

Pathological features of paraganglioma in the lumbar spinal canal

A case report

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Abstract

Introduction: This study aims to investigate the pathological features of a patient with paraganglioma in the lumbar spinal canal.

Case presentation: The patient was 36 years old male with electrical pain in the waist and buttock which occurred intermittently, and was not relieved under oral use of analgesics. Immunohistochemical staining was performed to diagnose the disease. The results revealed that the size of the tumor was 3.4 × 1.6 × 1.4 cm. The hematoxylin and eosin (H&E)-stained tumor cells mainly presented with an organ-like arrangement under low power microscope, showing prominent chrysanthemum-like, pseudo glandular or pseudo papillary arrangements. The surrounding area of the nest presented with sinusoids, and fibrosis and focal calcification could be observed in the interstitial space among the lesions. Immunohistochemistry results showed that the chief cells were positive for neuron-specific enolase (NSE), Syn and CgA, and Sertoli cells were positive for S-100.

Conclusion: Paraganglioma is a very rare malignant tumor. This tumor should be distinguished from ependymoma, meningioma and hemangioblastoma, to avoid misdiagnosis, and missed diagnosis.

Abbreviations: CEP = cauda equina paraganglioma, CT = computed tomography, EMA = epithelial membrane antigen, GFAP = glial fibrillary acidic protein, MRI = magnetic resonance imaging, NSE = neuron-specific enolase, PR = progesterone receptor.

Keywords: differential diagnosis, immunohistochemistry, lumbar spine, neuroendocrine tumor, paraganglioma

1. Introduction

Paraganglioma is common in clinical pathology, which can occur almost anywhere in the body. In 1891, Marchand reported the carotid body paraganglioma for the first time. To date, the locations of extra-adrenal paraganglioma reported in literature include the head and neck, chest, mediastinum, abdominal cavity, pelvic cavity, and urogenital tract. In the minority of patients, the tumor can occur in parts of the body without accessory ganglia, such as the heart,^[1] lung,^[2] gallbladder,^[3] thyroid,^[4] uterus,^[5] and vaginal wall.^[6] Paraganglioma is a unique neuroendocrine tumor that is often encapsulated and benign. This tumor is derived from special neural crest cells in the segmental or lateral

autonomic ganglia.^[7] Paraganglioma in the spinal canal is rare, which is mostly located in the spinal cord and cauda equina.^[8] The first case of cauda equina paraganglioma (CEP) was reported in 1970,^[9] and at least 210 cases of this disease have been reported to date.^[10–13] In this report, the morphological features, immunohistochemical characteristics and differential diagnosis of paraganglioma in the lumbar spinal canal were investigated.

2. Case report

This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of China-Japan Union Hospital of Jilin University. Written informed consent was obtained from all participants.

The patient was 36 years old male with electrical pain in the waist and buttock which occurred intermittently and was not relieved under oral use of analgesics. The results of non-enhanced and enhanced magnetic resonance imaging (MRI) of lumbar spine showed that the epidural and intramedullary spaces of L1 presented with hyperintense T1 signal and inhomogeneous T2 signal, the size was approximately 1.4 × 1.6 × 3.4 cm, and the margins were clear. The posterior part of the lumbar vertebrae was depressed because of compression, presenting with scattered fine calcifications (Fig. 1). A wide excision of the tumor was performed as the tumor boundary was not clear.

The specimens were fixed with 4% neutral formaldehyde solution and were subject to hematoxylin and eosin (H&E) staining and immunohistochemical labeling (En Vision two-step method). The primary antibodies included vimentin (dilution, 1:300), S-100 protein (1:60), glial fibrillary acidic protein (GFAP, 1:150), neuron-specific enolase (NSE, 1:150), Ki67 (1:150), pan-cytokeratin (CKpan, 1:150), epithelial membrane antigen (EMA,

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Figure 1. CT results: an irregular mass with a slightly high density was found at the spinal canal from the L2-5 vertebrae, the size is 7.1×2.2 cm, depression induced by compression was found in the posterior lumbar region, and scattered fine calcifications could be seen. CT=computed tomography.

1:150), smooth muscle actin (SMA, 1:200), progesterone receptor (PR, 1:50), and Syn, CgA and CD34 antibodies. All antibodies were provided by Fujian Maxim Biotechnologies and were subject to heat recovery in a rice cooker under pH-6 citric acid.

The size of the tumor was approximately $1.4 \times 1.6 \times 3.4$ cm, the margins were clear, and the tumor appeared to be encapsulated. Microscopic results showed that at low magnification, the tumor had no obvious capsule, the margins were clear, cells mainly presented with a nest-like arrangement (Fig. 2). The tumor

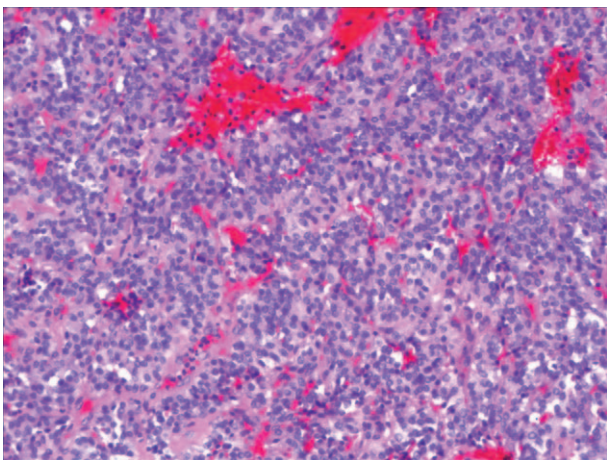


Figure 2. Under H&E staining with a $\times 40$ low power microscope, the tumor cells presented with a nest-like arrangement, and fine sinusoids were observed around the tumor. H&E=hematoxylin and eosin.

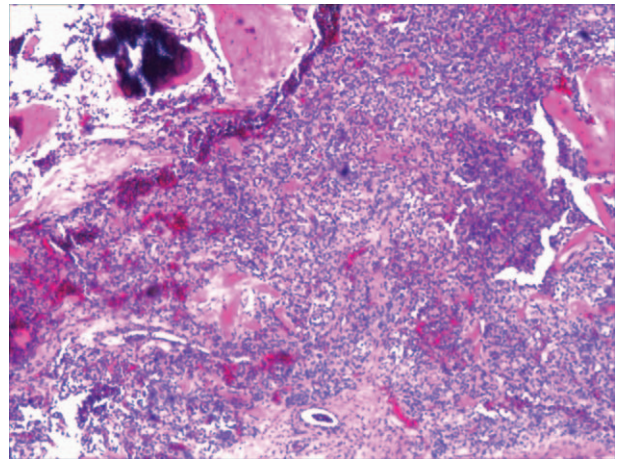


Figure 3. Under H&E staining with a $\times 40$ low power microscope, the tumor invaded the surrounding bone tissue. H&E=hematoxylin and eosin.

comprised of 2 kinds of cells: Some vascular wall presented with hyalinizing change, and fibrosis and calcification could be found in the space among the lesions (Fig. 3). Some tumor cells invaded the bone tissue (Fig. 4).

Vim, NSE, CgA, Syn, and CD56 were positive (Fig. 5), Ki67 was 1% (Fig. 6), GFAP, EMA, PR, and CD34 were not expressed, and Sertoli cells were positive for S-100.

Therefore, the histopathological diagnosis was paraganglioma with local invasion of bone tissue.

After surgery, the doctor advised the patient to do the radiation therapy because of local invasion of bone tissue, but the patient did not follow the advice and chose to give up the treatment.

Follow-up was done after 6 months. It was found that pain in the waist and legs disappeared within 1 month after surgery, space occupying lesion did not appear in the spine, and the patient was lost to follow-up.

3. Discussion

Paraganglioma in the spinal canal is a unique neuroendocrine tumor that is often encapsulated and benign. This tumor is derived from special neural crest cells in the segmental or lateral

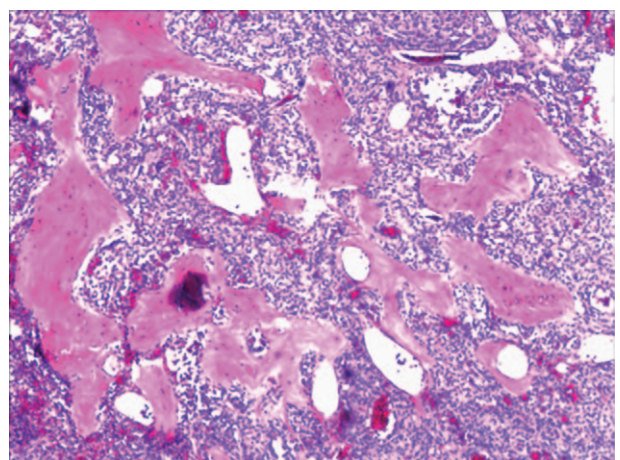


Figure 4. Immunohistochemical result: the cytoplasm was positive for Syn.

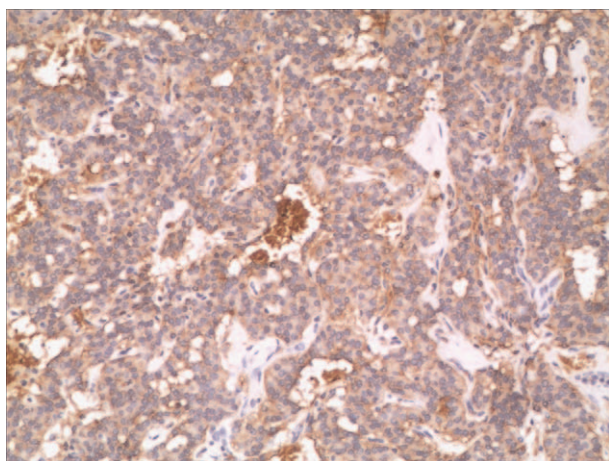


Figure 5. Immunohistochemical result: the cytoplasm was positive for CgA.

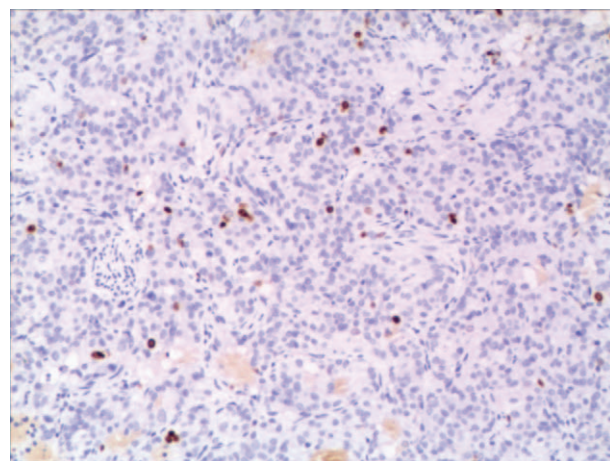


Figure 6. Under H&E staining at $\times 40$, Ki-67 was approximately 1%.

autonomic ganglia.^[7] The tumor comprises of uniform-sized chief cells accompanied by differentiated neurons, forming a compact nest-like (organ-like) structure, which is surrounded by a capillary network of Sertoli cells and fibers. Paraganglioma in the spinal canal is usually located in equine caudal regions. Therefore, it is also called CEP.^[8] Miller et al first described CEP in 1970. It was considered as an ependymoma with neuroendocrine function at that time.^[9] Furthermore, Lerman et al first explicitly proposed the concept of CEP in 1972.^[14] CEP is histologically equivalent to WHO grade I,^[15,16] and its cases account for 3.4% to 3.8% of cases of paraganglioma in the central nervous system,^[12] while other segments of the spinal cord are rarely affected. Studies have reported that paraganglioma occurred in the thoracic spinal cord of 15 patients,^[17,18] and most of them were located outside the spinal dura mater and contained intraspinal or paravertebral components, while another studies reported 2 patients who had paraganglioma in the cervical segment.^[19] Intracranial paraganglioma is often formed by the invasion of caroticotympanic paraganglioma into the cranial cavity.^[20] Rare primary intracranial paraganglioma has also been reported, in which the tumors were located in the sellar region, cerebellopontine angle, and cerebellar parenchyma.^[20,21]

Most tumors revealed homogeneous iso-density shadows on computed tomography (CT) images, which can be enhanced on enhanced scanning images. Typical MRI displays lesions with clear margins and occasionally displays some cystic areas, which have certain characteristics. The tumor presents with low to intermediate signal intensity on T1WI, and intermediate to high signal intensity on T2WI. Since the tumor is rich in blood vessels, an empty area will appear in the background of slow blood flow with an enhanced signal of the tumor. This is called “salt and pepper disease” on T2W1 images, which is one of the features of paraganglioma.^[22,23] The gross pathologic manifestations include an intact capsule, which is dark red or brown.^[24] Multifocal hemorrhage occurs after the removal of tumor surface tissues during the operation. According to the published literature, the tumor usually presents a smooth boundary and partially invades the bone tissue, but in the present case, the tumor cells were arranged in the nest-like arrangement involving the bone tissue.^[24]

Histology of CEP can be the same as that of paraganglioma at other sites, but has the following differences: hemangioma-like,

pseudo-chrysanthemum-like, pseudo glandular or pseudo papillary arrangements can be observed; divergent differentiation can also be observed, and is sometimes accompanied with neuroblastoma, gangliocytoma, ganglioneuroblastoma, and malignant peripheral schwannoma components.^[25,26] Therefore, it is classified as neuron-glioma by the WHO.^[16] Pytel et al reported one patient with CEP accompanied with gangliocytoma components, and the immunophenotype was the expression of CK.^[27] This may also be the difference in characteristics between CEP and paraganglioma in other sites of the body. It also expresses neuroendocrine markers such as CgA, Syn, CD56 and S-100. Considering the differential diagnosis, if the tumor simultaneously expresses CK and neuroendocrine markers, the metastasis of hepatocellular carcinoma and gastrointestinal neuroendocrine carcinoma should be excluded.^[28] When CEP presents with a pseudo chrysanthemum-like structure, it is very similar to ependymoma, and immunohistochemical staining identification is required.^[28] Ependymoma expresses GFAP and EMA but does not express neuroendocrine markers.^[28] When it has an obvious nest-like or sinusoids structure, it needs to be distinguished from carcinoid tumors.^[28] The immunohistochemical staining of carcinoid tumors is negative for S-100 protein.^[28] When it is rich in blood vessels, it needs to be distinguished from tumors that are rich in blood vessels, such as hemangioma-meningioma, which are positive for EMA, PR and Vim, and hemangioblastoma, which does not express Syn.^[28]

Spinal paraganglioma is mostly benign and rarely malignant. It is difficult to determine benign and malignant tumors by histology. In this report, immunohistochemical staining could be used to effectively analyze the shape of paraganglioma. Hence, it should be determined according to its biological behavior. If the tumor has lymph node metastasis or/and distant metastasis, it can be considered as malignant paraganglioma. Complete removal of tumor by 1-stage resection is the first choice for the treatment of paraganglioma in the spinal canal. If the 1-stage operation can completely remove the tumor, the prognosis is good.^[29] In this case, the tumor boundary were unclear, and invasion of bone tissue was observed. In the case of unclear tumor boundary, if the resection is incomplete, the recurrence would easily occur. Therefore, the range of excision should be extended to remove the tumor completely under the guidance of accurate pathological diagnosis. The prognosis of this case was good, and no recurrence was found in the follow-ups. In addition, the present study

improves pathologists' and clinicians' knowledge and ability of differential diagnosis about this rare disease.

In summary, surgical resection combined with radiotherapy can effectively alleviate clinical symptoms, and improve long-term survival rate.^[30]

Author contributions

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