Bölüm 13

ENDOMETRİOZİS HORMONLAR VE GENETİK

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Endometriotik odak sanıldığının aksine steroit bir organ değildir. Endometrioma klonalite bakımından diğer benign ovarian kistlerden farklıdır. Odaklar gelişimlerinin belli bir aşamasında reseptör bakımından aktif iken ilerleyen evrelerde ve renk kaybına uğrayan odaklarda bazı reseptörler kaybolmakta ya da ekspresyonları azalmaktadır. Retinoik asit gibi bazı enzimlerin kofaktörleri genetik olarak odaklarda defektif olabilmektedir. Bir genden ziyade gen zincirleri defektif olabilmekte ve ekspresyon özellikleri değişmektedir. Endometriomalarda ve hafif/orta derece peritoneal endometriozis olgularında yapılan cerrahi girişimler resptiviteyi genler üzerinden düzeltmekte ve gebelik şansını artırmaktadır. DPE'deki bir odak rezeksiyondan sonra veya tıraşlamadan sonra rezistan olduğu medikal bir ajana cevap verir hale gelmektedir. İnflamatuar ve HOXA genlerdeki ekspresyon değişiklikleri ötopik endometriumu fizyolojik implantasyon aşamasından uzaklaştırarak subfertiliteye yol açabilmektedir. **Editorial**

Özet

Endometriozis, sıklıkla reprodüktif yaştaki kadınlarda görülen, menapoz veya ooferektomi sonrasında gerileyen, östrojen bağımlı bir hastalıktır. İnsanlarda endometrial doku, menstruel siklus boyunca hem östrojen hem de progesteron etkisi altında düzenli değişim gösterir, bu nedenle endometrial hücreler, genetik rekombinasyon hatalarına karşı çok hassastır. Çeşitli genetik ve çevresel faktörler, endometriozis etyolojisinde öneme sahiptir. Endometriozisin genetik yanı ile ilgili çok önemli ipuçları olmasına karşın, hangi genetik mekanizmaların hastalıktan sorumlu olduğu henüz netliğe kavuşturulamamıştır. Ötopik endometrial dokuda, tümör baskılayıcı genler ile onkogenlerin ekspresyonlarındaki değişiklikler, endometrial hücrelerin uterus dışında yaşama ve çoğalmasına yatkınlık yaratmaktadır. Endometriozisin genetik karakterinin gün ışığına çıkartılması ve reseptör düzeyinde hormonal etkilerin ortaya konması, hastalığın tedavisindeki başarının da anahtarı olacaktır. Bu derleme, son gelişmeler eşliğinde endometriozisten sorumlu tutulan aday genler ve hormonlar gözden geçirilmiştir.

Giriş

Endometrial stromal hücreler (ESH), peritoneal mezotelyuma implantasyona yatkınlıkta en kritik hücrelerdir. Endometrial hücrelerin genetik farklılıklarının, implantasyon yatkınlığına etkisi herediter olduğu iddia edilmektedir (1). Simpson ve ark. tarafından yapılan çalışmada, birinci derece akrabasında ciddi endometriozis olan kadınlarda, ailesinde endometriozis olmayan kadınlara göre 6 kat daha fazla hastalık riski mevcuttur (2). Ciddi endometriozis'i olan 10 kadından birinin kızında

lerin çoğalmasını, yapışmasını ve apopitoza direnç göstermesine zemin hazırlayabilir. Endometriozisli hastalarda, hastalıkla ilişkili sabit bir gen polimorfizmi veya mutasyonu, gösterilememiş olsa da, üzerinde çalışılan birçok aday gen mevcuttur ve yakın gelecekte endometriozisin genetik yönünün daha net bir biçimde ortaya konulacağı açıktır.

Tablo 1: Endometriozis'in patogenezisinde yeri olan aday genler ve ürünleri

Gen	Ürün
HOXA-10	Transkripsiyon faktörü
MMP 3, 7, 9	Matriks metalloproteinaz'lar
17-βHSD-2	Hidroksisteroid dehidrojenaz tip 2 enzimi
C-MYC	Transkripsiyon regülatörü
BAX	Apoptozis
BCL-2	Anti-apopitozis
PTEN	Tümör baskılayıcı gen
mTOR	Onkogen
AKT1	Onkogen
4EBP1	Tümör baskılayıcı gen
CYP1A1/ 1B1	Sitokrom 1A1/ 1B1 enzimi
CYP450c17α	17α Hidroksilaz ve 17,20 Liyaz enzimleri
CYP45019a1	Aromataz enzimi
HOXA-11	Transkripsiyon faktörü
KRAS	Onkogen
Galaktoz 1-P üridil transferaz	Galaktoz 1-fosfat üridil transferaz enzimi
Glutatyon S-transferaz M1/T1	Glutatyon S-transferaz enzimi
TGF-β1	TGF-β1 sitokini
P53	Tümör baskılayıcı gen
N-asetil transferaz 1/2	N-asetil transferaz tip 1/2 enzimi

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