BÖLÜM 88

KARACİĞERİN DİĞER KALITSAL METABOLİK HASTALIKLARI

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METABOLİK KARACİĞER HASTALIĞIN KLİNİK ÖZELLİKLERİ

Metabolik karaciğer hastalıkları çeşitli şekillerde karşımıza çıkabilir (Tablo 1) (3).

Tablo 1. Metabolik karaciğer hastalığının başlangıç özelikleri (3)

Semptomlar	Bulgular
Kusma	Asit
Gelişme geriliği	Abdominal distansiyon
Hipoglisemik semptomlar	Hepatomegali
Hiperamonyemik semptolar	Splenomegali
Nöbetler	Sarılık
Nörolojik ya da motor yetenek kayıpları	Kısa boy
	Kardiyak disfonksiyon
	Katarakt
	Dismorfik bulgular

Genç hastalardaki bazı metabolik karaciğer hastalıkları, akut enfeksiyonlar ve zehirlenmeler gibi diğer hastalıkları taklit edebilir. Buna karşılık, metabolik karaciğer hastalığı olan daha yaşlı bir hasta kronik karaciğer hastalığı semptomlarıyla başvurabilir. Metabolik hastalıklar diğer birçok bozukluğu taklit edebildiğinden, yüksek bir şüphe indeksi gereklidir. Kolestaz ile başvuran herhangi bir bebeğin değerlendirmesi metabolik karaciğer hastalığını dikkate almalıdır. İlerleyici nöromüsküler hastalığı, gelişimsel gecikmesi veya gelişimsel kilometre taşlarında gerilemesi olan herhangi bir hasta da değerlendirilmelidir. Tüm yaşlardaki hastalarda yükselmiş serum aminotransferaz seviyeleri, hepatomegali, asidoz, hipoglisemi, asit, kanama diyatezi, hiperammonemi, koma, tekrarlayan kusma veya kilo alamama durumlarında metabolik karaciğer hastalığı hemen düşünülmelidir.

Ayrıntılı bir öykü genellikle metabolik karaciğer hastalığı olasılığını artırabilir. Akraba evliliği, çoklu düşük veya erken bebek ölümleri öyküsü metabolik bir bozukluğu düşündürebilir. Tanı konmamış karaciğer hastalığı, ilerleyici nörolojik veya kas hastalığı veya tanı konmamış gelişimsel gecikmeleri olan yakın akrabalar da şüphe uyandırmalıdır. Belirli gıdaların tanıtılması, üre döngüsü bozuklukları, galaktozemi veya fruktozemi hastalarında olduğu gibi semptomların başlangıcıyla ilişkili olabilir. Spesifik diyet kaçınmalarının öyküsü açıklayıcı olabilir. Metabolik karaciğer hastalığında önerilen başlangıç tarama testleri Tablo 2'de listelenmiştir. (4).

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mortalite ile ilişkilidir, bu nedenle klinik uygulamada onun yerine ERT ve SRT etkili bir şekilde kullanılmaktadır. Nörolojik belirti veya semptomların başlamasından önce başvuran tip 3 hastalarında hala düşünülmektedir (178). GH'ın gelecekteki potansiyel tedavisi gen terapisi ve enzim geliştirme terapisini içerebilir, bu olasılığı araştıran çalışmalar bulunmaktadır (179).

Makrofaj aktivasyonunun biyobelirteçleri (kitotriosidaz ve CCL-18) veya glukozilsfingozin (lyso-Gb1) tedavinin etkilerini izlemek için kullanılabilir. Başlangıç seviyeleri değişken olduğundan, her hasta kendi başlangıç seviyesine göre izlenmelidir (115,180).

SONUÇ

Gaucher hastalığının klinik özellikleri değişkendir ve hastalık her yaşta ortaya çıkabilir. Hastalığın tedavisinin temel hedefleri semptomların ortadan kaldırılması, geri döndürülemez komplikasyonların önlenmesi ve genel yaşam kalitesinin iyileştirilmesidir. Tedavisi fenotipik değişiklik, hastalığın belirtileri, şiddeti ve ilerlemesindeki değişkenlik nedeniyle her hastaya göre bireysel düzenlenir. Hastalık şüphesi olan ailelere ve tüm hastalara genetik danışmanlık ve hastalık hakkında eğitim verilmelidir.

Spesifik olmayan semptomlu hastalarda, hastalığın farkında olunmaması nedeniyle tanı gecikebilir. Zamanında tanı ve uygun erken tedavi, gelişecek komplikasyonları önleyebilir veya şiddetini azaltabilir. Bu nedenle hastalığın erken teşhisi çok önemlidir. Nörolojik komplikasyonların varlığı prognoz ve tedavi açısından önemli sonuçlar oluşturur, nörolojik komplikasyonlar tanıdan sonra en kısa sürede belirlenmelidir. Tip 1'in klinik seyri ve yaşam beklentisi değişkendir. Buna karşılık, tip 2 olan hastaların çoğu yaşamlarının ilk yıllarında ölür. Tip 3, Tip 1'den daha şiddetli ve agresif olabilir ancak ilişkili fenotiplerin geniş bir yelpazesi vardır.

Rekombinant ERT ile SRT klinik olarak önemli belirtileri olan ve nöropatik olmayan gaucher hastaları için tercih edilen tedavilerdir. ERT ve SRT, akut nöropatik tip 2 GH olan hastalar için önerilmez. ERT'ler etkin, yan etki açısından güvenli ancak maliyeti yüksek tedavilerdir. Ayrıca kemik hastalığı, kanama eğilimi venörolojik hastalığı yönetmek için destekleyici bakım önlemleri gereklidir.

Gaucher hastalarının ömür boyu takibi yapılmalı ve kişiye özel tedavi hedefleri belirlenmelidir. Tedaviye yanıt değişir, ancak genel olarak iyileşmeler tedavinin başlamasından sonraki altı ay içinde gerçekleşir. Tedaviye yanıt dalak ve karaciğer hacimlerinin azalması, trombositopeni ve aneminin düzelmesi, yorgunluğun azalması gibi durumları içerir. ERT ve SRT kan-beyin bariyerini geçemediği için, nörolojik ve pulmoner tutulum açısından tedavide mükemmel sonuçlar elde edilemediği görülmüştür. Gelecekte, bu genetik hastalığı gen terapisiyle tedavi etmek de mümkün olabilir.

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