BÖLÜM 2 BÖBREK TÜBÜLLERİNDEN KÖKEN ALAN TÜMÖRLER

2.1 BERRAK HÜCRELİ RENAL TÜMÖRLER

Berrak GÜMÜŞKAYA [1]

2.1.1. Tanım

- Renal epitelyal tümörlerden en sık karşımıza çıkan, tipik olarak berrak sitoplazmaya sahip, dallanan vasküler yapılarla ayrılmış kompakt yuvalar veya asiner büyüme paterni oluşturan, karakteristik olarak von Hippel-Lindau (*VHL*) gen inaktivasyonuna yol açan kromozom 3p alterasyonları içeren kortikal böbrek tümörüdür (1).

2.1.2. Köken/Patogenez

- Proksimal kıvrıntlı tübülü döşeyen epitelyal hücreden köken aldığı düşünülmektedir. VHL (von Hippel-Lindau) tümör baskılayıcı geninde (3p25-26) iki basamakta gerçekleşen kayıp, dengesiz translokasyon veya biallelik alterasyon sonucu oluşan VHL protein fonksiyon kaybı, somatik berrak hücreli RCC'lerin %50-82'sinde görülür (1).
- İlk basamakta 3p kaybı genellikle çocukluk ya da adolesan çağda birkaç yüz hücrede kromotripsis şeklinde gerçekleşir.
- İkinci allel ise somatik mutasyon ya da hipermetilasyon gibi epigenetik inaktivasyonla kaybedilir.
- VHL protein kaybı hipoksi 'inducible' transkripsiyon faktörü alfa (HIF1α)'nın birikimine yol açar.
- HIF1α birikimi, hipoksi ilişkili *VEGF*, *PDGFβ*, *GLUT1*, *TGFα*, *CA9*, *EPO* ve metalloproteinazları içeren genlerin transkripsiyonuna yol açar.
- Diğer sürücü mutasyonlar daha az oranlarda görülür (1).

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- İmmünohistokimyasal olarak keratin 7 (kuvvetli), CD10 ve CA9 komplet membranöz (kutu benzeri) pozitiftir.

- **Kromofob RCC ile ayırıcı tanısı:**
  - Makroskopide homojen açık ten rengi iyi sınırlı kitle izlenir. Mikroskopik olarak keskin hücre sınırlarına sahip geniş hücreler, ince retiküler sitoplazmalı olup, düzensiz nükleer sınırlara (kuru üzüm gibi) ve perinükleer halolara sahiptirler.
  - Berrak hücreli RCC'deki narin kapiller damar çatısı yoktur.
  - İmmünhistokimyasal olarak keratin 7, KIT pozitif; CA9 ve vimentin negatiftir (46).
- **Onkositom ile ayırıcı tanısı:**
  - Miksoid/hyalinize stromanın yer aldığı zeminde eozinofilik granüler sitoplazmalı ve küçük yuvarlak nükleuslu hücrelerin oluşturduğu yuvalar izlenir.
  - Berrak hücreli RCC'deki tipik vasküler çatısı yoktur.
  - İmmünhistokimyasal olarak KIT pozitif, vimentin ve CD10 negatiftir.
- **Adrenal kortikal karsinom ile ayırıcı tanısı:**
  - İnhibin, MelanA ve SF1 pozitif; PAX8 ile EMA ve keratinler negatiftir.
- **Overin berrak hücreli karsinomu ile ayırıcı tanısı:**
  - İmmünohistokimyasal olarak 34 beta E12 ve keratin 7 pozitiftir.
  - Böbrek dışı bölgelerde PAX8 negatif ancak böbrek içerisinde pozitif olabilir (46).
- **Tiroidin berrak hücreli karsinomu ile ayırıcı tanısı:**
  - İmmünohistokimyasal olarak tiroglobulin ve TTF1 pozitiftir.
  - PAX8'in her ikisinde de pozitif olduğu göz önünde bulundurulmalıdır (46).
- **Mezotelyoma ile ayırıcı tanısı:**
  - İmmünohistokimyasal olarak kalretinin, mezotelin ve keratin 5/6 pozitiftir.

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