28.
BÖLÜM

ALLOGREFT VASKÜLOPATİSİ HAYVAN MODELLERİ

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Akut organ reddi, gelişen cerrahi teknikler, yeni immünsüpresif tedaviler ve organ koruma teknikleri ile transplantasyonda önüne geçilmeye başlanmış bir sorundur. Transplantasyonda uzun dönem sağ kalımı azaltan kronik organ reddi ise halen önümüze çıkan en önemli zorluklar arasındadır. Kronik organ reddi sebepleri içerisinde yer alan ve uzun dönemde sağ kalımı etkileyen en önemli faktörlerden biri ise allogreft vaskülopatisidir. Allogreft vaskülopatisi kalp transplantasyonu sonrasında ilk 5 yıl içerisinde %50'ye varan oranlarda görülmektedir (1, 2)

Allogreft vaskülopatisi, immün ve immün dışı (iskemi, reperfüzyon, viral enfeksiyon, inflamasyon, hipertansiyon) sebeplerle greft arterlerinde meydana gelen intimal hiperplazi, ilerleyici stenoz ve kronik iskemi sonrasında greft reddine kadar uzanan bir süreç olarak karşımıza çıkar (1, 3, 4).

Vaskülopati, koroner arterler ve majör dallarından önce allogreftin arteriollerinde başlayan bir süreçtir. Bu sebeple başlangıç aşamasında fark edebilmek ancak endomiyokardiyal biyopsiler ile mümkündür. Hayvan deneyleri ise vaskülopatinin patogenezi anlamada büyük ölçüde yardımcı olmaktadır.

ALLOGREFT VASKÜLOPATISI NEDENLERI

İmmün Sebepler

Vaskülopati gelişiminde immün dışı sebeplerin çok büyük etkisi olduğu belirtilse de alloimmün yanıtın vaskülopatiyi başlatan sebep olduğu düşünülmektedir. Vaskülopati gelişiminde hem hümoral hem de hücre aracılı immün

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teknikle anostomoz edilir. Anostomoz hattında darlığı önlemek için 2-4mm kadar cuff aortotomi hattından anostomoz öncesi rezeke edilir. Soğuk ve sıcak iskemi zamanının 45 dakikadan fazla uzamamasına dikkat edilir. Greft abdominal palpasyon, ekokardiyografi ve elektrokardiyografi ile monitörize edilir.

Primat Modeli (Cynomolgus Maymunu)

Primat modeli uygulaması insana en yakın gen yapısı, anatomik ve fizyolojik benzerlikleri ile oldukça önemli avantajları olan bir model iken etik kaygıları, yüksek maliyetleri, ileri düzey deneyim gerektirmesi, bakımının zor olması, pratik olmayışı, erişim zorluğu ve yeterli miktarda ve hızlı çoğalamaması sebebiyle oldukça dezavantajlı bir modeldir.

Pierson ve arkadaşlarının yaptığı çalışmada heterotopik kalp transplantasyonu tekniği uygulanmıştır (52). Donör kalbin aortası alıcının abdominal aortuna ve donör pulmoner arteri alıcıda inferior vena cava'ya anastomoz edilmiştir. Benzer teknik vimentin molekülünün akut ve kronik organ reddi ve vaskülopati üzerine etkisinin araştırıldığı Azimzadeh ve arkadaşlarının çalışmasında da kullanılmıştır (20). Primat modelleri daha çok akut ve kronik transplant rejeksiyonunun mekanizmasının anlaşılmasında uygulanmıştır.

Hayvan modelleri, transplante greftlerde vaskülopatinin patojenezinin anlaşılması ve sürecin geciktirilmesi açısından yapılması gerekenler konusunda çok değerli bilgiler sağlar. Araştırmacı kullanacağı modeli, hipotezindeki deneysel amacına ve modellerdeki sınırlamalara göre seçmelidir. Aynı zamanda kullanılacak modelin seçilmesi hususunda araştırma yapılacak merkezin fiziki şartları ve ekip deneyimi çok önemlidir.

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