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Peripheral Neuroepithelioma of the Kidney

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Peripheral neuroepithelioma is a rare tumor, comprising less than 1% of all soft tissue malignancies arising from the peripheral nonautonomic nervous system. Most peripheral neuroepitheliomas reported were located in the extremities, thoraco-pulmonary region, and pelvic areas, and as many as 30 % of cases were associated with peripheral nerve. We report one case of peripheral neuroepithelioma arising in the kidney, mimicking renal cell carcinoma on the CT scan.

Key Words : *Kidney neoplasms, Neuroepithelioma, Tomography, X-ray computerized*

INTRODUCTION

Peripheral neuroepithelioma is a primitive neuroectodermal tumor (PNET) arising from peripheral nonautonomic nerves (Enzinger and Weiss, 1988). It was first described by Stout (1918) arising in association with the ulnar nerve, but association of the tumor with peripheral nerves has been reported to be less than 30 %. The tumor is rare, and it can be located anywhere in the body, most commonly in the peripheral extremities and chest wall. To our knowledge, this is the first reported case of peripheral neuroepithelioma arising in the kidney in Korea.

CASE REPORT

A 33-year-old woman was admitted with pain in the right flank area which she had suffered for one year. She also complained of intermittent facial flushing, urinary frequency and 5 kg weight loss during the previous six months. Physical examination revealed no abnormal findings. Blood pressure was 120/70 mmHg. Laboratory findings revealed no significant changes with a serum creatinine level of 0.8 mg /dl, and blood urea nitrogen of 16.3 mg/dl.

An abdominal ultrasonogram revealed a 5 cm round, heterogeneous echoic mass arising from the lateral aspect of the right kidney (Fig. 1). Computed tomography (CT) also showed a well-defined, round mass in the interpolar area of the right kidney. The mass was slightly hyperdense in precontrast study, and hypodense in postcontrast study with multiple low densities suggesting necrosis (Fig. 2). Preoperative diagnosis was renal cell carcinoma of the kidney.

A right radical nephrectomy was subsequently performed. On cut section, the tumor was well-confined within the renal capsule and well demarcated from the adjacent renal parenchyma by a thin fibrous capsule. Massive hemorrhagic necrosis was noted within the tumor (Fig. 3). The adrenal gland was grossly normal.

Microscopically, there was no definite fibrous capsule of the tumor. At the outer margin of the tumor, tumor cells penetrated the renal capsule and extended to the perinephric fat tissue in the focal area. The tumor was composed of sheets or lobules of closely packed small cells with intervening thin fibro-

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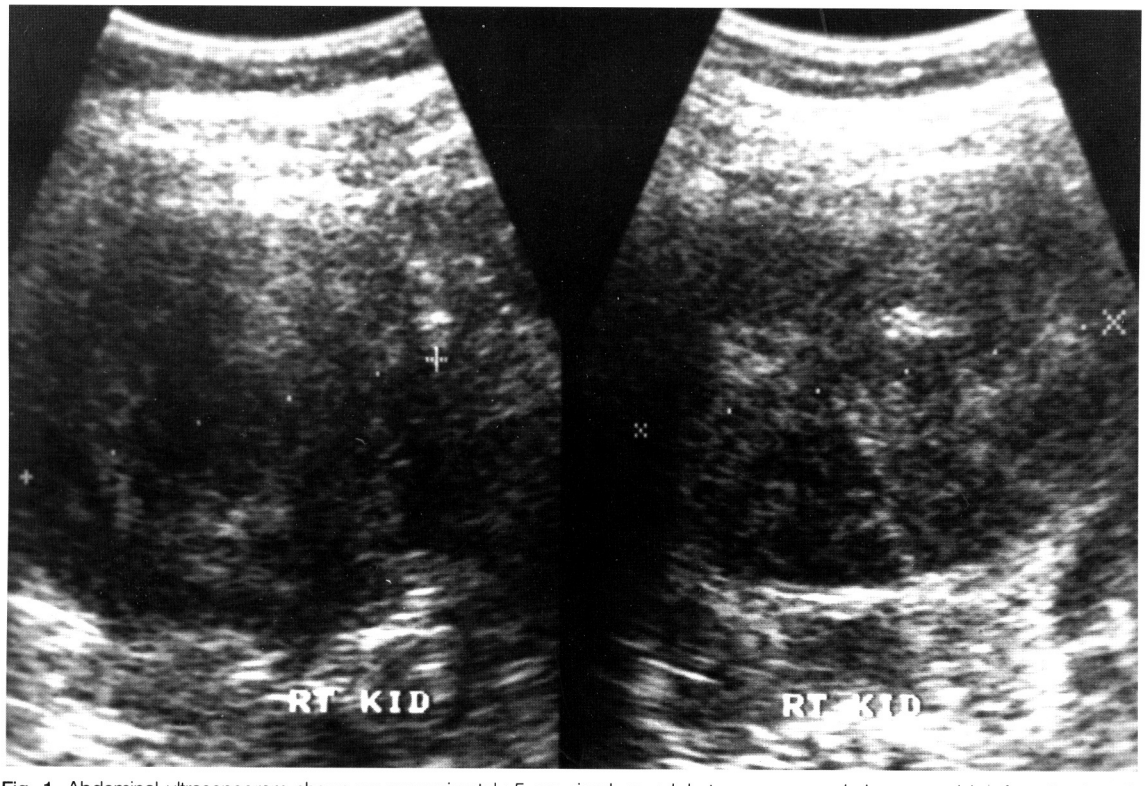

Fig. 1. Abdominal ultrasonogram shows an approximately 5 cm sized, round, heterogeneous echoic mass arising from the lateral aspect of the right kidney.

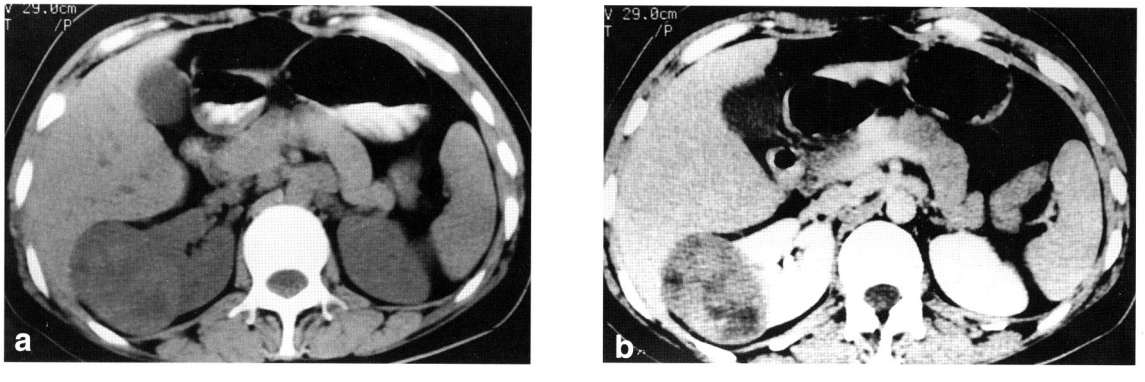

Fig. 2. Abdominal CT scan shows an approximately 6 × 4 cm sized, well-defined, round, slightly hyperdense mass protruding from the interpolar area of the right kidney in the precontrast image (2a) and the postcontrast image shows a hypodense mass with multiple low density area consistent with hemorrhagic necrosis (2b).

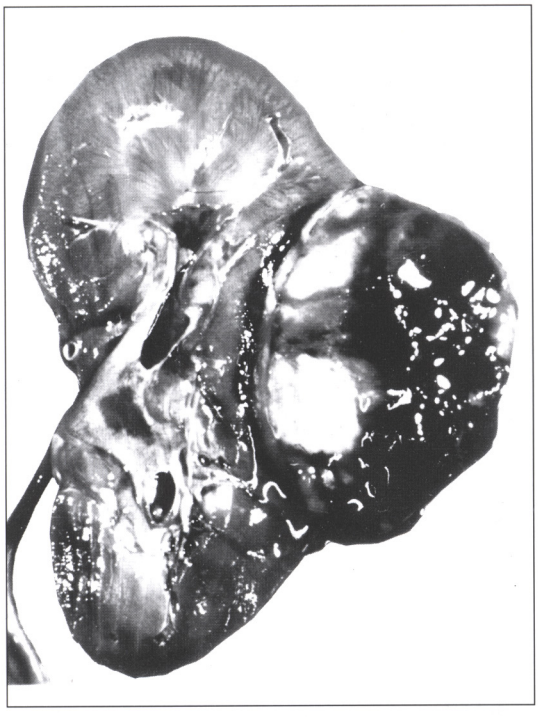

Fig. 3. Nephrectomized gross specimen reveals a 6.5 ×5 cm sized mass protruded laterally in the interpolar area of the kidney well-confined to the renal capsule, and the central massive hemorrhagic necrosis is demonstrated.

vascular septa. Tumor cells were uniform, with round to oval nuclei containing coarse but evenly dispersed chromatin and few minute nucleoli. Mitotic figures were numerous. Many Homer-Wright type rosettes and rare Flexner type rosettes were noted in the tumor (Fig. 4a). Immunohistochemistry revealed positive reaction for neuron specific enolase (Fig. 4b) and negative reaction for S-100 protein, vimentin and epithelial membrane antigen(EMA). Ultrastructurally, neoplastic cells were undifferentiated, having a high nucleus/cytoplasm ratio. Nucleoplasm tended to be clumped and marginated at the periphery, and one or two nucleoli were present. Intercellular junctions and elongated cytoplasmic processes were prominent. Cytoplasmic organelles such as mitochondria and rough endoplasmic reticulum were variable in number from cell to cell. Neither neurosecretory granules, microtubules nor neurofilaments was observed in tumor cells.

DISCUSSION

Peripheral neuroepithelioma is a PNET arising from peripheral nonautonomic nerve. However, the origin from a nerve can be identified only in about 30 % of cases(Enzinger and Weiss, 1988 ; Fletcher, 1990). Geschikter(1935) estimated its incidence as less than

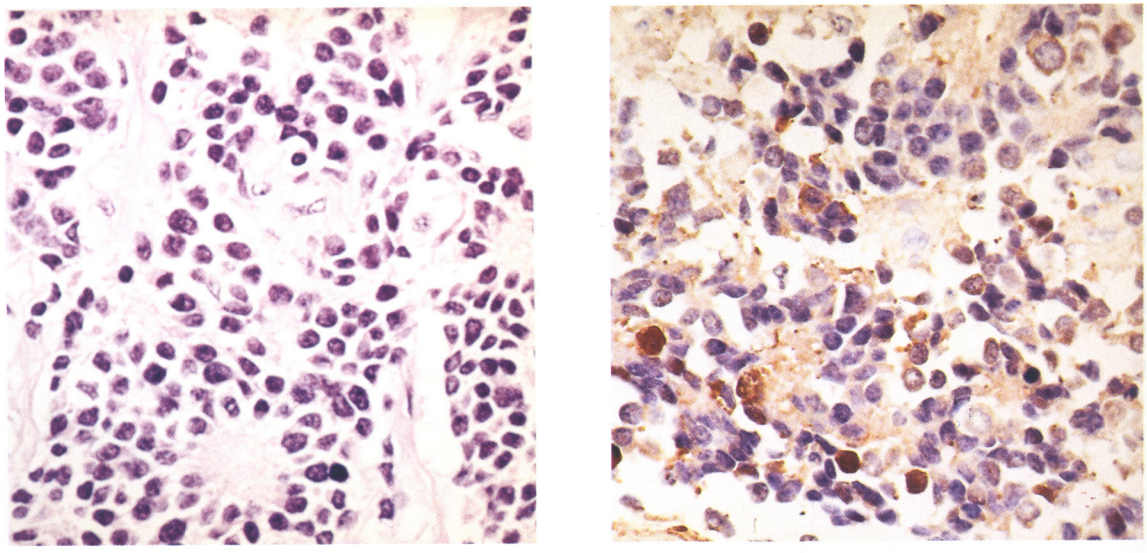

Fig. 4. Light microscopy reveals the tumor to be composed of densely small round cells with formation of Homer-Wright rosettes, H & E, reduced from ×100 (4a) and immunohistochemical study shows positive reaction for NSE, reduced from ×100 (4b).

1 % of all malignant tumors of peripheral nerve and Hashimoto and coworkers(1983) estimated its incidence as about 1 % of all sarcomas. It may occur at any age, but most commonly in adolescent and young adults with median age ranges from 11 to 22 years. There is no gender predisposition(Hashimoto et al., 1983 ; Enzinger and Weiss, 1988 ; Jürgens et al., 1988). The predilection sites vary according to the authors, most commonly in the extremities(Hashimoto et al., 1983 ; Enzinger and Weiss, 1988) and thoracopulmonary region(Jürgens et al., 1988 ; Marina et al., 1989). Peripheral neuroepithelioma arising from the kidney has been rarely reported(Weeks et al., 1991). The possible origin of this tumor in the kidney may be from the remnant of peripheral neuroectodermal tissue, or from the peripheral nerve.

Compared to classic neuroblastoma, this tumor is not always associated with increased level of catecholamine and its metabolites including norepinephrine, epinephrine, and vanilmandelic acid (VMA) in serum or urine(Dehner, 1986 ; Enzinger and Weiss, 1988).

There are no previous reports regarding the radiographic findings of the peripheral neuroepithelioma. In our case, ultrasonogram revealed a heterogeneous round mass. CT scan showed a well demarcated, slightly hyperdense mass in the precontrast image and hypodense mass with multiple low density area consistent with hemorrhagic necrosis in the postcontrast image. But there are no differential points from other renal masses including renal cell carcinoma and other PNETs including primary neuroblastoma.

Hashimoto et al.(1983) described gross appearances of the tumors, that were relatively well circumscribed in six of 15 cases, and there was infiltrative growth in seven cases and bony involvement was noted in two cases. It was frequently associated with necrosis or hemorrhage. In our case,the tumor was well circumscribed with a thin fibrous capsule and had central hemorrhagic necrosis.

On light microscopy, the tumors are composed of sheets or lobules of small rounded cells containing darkly stained, round or oval nuclei. These small cells are also seen in other tumors such as undifferentiated small cell carcinoma, Ewing's sarcoma, malignant lymphoma, and classical neuroblastoma. But this tumor forms Homer-Wright rosettes containing a central neurofibrillary material, and less often Flexner-Wintersteiner rosettes containing a central lumen or vesicle. In contrast to a neuroblastoma, PNET does not calcify, nor does it display mature elements such as ganglion cells, adult nerves, or mature neuropils(Hashimoto et al., 1983 ; Dehner, 1986 ; Enzinger and Weiss, 1988 ; Fletcher, 1990). In this case, the tumor was composed of small round cells, frequently forming Homer-Wright rosettes, and rare Flexner type rosettes. There is no cystic degeneration or calcification.

Immunohistochemical study of neuroepithelioma shows positive reaction for neuron specific enolase (NSE) in the cytoplasm, which suggests neuronal activity, and negative reaction for S-100 protein, suggesting non-Schwann cell or glial cell differentiation(Hashimoto et al., 1983 ; Enzinger and Weiss, 1988), which agrees with our findings. The most characteristic ultrastructural feature of the tumor is the elongated cell processes as shown in this case and small dense core granules (neurosecretary granule)(Enzinger and Weiss, 1988), which are not found in this case. Extrenal lamina or junctional complex insinuating epithelial differentiation of Wilms' tumor is not noted in this case.

Marina et al(1989) propose the potential criteria for the diagnosis of PNET to be as follows ; (1) Occurrence of rosettes. (2) Originating from or linked clearly to a peripheral nerve. (3) NSE positivity or Leu-7 positivity (4) Ultrastructural cytoplasmic processes, neurosecretary granule,and microtubules (5) Reciprocal translocation t(11 ;22)(q24 ;q12) (6) Proto-oncogenic expression (N-myc, c-myb, c-ets-1) (7) Activity of neurotransmitter biosynthetic enzymes (tyrosine hydroxylase, dopamine β hydroxylase, and choline acetyltransferase). At least two of the above findings or preferably three must be met and our case satisfies at least two criteria.

The peripheral neuroepithelioma is a highly aggressive tumor, locally recurrent and rapidly metastasizing to lung, liver, lymph node, bone, and brain. The outcome is poor with 5 year survival below 40 % in spite of aggressive combined treatment including surgery, chemotherapy, and radiation therapy(Marina et al., 1989).

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