

TÜTÜN VE AKCİĞER İMMÜNOLOJİSİ

6. BÖLÜM

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Giriş

Tütün kullanımı ne yazık ki dünya çapında yaygın olup, erişkin toplumun 1/3'ünün tütün kullandığı raporlanmıştır (1). Sigara, puro, pipo, elektronik sigara, vb. gibi ürünlerin tüketimi esnasında solunan tütün dumanında toksik, mutajenik ve karsinojenik etkileri olan 5000'den fazla kimyasal maddenin bulunduğu bilinmektedir. Tütün dumanındaki ana emisyon maddeleri arasında, nikotin, tar, karbon monoksit, karbon dioksit, formaldehit, amonyak, reaktif oksijen türevleri (ROS), reaktif nitrojen türevleri (RNS), serbest radikaller gibi immün disfonksiyona sebep olabilecek pek çok toksin yer almaktadır (2). Prevalansını azaltmaya yönelik bütün çalışmalara rağmen, dünyada her yıl yaklaşık 6 milyon kişi tütün kullanımına bağlı ölmektedir (3). Yaklaşık 600.000 kişi ise pasif maruziyetin yarattığı etkilerden dolayı ölmektedirler. Kronik obstrüktif akciğer hastalığı (KOAH), kanser, kardiyovasküler hastalıklar ve hipertansiyonun patogeneğinde yer almak dışında tütün kullanımı kronik inflamatuvar bileşeni olan romatoid artrit, Crohn hastalığı, psöriasis ve aterosklerozis gibi pek çok sistemik hastalığın gelişiminde tanımlanmış risk faktörüdür. Ayrıca, tütün kullananların mikrobiyal enfeksiyonlara duyarlılığının arttığı (solunum yolu enfeksiyonla-

rı, periodontit, bakteriyel menenjit gibi) ve yara iyileşmelerinin bozulduğu görülmektedir (4, 5). Bu sebeplerle, tütün dumanının immün homeostazi bozduğu bilinmektedir, ancak mekanizmaları hala net olarak açıklığa kavuşturulamamıştır.

Akciğer İmmünolojisine Genel Bakış

Akciğerlerin epitel yüzey alanı yaklaşık bir tenis kortu büyüklüğünde olup vücudumuzdaki en büyük epitelyal yüzeydir. Bu özellik göz önüne alındığında, gün içinde solunan hava ile birlikte alınan çok sayıda enfeksiyöz ajan, toksik gaz ve ince partiküllü maddelerin yarattığı tehdide meydan okuması gerekmektedir. Bunun içinse doğal ve edinsel immünitelyi içeren oldukça geniş bir yelpazeye sahip olan konak savunma mekanizmaları geliştirilmiştir. Alveolar ve kapiller membran bariyerleri gaz alışverişi için önemlidir; toksik ve enfeksiyöz patojenlerin hasar verici etkisinden korunmaları gereklidir.

Bakteri, virüs veya fungal patojenler (veya onların patern-ilişkili moleküler proteinleri [PAMPs]) ve çevresel allerjenler öncelikle membrana bağlı, sitozolik ve/veya endozomal doğal sensörler veya patern tanıyan reseptörler (PPRs) tarafından algılanır. Solunum epitel hücreleri hava yolu lümen içi antijenleri ile altta yatan havayolu

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Sonuç olarak, sigara dumanının Treg düzeyleri üzerine etkisi tam net değildir. Muhtemelen Treg hücre alt tipleri arasındaki dengesizlik pro-inflamatuvar alt tip lehine olması KOAH patogenezinde rol oynarken, bazı sigara kullananlarda Treg sayısının yüksek olması o hastaların solunum yolu enfeksiyonlarına yatkınlıklarını artırabilir.

B hücreler

B hücreler antikor ve sitokin salınımından sorumludurlar ve antijen sunum sürecinde yer alırlar. İnsan ve deneysel çalışmalardan elde edilen veriler sigara dumanının B hücre gelişiminde, fonksiyonunda ve immünooglobulin üretiminde baskılayıcı yaptığını önermişlerdir (112, 113). KOAH'lılarda küçük hava yollarında artmış sayıda B hücre olduğu gösterilmiş, ancak sağlıklı bireylerle karşılaştırıldığında KOAH'lıların periferik kanlarında hafıza B hücrelerinin daha düşük sayıda olduğu izlenmiştir (113, 114). Bu bulgularla uyumlu olarak sigara dumanı maruziyetinin B hücre farklılaşması sürecini çok erken bir evrede baskılayabildiği, fare kemik iliğinde pre-B ve pro-B hücrelerinde belirgin aşağı doğru regülasyon gösterilerek doğrulanmıştır (115, 116). Ek olarak sigara dumanına maruziyet immünooglobulin üretimini de baskılamaktadır. IgA, IgG ve IgM'nin sigara kullananların tükürüğünde ve periferik kanında azaldığı gösterilmiş olmakla birlikte bu baskılayıcı etki IgE sentezini etkilememektedir. Aksine sigara kullananların kanlarında IgE düzeyleri artmıştır (117, 118).

Sonuç olarak, sigara kullanımının hava yollarında B hücre depolanmasını arttırdığı; periferik kanda hafıza B hücre sayısını azalttığı; Ig A, IgG ve IgM salınımı azalttığı ama aksine IgE üretimini arttırdığı gösterilmiştir.

Sonuç

Sonuç olarak çok sayıda kanıt göstermiştir ki hem doğal hem de edinsel immünite sigara dumanı maruziyetine duyarlıdır. Sigara dumanı çok sayıda farklı pro-inflamatuvar, oksidatif ve karsinogenik etkilere sahip bileşenler içeren kimyasal

bir karışımdır ve bu yüzden bazen de maruziyet sonrası çelişkili etkiler izlenmektedir. Tütün immünolojik homeostazı bozmakta, çeşitli paradoks etkilere ve hastalıklara sebep olmaktadır. Sigara dumanı bir taraftan normal savunma fonksiyonunu azaltırken bir yandan da patolojik immün yanıtı artırabilmekte, neticede maruz kalan kişide yararlı değil her zaman zararlı etkiye sebep olmaktadır. Örneğin sigara dumanı genellikle enfeksiyonlara yönelik immün yanıtı zayıflatırken paradoks olarak otoimmüniteyi desteklemektedir. Sigara dumanının yarattığı etkilerin altında yatan immünoopatolojik mekanizmaları hâlâ net değildir ve ileri araştırmalara ihtiyaç vardır.

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