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METASTATİK ALK VE ROS-1 POZİTİF HASTALIKTA SİSTEMİK TEDAVİ SEÇENEKLERİ

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GİRİŞ

Küçük hücreli dışı akciğer kanseri (KHDAK) olan bir grup hastada 2.kromozomun inversiyonu yani echinoderm mikrotubule bağlı protein benzeri 4 (EML4) geninin 5' ucu ile anaplastik lenfoma kinaz (ALK) geninin 3'ucu yan yana gelerek yeni bir füzyon onkogeni olan EML4-ALK'i oluşturur [1]. Bu füzyon onkogen yeniden düzenlemesi, hem in vitro hem de in vivo olabilir ve KHDAK'nin farklı bir klinikopatolojik alt kümesini tanımlar. KHDAK 'lerin yaklaşık yüzde 5'inde bulunur [2]. EML4-ALK füzyon onkojeni veya varyantlarını içeren tümörler, hiç veya hafif sigara öyküsü, genç yaş; signet halkası veya asiner histolojisi olan adenokarsinom dahil olmak üzere spesifik klinik ve patolojik özelliklerle ilişkilidir. ALK gen düzenlemeleri epidermal büyüme faktörü reseptörü (EGFR) ve Kirsten sıçan sarkoması viral onkojen homolog (KRAS) mutasyonları ile karşılıklı mutasyondur [3]. Bu füzyon geninin KHDAK'de taranması önemlidir, çünkü "ALK pozitif" tümörler (yeniden düzenlenmiş bir ALK gen / füzyon proteinini barındıran tümörler), ALK-hedefli tedavilere oldukça duyarlıdır. ALK füzyon onkojeni ve ROS1 mutasyonu ile ilişkili KHDAK›nin moleküler patogenezi, klinik özellikleri ve tedavisi burada tartışılmaktadır.

ALK POZİTİF HASTALIĞA GENEL BAKIŞ

ALK pozitif akciğer kanseri olan hastalar bu geni taşımayanlara göre nispeten daha gençtir [4,5]. Crizotinib onayını desteklemek için kullanılan iki çalışmanın veri tabanına göre ALK pozitif 255 hastada; medyan yaş 52 idi [5]. ALK füzyon geni hiç veya hafif (<10 paket-yıl) sigara öyküsü ile güçlü bir şekilde ilişkilidir [1,4,5]. ALK pozitif akciğer tümörlerinin büyük çoğunluğu adenokarsinomdur.

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dışında ceritinibde ilk basamakta etkinliğini kanıtlamıştır ama alektinib ve brigatinibin ROS1 mutasyonuna etkinliği yoktur. Crizotinib direnci sonrası Lorlatinib etkin bir tedavi seçeneğidir.

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