

# BÖLÜM 13

## AKROMEĞALİ

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### GİRİŞ

Akromegali, somatik büyüme ve proporsiyonun bozulmasıyla giden olağanüstü bir klinik sendromdur. Eski tarihlerden beri doktorlarda merak uyandırmıştır. Bununla birlikte, Pierre Marie 2 hastasını gözlemleyerek ve başkalarının önceden tarif ettiği 5 hastayı farkederek hastalığın ilk klinik tanımını ancak 1886'da yayınlamıştır<sup>1</sup>. Akromegali, büyüme hormonu (GH) ve insülin benzeri büyüme faktörü-1'in (IGF-1) kontrolsüz sekresyonundan kaynaklanır. Amerika Birleşik Devletleri'nde hipofiz tümörlerinin yıllık insidansı yılda milyon nüfus başına 45 vakadır<sup>2</sup>. Akromegalinin bu vakaların yaklaşık %25'ini oluşturduğunu varsayarsak, bozukluğun insidansı milyonda 10 vaka olarak hesaplanır.

Akromegali hipofizer ya da ektrahipofizer hastalıklardan kaynaklanabilir<sup>3</sup>. Hastalığın etyolojisinden bağımsız olarak, hastalık GH ve IGF-1 yüksekliği ve hipersomatotropizm belirtileri ve bulgularıyla karakterizedir<sup>4</sup>. Akromegali hastalarının %95'inden fazlası kontrolsüz GH salınımı yapan, bir hipofizer adenom nedeniyle gelişir<sup>5</sup>. GH salgılayan adenomların %60'ı yoğun veya seyrek boyanan sitoplazmik GH granülleri içerir ve yavaş (yoğun granüllü) ya da hızlı (seyrek granüllü) büyürler<sup>6</sup>. GH hücresi ve prolaktin (PRL) hücresini mix içeren adenomlar 2 farklı ayrı tip hücreden oluşmaktadır, somatotroplar GH, laktotroplar PRL eksprese eder<sup>7</sup>. Bimorf tümörler, orta derecede yüksek serum PRL seviyeleri ile akromegaliye neden olur. Asidofil kök hücre adenomları monomorf ortak GH ve PRL kök hücresinden kaynaklanan ve her iki hormonu da eksprese eden tümörlerdir<sup>8</sup>. Genellikle hızla büyürler ve invazivdirler, baskın klinik akromegali yerine hiperprolaktinemi olabilir.

Buna karşılık, monomorf mammomatotroph hücre adenomları hem GH hem de PRL eksprese eden tek bir olgun hücreden oluşur. Serum PRL düzeyleri sıklık-

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yapılmış bir çalışmada<sup>14</sup> akromegalili kadınların yaş ve cinsiyet uyumlu kontrollele karşılaştırıldığında daha yüksek ölüm riski gösterdiği görülmüştür.

Daha önceki çalışmalarda bildirilen aşırı mortalite, öncelikle iskemik kalp hastalığı ve serebrovasküler hastalık gibi kardiyovasküler hastalıklar nedeniyledir, malignitelerden daha az etkilenmektedir<sup>121</sup>. Son zamanlardaki çalışmalarda akromegalide kanserin önde gelen ölüm nedeni olduğu bildirilmiştir<sup>119,120,122</sup>. Bu da muhtemel belirli bir kanser riskindeki artıştan ziyade, hastalığın ve buna bağlı komorbiditelerin daha iyi kontrol altına alınmasıyla daha uzun yaşam beklentisi olmasıyla ilişkili görülmektedir. 1195 akromegalili hasta içeren, 1997'den 2013'e kadar takip edilen Tayvan'da yapılmış bir kohort çalışmasında, 87 yeni tanı kanser hastası gösterilmiştir<sup>123</sup>. Bu sonuca göre kanser insidans hızı 1000 kişi-yılda %10.6 olarak hesaplanmıştır. Bununla birlikte, akromegali ile en çok ilişkili iki kanserle ilgili çalışmalar<sup>103,124</sup>, yani kolon ve tiroid kanseri, bu riskin klinik olarak anlamlı olmayabileceğini öne sürmektedir. 178 hasta ve 356 kontrol karşılaştırıldığında, kolorektal polipler akromegali hastalarının %67'sinde ve kontrol grubunun %24'ünde bulunmuştur (p < 0,001), ancak histolojik alt tiplerde fark yoktur<sup>125</sup>.

Özetle, akromegali erkeklerde kadınlara göre daha genç yaşta ortaya çıksa da, kadınlarda hem insidans hem de mortalite riski artmış görünmektedir. Biyokimyasal kontrol, glukoz metabolizması, OSA, kardiyovasküler hastalık ve VF'de iyileşmeleri yansıtabilecek şekilde hasta sonlanımı ile ilgili en güçlü tahmin edici olmaya devam etmektedir. Bununla birlikte, yapısal kalp ve eklem değişikliklerini düzeltmek olası değildir. Akromegali hastalarında gözlenen mortalitedeki düşüş daha etkili tedaviler kullanmakla ilişkili gibi durmaktadır. Biyokimyasal kontrol sağlanmasıyla mortaliteyi arttıran kardiyovasküler ve respiratuvar komorbiditeler azalıyor gibi durmaktadır. Tiroid malignitesi sıklığı akromegali hastalarında, akromegali olmayanlardan daha fazla değildir. Tanıda kolonoskopi ile tarandıktan sonra, ileri testler gerekliliği genel popülasyonla benzerdir.

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