ADRENAL GANGLIONEUROMA ASSOCIATED WITH PRIMARY KIDNEY CANCER. REPORT OF TWO CASES AND LITERATURE REVIEW

Karla Tomić1, Goran Štimac2, Ognjen Kraus2, Leonardo Tomić1, August Mijić3 and Božo Krušlin4

1Department of Pathology, Dr. Josip Benčević General Hospital, Slavonski Brod; 2University Department of Urology; 3University Department of Surgery; 4Ljudevit Jurak University Department of Pathology, Sestre milosrdnice University Hospital, Zagreb, Croatia

SUMMARY – Two cases of adrenal ganglioneuroma associated with ipsilateral primary kidney cancer, according to literature review a very rare combination, are presented. Both patients underwent adrenalectomy and nephrectomy. Specimens were formalin fixed, paraffin embedded, cut at 5 μm and routinely stained with hematoxylin and eosin. Primary antibodies to neurofilament protein and S-100 were used to confirm ganglion cells in the ganglioneuromas. Histopathological analysis revealed adrenal gland ganglioneuroma with ipsilateral kidney carcinoma. One of them was renal cell carcinoma and the other one was urothelial carcinoma of the renal pelvis. This combination of malignant kidney tumor and adrenal gland ganglioneuroma is extremely rare, and after literature review we concluded that both cases presenting this combination of tumors were probably incidental.

Key words: Adenocarcinoma – pathology; Adenocarcinoma – surgery; Adrenal gland neoplasms – surgery; Ganglioneuroma – pathology; Ganglioneuroma – surgery; Kidney neoplasms – surgery

Introduction

Ganglioneuromas belong to fully differentiated sympathetic nervous system tumors that arise from primitive sympathogonia. They are entirely composed of ganglion cells and schwannian stroma, without neuroblasts, intermediate cells or mitotic figures seen in neuroblastosmas and ganglioneurolastomas1,2. Approximately 96% of all cases occur in the first decade of life, and 3.5% in the second, without sex predilection3. The most common locations are the posterior mediastinum (41.5% of cases), retroperitoneal (37.5%), adrenal gland (21%) and neck (8%)1. Ganglioneuroma most often manifests as an asymptomatic mass discovered on a routine radiographic study. In only rare cases, they secrete sufficient quantities of vanillylmandelic acid (VMA) or homovanillic acid (HVA) to manifest with flushing and other symptoms of catecholamine excess. Some authors support the idea that the majority of ganglioneuromas develop de novo rather than by maturation from preexisting neuroblastoma4. The etiology of neuroblastomas and ganglioneuromas is still unknown, and a few studies suggested a weak association between neuroblastomas and paternal occupational exposure to electromagnetic fields, but none of these associations has been confirmed5.

Renal cell carcinoma (RCC) accounts for more than 90% of all malignancies that occur in adult kidneys in both sexes6. Approximately 30% of all patients with RCC have already developed distant metastases at the time of diagnosis, and the most frequently involved organs are lungs and bones. At the clinical level, these metastases are often solitary, and can be confused with primary tumors of the organs in which they lodge2.

Tumors of the ureter and renal pelvis account for 8% of all urinary tract neoplasms, and 90% of these are urothelial carcinomas.

Correspondence to: Karla Tomić, MD, Ljudevit Jurak University Department of Pathology, Sestre milosrdnice University Hospital, Vinogradska cesta 29, HR-10000 Zagreb, Croatia
E-mail: karlamed@yahoo.com
Received August 2, 2006, accepted in revised form October 6, 2006
Case Reports

Patient No. 1

A 54-year-old man presented with left sided lumbar pain and hematuria persisting for several months. Computed tomography (CT) scan showed a lesion of the left kidney measuring up to 11 cm with intrallesional calcifications. CT scan also revealed a suspect lesion in the left adrenal gland measuring up to 3 cm in the largest diameter, suggesting metastatic disease. The patient was treated with radical nephrectomy.

Pathologic examination of the left kidney revealed a tumorous mass measuring 9 cm in the largest diameter, without extension beyond the kidney or infiltration of the renal pelvis or hilar blood vessels. On sections of the left adrenal gland, a yellowish, well-demarcated tumor measuring 3.2 cm in the greatest diameter was found (Fig. 1). Microscopically, the renal tumor consisted of solid nests, tubular and alveolar structures composed of atypical epithelial cells, with clear cytoplasm and nuclei easily recognizable with the X10 objective. Microscopically, adrenal gland tumor was composed of schwannian stroma and ganglion cells that immunohistochemically showed positive reaction for S-100 and neurofilament protein.

Patient No. 2

A 50-year-old female was admitted to the hospital for hyperparathyroidism and immunohemolytic anemia, when intravenous urography and CT scan demonstrated an expansive mass of the left kidney of up to 4.5 cm and a large tumor measuring up to 10 cm in the largest diameter in the left adrenal gland. Several months before she had noticed hematuria with lumbar pain on the left side. Cytological analysis of the urine showed high-grade carcinoma. Laboratory analysis did not show elevated levels of VMA or catecholamine. Nephroureterectomy followed by ipsilateral adrenalectomy was performed.

Grossly, on the sections of the left kidney, a grayish, papillary tumor in the renal pelvis was found, measuring 4 cm in the greatest diameter. Macroscopic examination of the left adrenal gland revealed an encapsulated, yellow tumor measuring 13x10x6 cm. Renal tumor was microscopically composed of papillae with disordered architectural and cytological features, and marked variation in nuclear size, shape and chromatin pattern. Mitoses were frequent and occurred at all levels. Tumor cells were infiltrating the subepithelial stroma but without invasion of the muscular layer. The adrenal gland tumor was composed of schwannian stroma and ganglion cells (Fig. 2).

In both patients, the histopathological diagnosis was adrenal gland ganglieneuroma associated with RCC and urothelial carcinoma of the renal pelvis.

Discussion

It is reported that ganglieneuromas may arise from the maturing neuroblastosomas and ganglieneuroblastomas, or they may arise de novo. Neuroblastoma, the immature form of ganglieneuroma, is known for deletions on chromosomal locus 1p (deleted in almost all cases)
and allelic loss of 11q (it occurs in 30%-50% of cases), making them the most common deletions detected in neuroblastomas. Trisomy for the 17q is another karyotypic abnormality that has been detected frequently in neuroblastomas. Allelotyping and comparative genomic hybridization studies have suggested that gain of the long arm chromosome 17 may occur in over half of all neuroblastomas, which appears to be associated with a more aggressive subset of neuroblastomas and has a prognostic value for adverse outcome. Koch et al. in their study of one adrenal ganglioneuroma did not detect allelic losses at the 1p36 and 17p13 (the p53 gene locus), suggesting that these loci are not involved in tumorigenesis. Another study investigated p53 protein and its messenger ribonucleic acid in human adrenal tumors, showing a very low p53 protein content in ganglioneuromas. On the basis of these last two investigations, and different distribution of ganglioneuromas and neuroblastomas, it is quite possible that the majority of ganglioneuromas arise de novo, without genetic aberrations described in neuroblastomas.

Cytogenetic analysis of upper urinary tract urothelial carcinomas indicates that these carcinomas share similar genetic alterations as urothelial carcinoma of the urinary bladder. Deletions of chromosome 9 occur in 50%-75% of all patients. Up to 20%-30% of all upper urinary tract cancers demonstrate microsatellite instability and loss of the mismatch repair proteins MSH2, MLH1 or MSH6.

Although most clear cell RCCs are not related to von Hippel-Lindau disease, 3p deletions are very common in most of the sporadic cases of RCC. The role of p53 gene expression in RCC is controversial, and few studies suggest that p53 overexpression is associated with poor prognosis and sarcomatoid transformation.

After review of the literature about the genetic and etiologic factors of all tumors described above, it can be concluded that combinations of adrenal gland ganglioneuromas and primary kidney cancers are rare, very probably incidental, but preoperatively difficult to distinguish from metastasis.

References

Sažetak

GANGLIONEUROM NADBUREŽNE ŽLIJEZDE U KOMBINACIJI S PRIMARNIM KARCINOMOM BUREŽA: PRIKAZ DVAJU SLUČAJEVA

K. Tomić, G. Štimac, O. Kraus, L. Tomić, A. Mijić i B. Krušlan

U radu su prikazana dva slučaja ganglioneuroma u nadbubrežnoj žlijezdi u bolesnika s primarnim tumorima bureža, gdje je u jednom bolesnika primarni tumor bureža bio karcinom burežnih stanica, dok je u drugom slučaju tumor bureža bio urotelni karcinom nakapnice. U oba slučaja prijeoperacijski nalaz kompjutorizirane tomografije je uz tumore bureža otkrio i tumore u nadbubrežnim žlijezdoma za koje se smatralo da su metastaze. Iako je kombinacija malignog primarnog tumora bureža i ganglioneuroma u nadbubrežnoj žlijezdi izrazito rijetka, vrlo je vjerojatno da su to slučajni nalazi, a prijeoperacijski je takve lezije skoro nemoguće razlikovati od metastatskih bolesti.

Ključne riječi: Adenokarcinom – patologija; Adenokarcinom – kirurgija; Neoplazme nadbubrežne žlijezde – patologija; Ganglioneurom – patologija; Ganglioneurom – kirurgija; Neoplazme bureža - kirurgija