

Case Report

Paraganglioma of the vulva: a case report and review of the literature

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Received July 6, 2013; Accepted August 19, 2013; Epub September 15, 2013; Published October 1, 2013

Abstract: Paraganglioma is a neuroendocrine neoplasm, which is extremely rare in the vulva and only one case has been reported. Here we present a case of vulvar paraganglioma in a 48-year-old woman and a literature review. The patient found a lump located in the genitals below the symphysis pubis 3 months before presentation when she complained that the lump was increasing in size. A 3.2 cm x 2.3 cm x 1.5 cm nodule was excised from subcutaneous soft tissue in the vulva. Microscopy showed a diversity of cell morphologies and structures in the rich vascular network of the tumor separated the chief cells into round cell nests (Zellballen pattern). Some areas of the tumor presented epithelioid and spindle-shaped cells with increased cell density and indistinct structural characteristics. Hyaline degeneration of collagen fibers or mucoid degeneration was found in tumor interstitium. Immunohistochemical staining showed diffused expression of synaptophysin in the chief cells, focal expression of S-100 protein in the sustentacular cells and high expression of CD34 in the vascular components. Based on morphological and immunohistochemical results, a rare paraganglioma of the vulva was diagnosed.

Keywords: Paraganglioma, vulva, Syn, S-100, immunohistochemistry

Introduction

Paraganglia are neural crest derived neuroendocrine organs widely distributed in the human body and can be divided into two types: the adrenal medulla paraganglia that are located in the adrenal medulla, and extra-adrenal paraganglia that are primarily distributed along the paravertebral and the main arteries in the para-axial region of the trunk from the skull to the pelvic organs. Thus, the paraganglia systems include the adrenal medulla, carotid body and aortic body chemoreceptors, vagus nerves and nodose ganglia located in the mediastinum, peritoneal and retroperitoneal areas. Paraganglia are comprised of two main cell types: chief cells and sustentacular cells. The chief cells are surrounded by sustentacular cells with a fibrovascular network and are packed into a characteristic, round cell nest pattern (Zellballen). Paragangliomas are tumors that represent this characteristic, typically occurring in the throat [1], orbit [2], abdomen [3] and prostate [4]. ENREF 5 Paragangliomas in the genito-urinary system occur mainly in the

bladder [5], followed by the uterus [6] and ovaries [7]. Paragangliomas of the vulva in females are extremely rare, and only one case has been reported so far [8]. Here we present a newly diagnosed case of a vulvar paraganglioma in a 48-year-old woman and review the related literature.

Case report

A 48-year-old woman with regular and normal menstrual periods, G2P2, and no history of dysmenorrhea or induced abortion, underwent fallopian tube ligation 20 years ago. The patient found a hard lump located in the genitals below the symphysis pubis 3 months ago, and presented to the hospital with a complaint of a lump which was progressively increasing in size. The patient was diagnosed as having a vulvar "fibroma". Her mental status, diet, sleeping pattern, energy levels, bowel movements and urination were normal, and there had been no recent weight change. Physical examination: body temperature: 36.5°C, pulse rate: 72 bpm, respiratory rate: 18 bp, blood pressure: 140/86



Figure 1. Gross morphology of the paraganglioma. A 3.2 cm x 2.3 cm x 1.5 cm solid mass was observed.

mm/Hg. She was awake and alert, her abdomen was soft, and there was no rebound pain or tenderness. She had a parous vaginal introitus. A walnut sized lump was found in the vulva below the symphysis pubis, which was solid, mobile, and not tender. Cervical hypertrophy was found, slightly congestive, but no obvious mass was found in the uterus and bilateral adnexa. She had a normal sinus rhythm. The lungs, liver, gallbladder, spleen, pancreas, bilateral kidney, ureter and bladder were all normal.

The paraganglioma tissue was excised from the patient and subjected to gross inspection. We observed a 3.2 cm x 2.3 cm x 1.5 cm solid mass (**Figure 1**) with a gray color and firm consistency on the cut surface. Microscopic inspection showed that the tumor boundary was clear. The morphology and structure of the tumor cells varied from polygonal to oval. In typical areas, chief cells were separated by fibrovascular stroma, and arranged in distinctive round cell nests (Zellballen pattern) (**Figure 2A**). Tumor cell borders were indistinct with abundant cytoplasm and numerous small eosinophilic granules. Cytoplasmic hyaline vacuolation, pleomorphic nuclei, fine chromatin and clear eosinophilic nucleoli were observed in some tumor cells (**Figure 2B**). Some tumor cells had an epithelial-like morphology with abundant cytoplasm (**Figure 2C**), and organ-like structures were indistinguishable due to high cell density and spindle cell-like arrangement or clumps of confused cells (**Figure 2D**).

Abundant hyaline degeneration of fine collagen fibers (**Figure 2E**) or mucoid degeneration (**Figure 2F**) was found in the stroma of the spindle cell-like region of the tumor. Transitional zones were observed in these different morphological regions. A small number of nuclear mitotic figures, but not pathologic nuclear mitotic figures or necrosis were observed in focal areas.

For immunohistochemical analysis, tumor specimens were surgically excised and fixed in 10% neutral buffered formalin overnight. Serial sections of paraffin-embedded tissue samples were cut at a thickness of 4 μ m. The sections were subjected to hematoxylin-eosin (H&E) staining and immunohistochemical staining with Syn, CK7, PCK, S-100, CD34, CgA, SMA, desmin, h-caldesmon and HMB45 antibodies (Gene Tech, Shanghai, China) and PV6000 testing Kit (Invitrogen, Grand Island, USA). The results showed that diffuse expression of Syn (**Figure 3A**), focal expression of CK7, PCK in chief cells and S-100 in sustentacular cells (**Figure 3B**), and negative expression of CgA, SMA, desmin, h-caldesmon and HMB45 were detected in tumor tissues. In addition, strong CD34 staining was detected in vascular components (**Figure 3C**). Based on these pathological characteristics, the patient was diagnosed as having a vulvar paraganglioma.

Discussion

Paraganglioma is a rare tumor that arises from paraganglia of neural crest origin and accounts for only 0.012% of all neoplasms. A diagnosis of paraganglioma is mainly based on pathological morphology [9]. According to histological morphology, paraganglioma can be divided into adrenal paraganglioma (or pheochromocytoma) and extra-adrenal paraganglioma. The typical histology of paraganglioma shows that tumor cells are clustered in honeycomb or nests patterns (Zellballen), which are separated by broad bands of fibrous tissue with prominent vascularization and argyrophilic fibers. The location of the paraganglioma in this case is extremely rare as are its various microscopic features. It is difficult for the pathologist to make a correct diagnosis because not all tissues within paraganglioma are characterized by typical features. This is especially true when microscopy shows prominent epithelioid or spindle cell features without obvious organelle-

Paraganglioma of the vulva

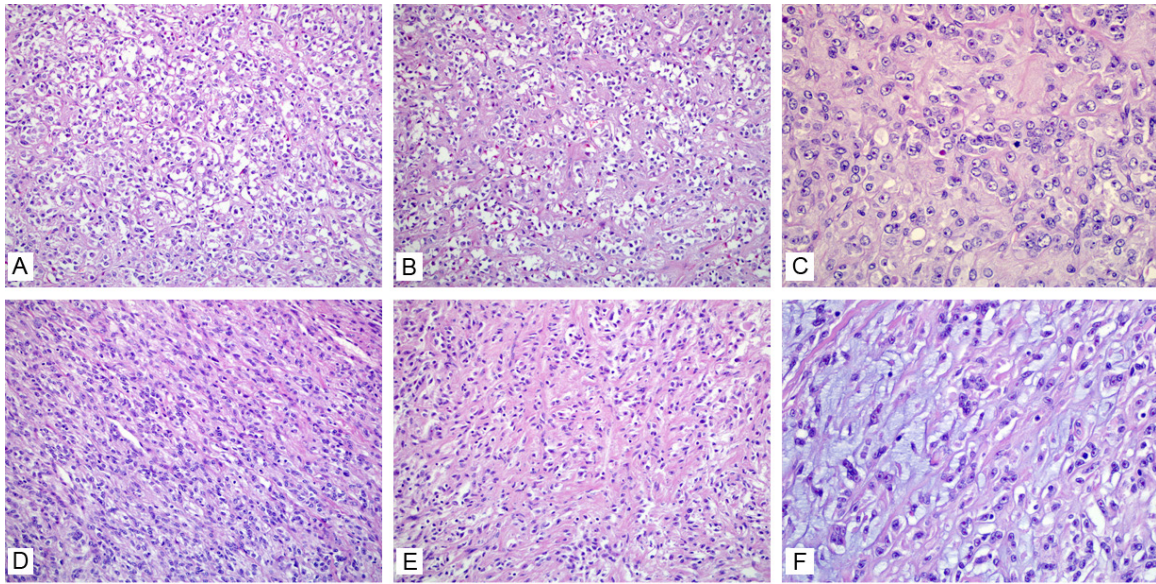


Figure 2. Histopathological features of the paraganglioma. A: Tumor cells were separated by abundant networks of blood vessels, arranged in organoid nests or glandular patterns (HE x20); B: Cytoplasmic hyaline vacuolation was observed in some tumor cells (HE x20); C: Some tumor cells had an epithelial-like morphology with abundant cytoplasm (HE x40), a nuclear mitotic figure was observed; D: Spindle-shaped tumor cells were arranged in high density (HE x20); E: Abundant hyaline degeneration of fine collagen fibers was found in the interstitium (HE x20); F: Mucoid degeneration in the interstitium (HE x40).

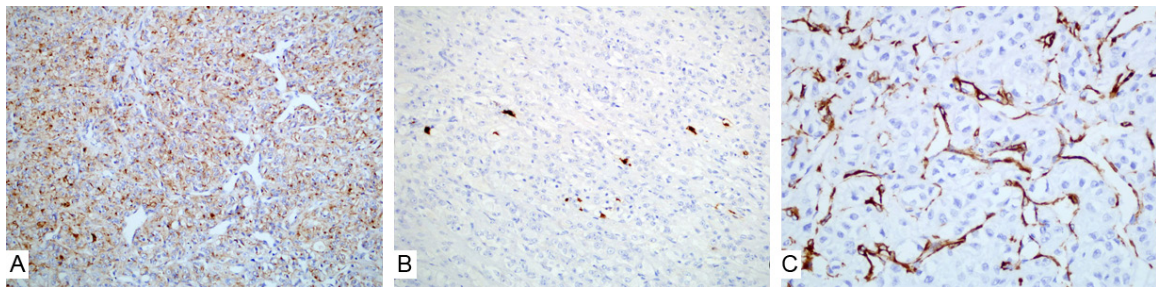


Figure 3. Immunohistochemical staining of the paraganglioma. A: Diffuse expression of Syn in chief cells (IHC x20); B: Expression of S-100 in sustentacular cells (IHC x20); C: High expression of CD34 in vascular components (IHC x40).

like structures. It could be misdiagnosed as a sarcoma. Therefore, it is important to examine the whole slice carefully for typical areas and features of paraganglioma. Immunohistochemical staining showed diffuse expression of Syn in chief cells and positive staining of S-100 in a few of the peripheral cells of nests, indicating the unique characteristics of two kinds of cell components and their organization in paraganglioma.

The differential diagnosis mainly includes alveolar soft part sarcomas (ASPS). Both paraganglioma and ASPS consist of polygonal cells that are arranged in a nest-like pattern and sepa-

rated by abundant interstitial capillaries. However, ASPS commonly occurs in deep soft tissue in a limb. Under optical microscopy, ASPS cells are large, with various acinar structures and coarse eosinophilic particles in the cytoplasm. Abnormal cells are more obvious than in paraganglioma, and positive crystal can be found by PAS staining. In addition, by immunohistochemical staining ASPS shows positive expression of CK and EMA, and vimentin, HHF35 and desmin, and occasionally NSE and S-100 could be detected in some cases.

It is not always possible to predict the clinical course and prognosis of paraganglioma. Some

characteristics are thought to imply either a benign or malignant neoplasm, including tumor size, nuclear polymorphism, mitosis and necrosis, DNA index, karyotype analysis and other indicators, but the outcome is not certain. The pathological morphology of paraganglioma is not necessarily consistent with its biological behavior, because metastasis may also occur in paraganglioma with “benign” morphology. Therefore, we cannot depend on pathological morphology alone to distinguish between malignant and benign paraganglioma [10]. Unfortunately there are no reliable criteria for differentiating benign and malignant paraganglioma, and histological changes alone cannot be used to predict tumor recurrence and metastasis [11].

Paraganglioma generally grow slowly. The average growth rate is 1.0 mm/year, and the average tumor doubling time is 4.2 years [12]. Surgical resection is a primary treatment for this tumor, and it is not sensitive to radiotherapy or chemotherapy [13]. Therefore, complete tumor resection is the key treatment to prevent relapse and improve survival rates. The prognosis of paraganglioma is often dependent on multiple factors, such as the type of surgery (biopsy, complete resection or local resection), tumor size and surgical margin, cell atypia, nuclear mitotic figures, necrosis, lymph node metastases and invasion of blood vessels [14]. In this case, the paraganglioma of the vulva was completely resected, the tumor volume was small and the surgical margin was clean. The patient remained well after follow-up for 8 months. To our knowledge, this is the second report on a case of a vulvar paraganglioma.

Acknowledgements

We want to thank Dr. Dengfeng Cao (Peking University Cancer Hospital) for his critical review of this manuscript.

Disclosure of conflict of interest

The authors report no conflict of interest.

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