksi - kolest - 4 - en - 3 - one muhtemelen 7-α-dehidroksilasyon içeren bir yolla kolestanole dönüştürülür. CTX'li hastaların safra asidi sentezi hızının azalması nedeniyle, safra asitleri ile kolesterol 7α-hidroksilazın normal geri besleme inhibisyonu bozulur. Bu, safra asidi prekürsörlerin-

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preimplantasyon genetik tanı mümkündür. [19] Etkilenen bireyler ve ailelerine genetik danışmanlık verilmelidir.

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