



Paraganglioma of Bladder

Mesaneje Paraganglioma

İpek Işık Gönül

Gazi University Medical School, Clinic of Pathology, Ankara, Turkey

Introduction

Paragangliomas are the tumors of the paraganglionic tissue in our body. Depending upon their size and anatomic location, paragangliomas can cause a variety of signs and symptoms but their morphology alone is almost the same.

Paragangliomas represent an uncommon neoplasms of the urinary bladder (1). Their origin is uncertain but they are thought to arise from the paraganglionic tissue that can be found in the wall of the urinary bladder (2). Although the most common clinical presentation is hematuria, bladder paragangliomas may cause voiding-associated or voiding exacerbated symptoms of hypertension, headache, palpitations, blurred vision and/or sweating due to their hormonally active status. The tumors may arise at any age, occur more or less equally in both sexes and rarely may be associated with neurofibromatosis, multiple endocrine neoplasia type 2 and von Hippel-Lindau disease (3). Although most paragangliomas are sporadic, germline mutations in the succinate dehydrogenase family of genes encoding subunit A, B, C and D (SDHA, SDHB, SDHC, SDHD) of the mitochondrial respiratory chain complex II are one of the genetic causes of hereditary cases (3).

Macroscopically, the tumors are typically lobulated, solid, submucosal or intramural dome-shaped masses covered by intact urothelium. Their size may vary from a few cm to 10 cm in diameter, but most are small. Light microscopy usually shows discrete nests

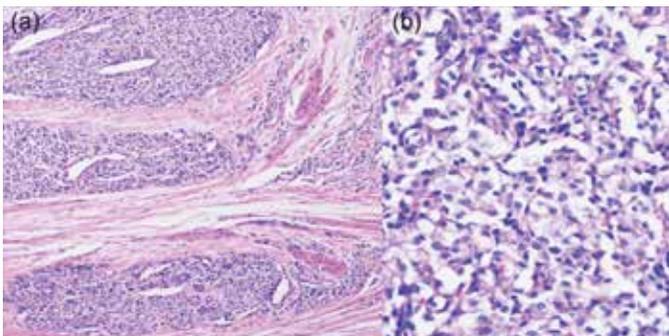


Figure 1. a) Infiltrative growth pattern of paraganglioma in the muscularis propria (Detrusor muscle) of bladder wall, **b)** classical Zellballen pattern of paraganglioma with discrete cell nests

of neoplastic chief cells in the characteristic Zellballen pattern with intervening vascular septa (Figure 1), but this feature is not always conspicuous and some tumors grow diffusely. The neoplastic cells are round or polygonal epithelioid cells with abundant eosinophilic or granular cytoplasm. Tumor cell nuclei are centrally located and are vesicular with finely granular chromatin. The cell nests are surrounded by S-100 (+) sustentacular cells (Figure 2) (4). Morphological features such as nuclear pleomorphism,

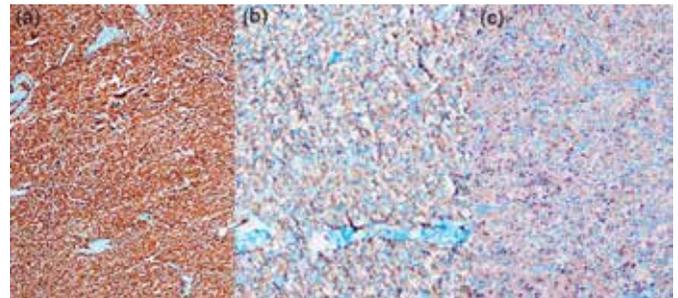


Figure 2. a) Immunohistochemistry showing NSE, **b)** synaptophysin and **c)** chromogranin were diffusely positive in the chief cells of the paraganglioma

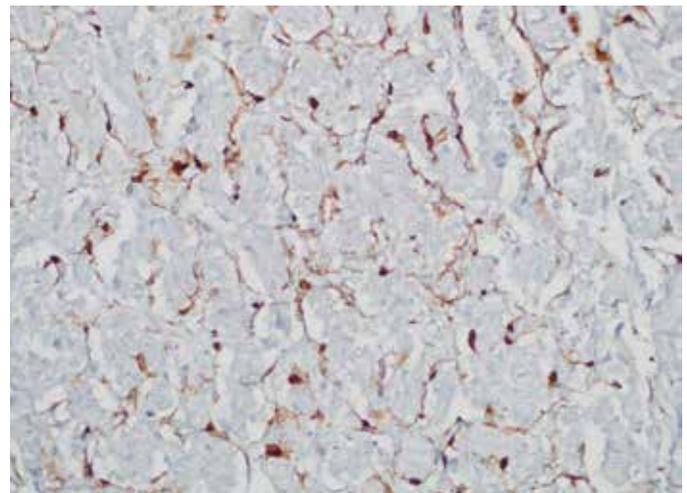


Figure 3. a) Immunohistochemistry showing NSE, **b)** synaptophysin and **c)** chromogranin were diffusely positive in the chief cells of the paraganglioma

Correspondence

İpek Işık Gönül MD, Gazi University Medical School, Clinic of Pathology, Ankara, Turkey

Phone: +90 312 202 54 88-89 E-mail: dripek@gmail.com Received: 02.08.2015 Accepted: 02.08.2015

mitotic figures, atypical mitosis or presence of necrosis are not a reliable predictor for malignant behaviour. Approximately 10% of the neoplasms are malignant and this is best predicted by depth of invasion into the bladder wall and confirmed by the presence of regional or distant metastasis (1). If present, the metastases mostly involve regional lymph nodes, lung, liver and skeleton.

The neoplastic chief cells are argyrophilic and positive for neuroendocrine markers including neuron-specific enolase, chromogranin and synaptophysin (Figure 3). A variety of hormonal substances, including serotonin, vasoactive intestinal polypeptide, gastrin, substance P, somatostatin, and bombesin may also be found to be positive immunohistochemically in the chief cell cytoplasm.

For bladder paragangliomas, the most important differential diagnosis is urothelial carcinoma. Based on a series of Zhou et al. (5), 20% of the tumors were initially misdiagnosed as carcinoma. In the context of a muscle invasive nested lesion, paraganglioma may be interpreted erroneously as invasive nests of urothelial carcinoma. However, the infiltrative nests of urothelial carcinoma lack the prominent vascular network of paraganglioma and are usually separated by variable amounts of stromal tissue and do not form a circumscribed mass. Other tumors which may mimic paraganglioma are prostatic adenocarcinoma, metastatic large cell neuroendocrine carcinoma, granular cell tumor, alveolar soft part sarcoma, metastatic renal cell carcinoma, carcinoid tumors and malignant melanomas. All of these tumors have their characteristic morphology and immune profile (4). Therefore, the differential diagnosis may easily be made.

Treatment of urinary bladder paraganglioma is primarily surgical by transurethral resection, partial cystectomy, or radical cystectomy (4).

Key Words: Bladder, paraganglioma, SDH

Anahtar Kelimeler: Mesane, paraganglioma, SDH

Concept: İpek Işık Gönül, **Design:** İpek Işık Gönül, **Data Collection or Processing:** İpek Işık Gönül, **Analysis or Interpretation:** İpek Işık Gönül, **Literature Search:** İpek Işık Gönül, **Writing:** İpek Işık Gönül, **Peer-review:** Internal peer-reviewed, **Conflict of Interest:** No conflict of interest was declared by the authors, **Financial Disclosure:** The authors declared that this study has received no financial support.

References

1. Cheng L, Leibovich BC, Chevillet JC, Ramnani DM, Sebo TJ, Neumann RM, Nascimento AG, Zincke H, Bostwick DG. Paraganglioma of the urinary bladder. Can biologic potential be predicted? *Cancer* 2000;88:844-852.
2. Homma K. Paraganglia of the urinary bladder. *Cancer* 1994;139:465-469.
3. Pasini B, Stratakis CA. SDH mutations in tumorigenesis and inherited endocrine tumours: lesson from the pheochromocytoma-paraganglioma syndromes. *J Intern Med* 2009;266:19-42.
4. Grignon DJ. Tumors of the urinary bladder. In: Amin MB, Grignon DJ, Srigley JR, Eble JN *Urological Pathology*, 1st ed. Philadelphia, Wolters Kluwer /Lippincott Williams&Wilkins, 2014, pp 340-460.
5. Zhou M, Epstein JI, Young RH. Paraganglioma of the urinary bladder. A lesion that may be misdiagnosed as urothelial carcinoma in transurethral resection specimens. *Am J Surg Pathol* 2004;28:94-100.