



BÖLÜM 1

BOTULİNUM NÖROTOKSİNİN TARİHÇESİ

Turan POYRAZ¹

"Bütün maddeler zehirdir, zehir olmayan madde yoktur. Doğru doz, zehiri ilaçtan ayırrır."

Dr. Paracelsus (1493-1541)

I. BOTULİNUM NÖROTOKSİNİN YAPISAL VE TERAPÖTİK ÖZELLİKLERİ

Botulinum Nörotoksin (BoNT) ya da diğer adıyla 'sihirli toksin' ile istenmeyen intoksikasyonlar nadiren görülmesine karşın, yaşanan kayıplar halkın ve tıp camiasında endişe uyandırmaya yetmiştir. BoNT, Clostridium botulinum bakterisi tarafından üretilen bir nörotoksindir (1, 2). Clostridium botulinum, çubuk şeklinde, gram pozitif, anaerobik bir bakteridir. Bu bakteriden üretilen nörotoksin, tehlaklı bir gıda zehirlenmesi olan botulizmden sorumludur. Günümüze kadar sekiz farklı serotip nörotoksin (A, B, C1, C2, D, E, F ve G) tanımlanmıştır (2, 3). Nörotoksinin A ve B tiplerinin insanda hastalığa neden olduğu bilinmektedir. Yine bu iki tip, daha uzun etki süreleri nedeni ile tıbbi ve terapötik olarak kullanılmaktadır. Temel etki mekanizması; Toksin, hemaglutininlerin ve nonhemaglutininlerin moleküller bir kompleksinde bulunmaktadır ve bakteriden tek bir zincir olarak salınır. Daha sonra sinaptik terminal için bağlanma alanını içeren bir ağır zincire ve toksinin aktif kısmı olan, metalloproteaz içeren bir hafif zincire böülüner. Sinapsta toksin, Çözünebilir NSF Ek Protein Rezeptör ('Soluble NSF Attachment Protein Receptor' SNARE) proteinini parçalar. Böylece toksinin sinaptik yarıktan çıkışını engeller. Toksin, presinaptik asetilkolin salınımını durdurur, böylece kas kasılmasıandan sorumlu sinir uyarılarını önler (4).

¹ Öğr. Gör. Dr., İzmir Ekonomi Üniversitesi, Sağlık Hizmetleri Meslek Yüksekokulu, Yaşlı Bakım Bölümü
Serbest Hekim, turanpoyraz@gmail.com



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