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Case Report

Malignant paraganglioma of testis and spermatic cord: a case report

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Abstract: To date, extra-adrenal chromaffin cell tumors in spermatic cord and testis areas are still rarely reported. In this case report, we presented one case of a malignant paraganglioma in the testis and spermatic cord of a patient who had initially been admitted to hospital for recurrent headaches and paroxysmal palpitation. This is the first case report of a paraganglioma in the testis and spermatic cord with multiple metastases. Firstly, the paraganglioma was found exclusively in the testis and spermatic cord, invading the testicle and the spermatic cord; Secondly, it was malignant with lymph node metastasis around the abdominal aorta, right inguinal and right external iliac; Thirdly, It has the ability to secrete high amounts of catecholamines. By combining this case with previous studies of others, we further discussed the clinical characteristics, diagnosis and treatment of the disease.

Keywords: Testis, spermatic cord, paraganglioma, diagnosis, treatment

Introduction

Paraganglioma is a rare soft tissue neuroendocrine tumor that originating from neural crest cells and belonging to apudoma. It can synthesize, store and secrete catecholamines and produce multiple peptide neurohormone and chromogranin particles. Paraganglioma is mainly located in where is abundant in secondary ganglion, such as the abdomen, the retroperitoneal axis along the abdominal aorta, chest, head and neck and so on. The paraganglioma of testis and spermatic cord is extremely rare. The first report of spermatic cord paraganglioma was documented in 1971 by Eusebi & Massarelli [1]. Herein, we reported a case of malignant paraganglioma in the testis and spermatic cord with multiple metastases.

Case report

The patient, a 28-year-old man, was admitted with the symptoms of recurrent headaches for 17 years, paroxysmal palpitation, sweating and pale for 6 months. There was no history of urinary symptoms or trauma of the scrotum. Initial clinical examination revealed two non-tender and fixed mass in the right scrotum. The left testicle and spermatic cord was normal. There were palpable inguinal lymph nodes on the right. Serum norepinephrine, dopamine, metanephrine and 24 hours of urine VMA are beyond normal range. He had a history of high blood pressure and type I diabetes mellitus. His family history was unremarkable. CT and MRI scan revealed a right testicle mass measured 15 mm*11 mm and a right spermatic cord measured 26 mm*32 mm accompanied with Lymph node enlargement around the abdominal aorta, right inguinal and right external iliac (**Figure 1**). PET-CT scan showed increased glucose metabolism masses/nodules in right spermatic cord, right inguinal and the retroperitoneum region (**Figure 1**). Somatostatin receptor imaging showed high expression of somatostatin receptor in the right testicular, right retroperitoneal, right iliac vascular and right groin.

Scrotum exploration with right inguinal incision was performed. Intraoperative frozen section diagnosis showed that the occupied lesions in the right testis and spermatic cord were malignant. So the patient underwent right orchiectomy, right spermectomy and lymphadenectomy of right inguinal, bilateral pelvic, retroperitoneal and mesenteric. During the operation, two sep-

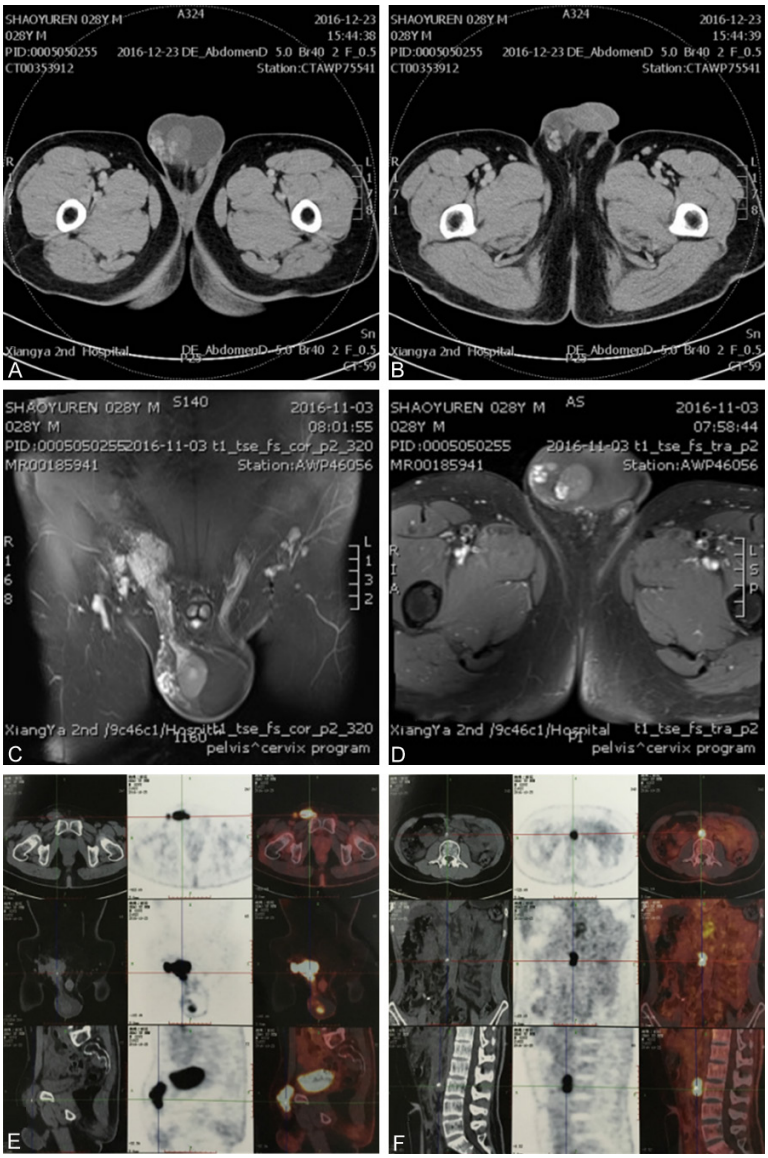

Figure 1. A. CT of the testis paraganglioma. Multiple nodules in the right testis with hydrocele of tunica vaginalis. B. CT of the spermatic cord paraganglioma. A round-like lump in the right spermatic cord with clear boundary. C. MRI coronal section of the spermatic paraganglioma. D. MRI cross section of testis and spermatic cord paraganglioma. E. PET-CT imaging of spermatic cord and testis paraganglioma. A round-like lump of increased glucose metabolismu in right spermatic cord with clear boundary. F. PET-CT imaging of retroperitoneal lymph node. Increased glucose metabolismu nodules and masses in the retroperitoneum.

arate masses with grey-and-yellow appearance in the right testis and spermatic cord were resected respectively. The highest blood pressure was 200/128 mmHg in the process of dissection and removal of testes and spermatic cords, and the lowest blood pressure after resection of tumor was 110/70 mmHg. There were no perioperative complications. Pathological examination demonstrated ectopic pheochromocytoma of right testis and right spermatic cord accompanied with lymph node metastasis around the abdominal aorta, right inguinal and right external iliac regions. Immunohistochemistry showed that tumor cells were EMA (-), HMB45 (-), Syn (++), Ki-67 2%+, CD56 (++), S100 (-), NSE (++), SMA (-), CgA (++), and ACTH (-) (**Figure 3**).

Discussion

To our knowledge, this is the first report in which paraganglioma was found both on the testicular and spermatic cord and accompanied with multiple metastases. Makris *et al.* reported a case of giant testicular malignant paraganglioma in 2014, the tumor's size was almost 17.5 cm×10 cm×9.5 cm [2]. In this case, the absence of important hemodynamic variances along with the normal levels of the catecholamines in the serum and the urine is remarkable. The authors of previous case reports considered that the small size of the paragangliomas and the consequently limitation in the secretion of catecholamines were responsible for the absence of significant hemodynamic symptoms. Makris *et al.* supposed that the extra-adrenal chromaffin cell tumors located especially in the paratesticular areas as well as those in the testis may lack the ability to secrete high amounts of catecholamines regardless of their size [2]. In our case, the size of the testis and spermatic cord paraganglioma was 1 cm×1 cm ×1 cm, 3.5 cm×2.5 cm×2.8 cm, respectively (**Figure 2**). However the patient had the clinical symptoms of headache, palpitation, sweating. The blood pressure significantly increased

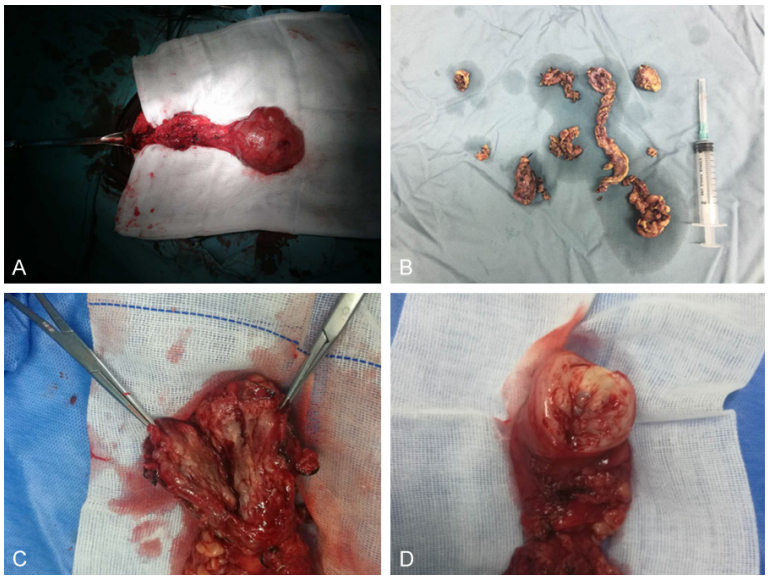

Figure 2. Gross appearance. A. Paraganglioma in testis and spermatic cord. B. Dissected lymph node. C. Paraganglioma in spermatic cord. D. Paraganglioma in testis. The lump is circumscribed and grey-and-yellow in colour.

when we touched the tumor, and decreased obviously after resection of the tumor. Postoperative blood pressure remained in normal range. Preoperative 24 hours urine VMA, plasma norepinephrine, dopamine and norepinephrine of the patient were higher than normal level. These points suggested that the testis and spermatic cord paraganglioma may still have endocrine function. Therefore, preoperative endocrine examination is of great value for the diagnosis of testicular and spermatic cord paraganglioma.

The majority of the paraganglioma is benign, and the malignant rate is around 30% [3]. There is a lack of uniform criteria for distinguishing benign and malignant paraganglioma. Malignant paraganglioma is usually found in the extra-adrenal gland, it is characterized by the invasion of adjacent tissues, the appearance of rough nodules, the necrosis of the tumor fusion and the absence of hyaline bodies in the cytoplasm under the microscope. Moreover, the vascular and capsular invasion is the basis for diagnosis of malignancy [4]. However, The benign and malignant paraganglioma cannot be distinguished by morphology of the tumor, so the recurrence and metastasis is essential for the diagnosis of malignant paraganglioma. Besides, the lymph node metastasis can be used as a good differentiating indicator [5]. In this case, the lesion invaded the normal testis, spermatic cord, and lymph node around the abdominal aorta. Tumor metastasis was also found in the area of right groin and external iliac. These evidences suggested that the tumor was malignant.

Surgical treatment is the first choice for the paraganglioma, and it is also the most effective method. Resection may be also clinically important in the management of patients with metastatic paraganglioma, it can be effective in normalizing or reducing levels of fractionated catecholamines and metanephrines, thus improving hormone-related symptoms and hypertension. Surgical resection, either complete or incomplete, is associated with durable survival despite a high rate of tumor recurrence [6]. Adequate preoperative preparation is the key to the success of surgery, patients with no significant high blood pressure or lack of typical symptoms were recommended to receive preoperative catecholamine blockade treatment. Reoperation is effective treatment when the tumor recurred. The role of chemotherapy in malignant paraganglioma is limited [7]. Chemotherapy with cyclophosphamide, vincristine and dacarbazine (CVD) can be used for palliative treatment of malignant pheochromocytoma and paraganglioma. Data on the effects of a combination of chemotherapy with cyclophosphamide, vincristine and dacarbazine (CVD) on malignant paraganglioma/pheochromocytoma suggested that a partial response concerning tumor volume could be achieved in about 37% of patients and a partial response on catecholamine excess in about 40% of patients [8]. Complete resection of malignant paraganglioma is difficult to achieve. The tumor is easy to recur after resection. Local radiotherapy can be used to control the growth of the tumor after recurrence, either with or without adjuvant radiotherapy after surgery. The scope and dose of radiotherapy need to be further studied. For ^{131}I-MIBG imaging positive malignant paraganglioma patients with surgical contraindication or the presence of metastatic tumor, ^{131}I-MIBG can be used as a

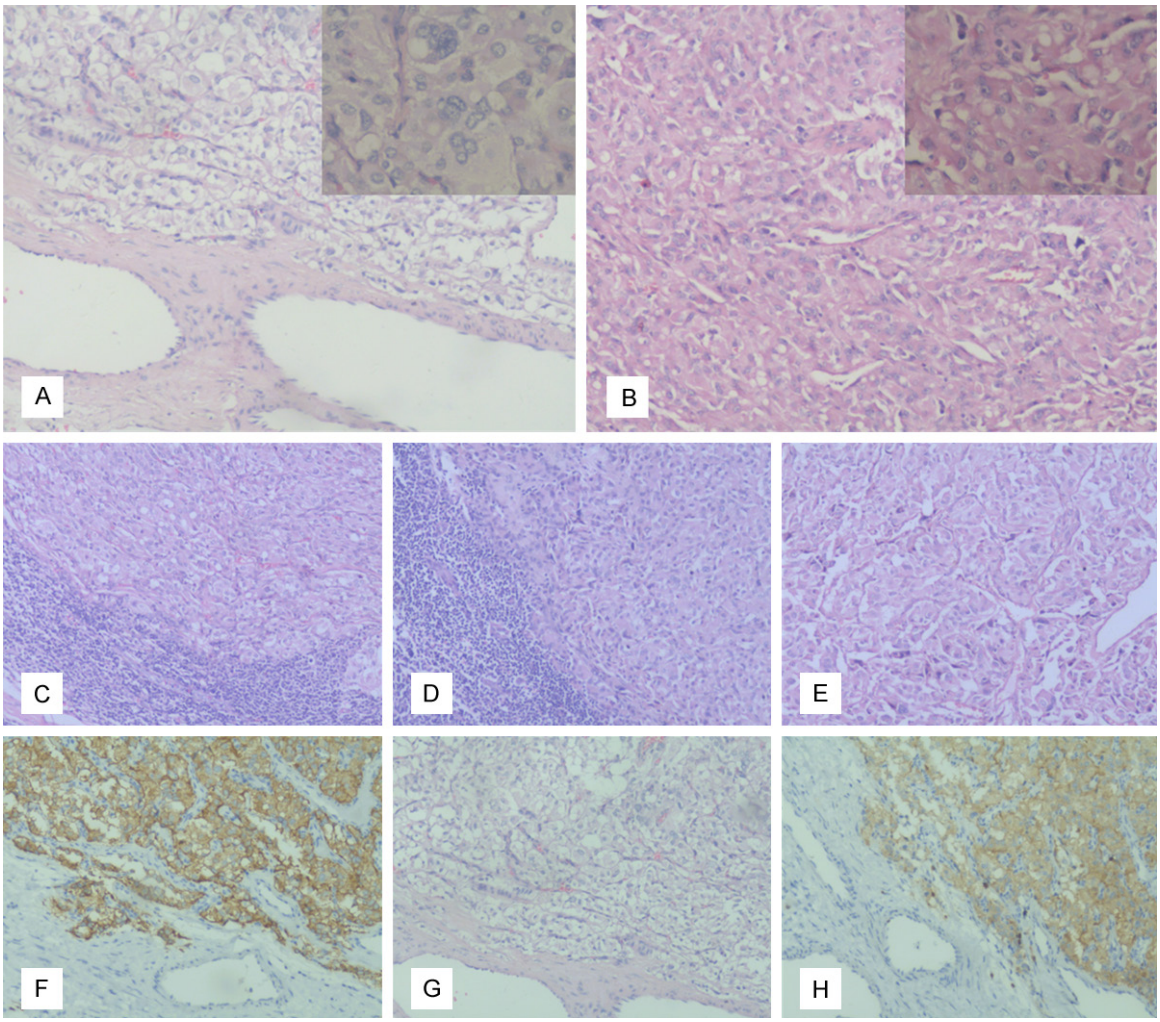

Figure 3. Pathological results. A. The testis paraganglioma (HE, ×100, ×400). The tumor cells were round or polygonal with rich cytoplasm. The nucleus were round or oval with obvious nucleolus, nuclear atypia was usual and nuclear fission was rare. B. The spermatic cord paraganglioma (HE, ×100, ×400). The morphology of tumor cells was consistent with testicular tumor tissue under light microscope. C. Metastatic lymph node around right inguinal (HE, ×100). D. Metastatic lymph node around right external iliac (HE, ×100). E. Metastatic lymph node around abdominal aorta (HE, ×100). F. Syn positive (Envision, ×100). G. Ki-67 positive (Envision, ×100). H. CgA positive (Envision, ×100).

priority for treatment [9]. Radioactive isotope therapy may achieve long-term remission of the tumor.

Acknowledgements

The patient was admitted to the Second Xiangya Hospital of Central South University, where we treated him.

Disclosure of conflict of interest

None.

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