BÖLÜM 92

ÇOCUKLUK ÇAĞI LÖKODİSTROFİLERİ

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GİRİŞ

Lökodistrofiler santral sinir sitemi (SSS) beyaz cevherini etkileyen herediter heterojen bir hastalık grubudur.[1] Son dönemde ileri görüntüleme yöntemleri ve ileri genetik testler (Whole Exom Sequencing (WES), Whole Genom Sequencing (WGS) sayesinde lökodistrofiler hakkında daha fazla bilgi sahibi olabilmekteyiz.

Manyetik rezonans görüntüleme (MRG) ve ileri görüntüleme teknikleri hastalığın tanısı, prognozu ve tedaviye yanıtın değerlendirilmesinde oldukça yararlı bilgiler vermektedir. Bunun yanı sıra patoloji temelli tanı da teşhiste, prognozu belirlemede ve tedaviye yanıtı değerlendirmede etkili bir yöntemdir.[1]

Lökoensefalopati terimi SSS'de beyaz cevheri yaygın ve baskın olarak tutan tüm hastalıkları tanımlamak için kullanılmaktadır. Bu hastalıklar kalıtsal (herediter) ya da edinsel olabilir. Günümüzde yüzden fazla tanımlanmış kalıtsal lökoensefalopati mevcuttur. Lökoensefalopatiler, genetik lökoensefalopatiler ve lökodistrofiler olmak üzere iki gruba ayrılır.[2]

Lökodistrofiler primer olarak SSS'i etkileyen hastalıklar iken, lökoensefalopatiler sistemik hastalıklar olup, sekonder olarak SSS'i beyaz cevher tutulumu olan hastalıklardır.[3,4] Bunun yanısıra son zamanlarda genetik lökoensefalopati yerine "lökodistrofi" terimi yaygın olarak kullanılmaktadır.[5]

Lökodistrofilerin tanısında MRG önemli bir tanı aracıdır. Bilgisayarlı tomografi (BT) beyaz cevherde hipointensiteyi gösterebilir ancak ayrıntıları belirlemede oldukça yetersizdir. Beyaz cevher maturasyonu ve miyelinizasyonunu ilk 6 ayda T1 ağırlıklı serilerde, 6-18. ylarda T2 ağırlıklı daha iyi değerlendirilir.[1]

Normal beyin dokusu miyelinizasyonu çocuklarda oldukça iyi bilinen belli bir sıra dahilinde yaklaşık ilk iki yaşta tamamlanır.[6,7] Miyelinize olmuş beyin yapıları gri cevherle karşılaştırıldığında T1 serilerde hiperintens (beyaz), T2 serilerde ise hipointens (siyah) görülür.[6,7] Buna karşılık demiyelinize alanlar ise T1 ağırlıklı serilerde hipointens (siyah), T2 ağırlıklı serilerde hiperintens (beyaz) izlenir.

T2 ağırlıklı serilerde 1,5 yaşına gelmiş bir çocukta serebral beyaz cevher hala hiperintens (beyaz) görülüyorsa altta yatan bir beyaz cevher hastalığı göz önünde bulundurulmalıdır.[6,7] Buradaki patoloji miyelin yapımıdaki yetersizlik ya da beyaz cevheri etkileyen myelini bozan başka bir durumdan kaynaklanabilir. (**Resim 1.**)

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terozigot mutasyon sonucu oluşmaktadır. Klinik olarak geç çocukluk ya da erken adolasan dönemde başlayan progresif nörolojik disfonksiyon, serebellar ataksi, kognutif bozulma,-tendon ksantomları, prematür ateroskleroz, katarakt, periferik nöropati,myopati bulguları izlenir. Kronik diyare ve uzamış yenidoğan sarılığı öyküde bulunabilir. Aşil tendonu, beyin ve akciğer dokusunda kolestrol ve kolestrol esterlerinin birikimi söz konusudur. Teşhiste serum kolestanol düzeyleri ve safra alkollerinin yüksekliği önemlidir. Kranial MR'da serebral ve/veya serebellar atrofi yanısıra serebellum, beyin sapı ve bazal ganglionlarda fokal hiperintens alanlar izlenmektedir. Tedavide oral kenodeoksikolik asit tedavisi hastalığın progresyonunu yavaşlatmada etkilidir.

L-2 Hidroksi Glutarik Asitüri

OR, geçişli L-2 OH glutarat dehidrogenez enzimini kodlayan L2HGDH geninde homozigot mutasyona bağlı oluşan bir hastalıktır. Kromozomun 14q21 bölgesinde yer alır. Hayatın ilk yılında psikomotor retardasyon ve epilepsi bulguları ile başlar, piramidal ve serebellar bulgular, spastisite, bilşsel kayıp ile ilerler. Hastalar makrosefaliktir. Hastalarda beyin tümörü insidansı yüksektir.[73] Kranial MRG'de subkortikal beyaz cevher tutulumu, serebellar atrofi, putamen, globus pallidus ve dentat nükleus tutulumu ön planda izlenir. (**Resim 7)** İdrar organik asit incelemesinde hidroksiglutarik asit atılımı oldukça yüksektir. Mutasyonun gösterilmesi ile tanı doğrulanır. Prenatal tanı amniotik sıvıda L-2 hidroksi glutarik asit ölçümü ile mümkündür. Spesifik bir tedavisi yoktur. Yavaş ilerleyen bir seyri vardır.

Klasik Konjenital Musküler Distrofi (Merozin Negatif)

Hipotoni, güçsüzlük ve serebral hemisferlerde yapısal bozukluk olmaksızın demiyelinizasyon ve kreatin kinaz (CK) enzim yüksekliği ile karakterizedir. Motor gelişim basamaklarını geç kazanır. Kromozom 6q22-23'te lokalize LAMA2 geninde merozin (alfa2 laminin) olarak bilinen merozin eksikliği vardır. Kranial MR'da yaygın beyaz cevher tutulumu izlenir. PMD ayırıcı tanısında düşünülmelidir, ancak bu hastalarda nistagmus izlenmez.

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