Paraganglioma of the cauda equina: a case report and review of the literature

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Abstract: Spinal paragangliomas are relatively rare non-secreting tumors. They often form intradural compression of the cauda equina. These tumors are mostly benign and can be completely resected by surgery. Therefore, the risk of local recurrence in these tumors isestimated to be low according to the literature. Here we report a rare case of the recurrent paraganglioma of the cauda equina and review the clinical presentation, magnetic resonance imaging, pathology and treatmentsbased on the literature.
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1.Introduction

Paragangliomas arise from the paraganglial cells of the autonomic nervous system and are usually benign neoplasms of neural crest origin.(Houten et al.,2002) Paragangliomas have been reported to occur in multiple regions of the central nervous system including the petrous ridge, pineal region, sella turcica, sphenoid sinus, cavernous sinus, cerebellum and spinal canal.(JSousa et al.,2005;Faro et al.,1997; Lamer et al.,1997; Zileli et al.,2008; Sundgren et al., 1999) Spinal paragangliomas are relatively uncommon and frequently present as intradural tumors involving the filum terminale,(Lerman et al.,1972;Miller and Torack 1970) cauda equina (Horoupian et al.,1974;Li et al.,2007) and lumbar spine regions.(Shin et al., 2001;Fitzgerald et al., 1996;Jeffs et al., 2003) In addition, paragangliomas involving the intradural thoracic or cervical cord have also been reported but are extremely rare.(Fitzgerald et al., 1996) Although spinal paragangliomas are thought to be benign, the risk of the local recurrence in these tumors has been estimated to be 3 times higher than that in the adrenal pheochromocytomas.(Jeffs et al., 2003) Although paragangliomas are frequently reported, recurrent cases are rare. For example, Fitzgerald et al showed that malignant paragangliomas were found in more than 6.5% of their patients and local recurrence rate in 12% of them and no document reported a rapid recurrent case in cauda equina. Here we describe a rare case of local recurrent paraganglioma of the cauda equine, which recurred twice within a year. The case challenges the general idea that paragangliomas are benign and grow slowly. We also review the relavent literature on this disease.

2.Case report

In 2007, a 62-year-old man was presented with a history of progressive back pain for three years and numbness in the lower limbs for several months. The physical examination was normal. A magnetic resonance imaging (MRI) scan of the lumbar spine revealed an intraspinal mass on the L5-S1 segment. The mass was isointense on T1-weighted images, hyperintense on T2-weighted images, and showed intense heterogeneous enhancement after injection of Gd-DTPA A L5 laminectomy was performed and an intradural mass arising from the cauda equina was exposed. A nerve root of cauda equina was involved and infiltrated by the tumor. The tumor compressing the cauda equina was excised en bloc. Histopathology showed a typical feature of paraganglioma.

In May 2009, the patient was admitted again with a chief complaint of back pain for 3 months. The physical examination did not reveal abnormalities. MRI revealed a mass lesion in the original site at the L5 level with a hypointense T1-weighted signal and an intermediate heterogenous T2-weighted signal (Fig.1A, B). A surgical resection of the mass was performed through the previous approach. Histopathology showed typical features of paraganglioma (Fig.1C).

In March 2010, the patient was admitted for the third time presented with more severe pain in his back. MRI showed a larger mass at the L5-S1 level with heterogeneous signal intensity on T2-weighted images (Fig.2A). After GDPA injection the lesion

showed intense patchy enhancement with tubular signal voids within the tumor (Fig.2B). Decompressive surgery in terms of subtotal resection of the mass was performed. Immunohistochemical staining showed positivity in MNP-9, EGFR, MGMT, VEGF, PTEN, MDM-2, GST, P53 and Ki-67(Fig 2C and D).The diagnosis was still paraganglioma. Postoperative chemotherapy combined with radiotherapy was adopted for 5 months but the outcomes were disappointing

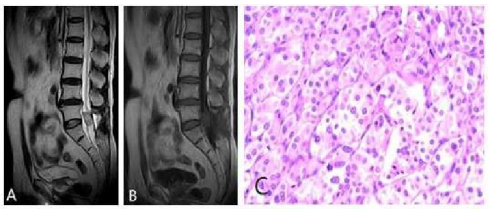

Fig.1 A,B) A mass of the original site at the L5 level with intermidate T2-weighted signal and T1-weighted signal. C) Histological image shows characteristic of paraganglioma. (original magnification, ×400)

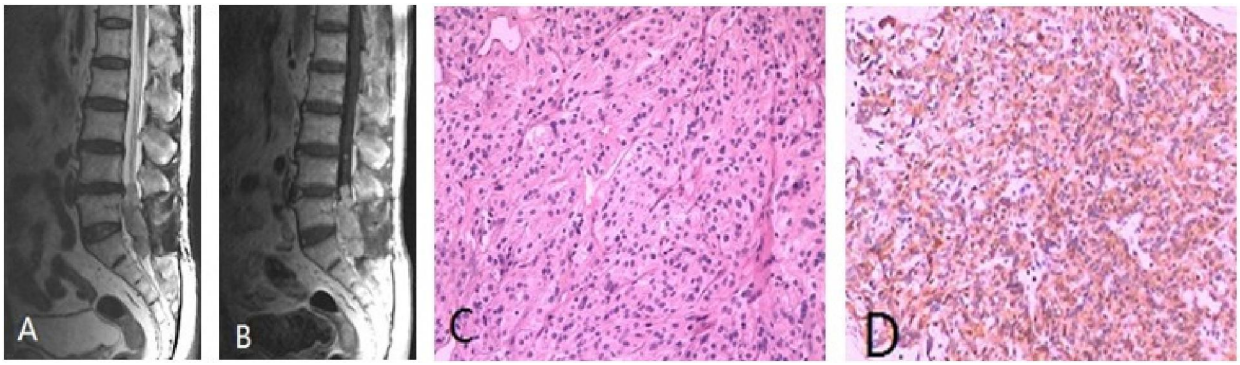

Fig.2A) A larger mass at the L5-S1 level with a moderately heterogenous T2-weighted signal. B) A contrast enhancing mass with tubular signal voids filled the spinal canal. C), Histopathology showed characteristic of paraganglioma. (original magnification, ×100) D) Immunohistochemical staining showed positivity in VEGF. (original magnification, ×100).

3.Discussion

Paragangliomas are neuroendocrine tumors of neuroectoderm derived from the neural crest and are found in several locations including head, neck, abdomen, and central nervous system. The primary tumors located in the adrenal medulla are called pheochromocytoma, while the extra-adrenal tumors of the neural crest origin account for 15% among all paragangliomas. Generally, adrenal pheochromocytomas secrete catecholamines, instead, paragangliomas are usually non-secreting lesions and 80% to 90% occur in carotid bodies or jugular bulbs.（Shin et al., 2001) In addition, paragangliomas have a higher rate of local recurrence than pheochromocytomas. Spinal paragangliomas arise from the sympathetic neurons in the lateral horns of the spinal cord, with approximately 90 cases reported in the literature.5 Most spinal paragangliomas in the literature occur in the cauda equina region. Paragangliomas occurred in the cauda equina region were first documented in the early 1970s. Since then more than 50 cases have been reported.(Houten et al.,2002) Paragangliomas of the cauda equina are generally intradural, whereas most thoracic paragangliomas are extradural and 20% have metastatic potential.13 Clinical presentation depends on the location and size of the tumor. For example, the typical symptoms of paragangliomas occurred in the cauda equina include low back pain, weakness and numbness in the lower limbs, sciatica, paresis, paresaesthesia and sphincter disturbances. On neurological examination, the patient may be found to have the abnormal sensation and proximal muscle power. On MRI, spinal paragangliomas revealed relatively well defined mass with low to intermediate signal intensity on T1-weighted images and intermediate to high signal intensity on T2-weighted images. Contrast-enhanced MRI presents with intense heterogeneous enhancement called “salt and pepper pattern”, which may be the characteristic findings of spinal paragangliomas.(Van Gils et al.,1994) The differential diagnosis of spinal paragangliomas on MRI include ependymoma, meningioma, schwannoma, dermoid and epidermoid cysts, lipoma, astrocytoma and metastatic tumours. The characteristic histological architecture of paragangliomas shows a hypervascularized tumor bed containing round and polygonal cells grouped in clusters called “Zellballen”. In detail, typical “Zellballen patern” presented as cords of chief neuroectodermal cells surrounded by sustentacular cells.(Lázaro et al.,2003) Immunohistochemical techniques to detect neuron specific enolase, leu-enkephalin, S-100 protein, synaptophysin and chromogranin are thought to be available tools.

(Kliewer et al.,1989) As most of spinal paragangliomas are non-secreting tumors, their preoperative diagnosis are relatively difficult compared to secreting pheochromocytoma. Although functional spinal paragangliomas are rare, the careful preoperative evaluation including blood pressure and urinary catecholamine metabolites is still necessary in order to prevent hypertensive crisis during tumor manipulation. It is suggested that prior to radiotherapy or surgery, preoperative hyperadrenal states is an important evaluation for patients with paragangliomas. It is also critical to treat endocrine-active paragangliomas before and after operation, including the management of preoperative hypertension and, if necessary, postoperative hypotension.

The majority of patients can be treated effectively by surgery. Metastatic spinal paragangliomas can treated with surgical decompression followed by radiotherapy. In some studies, iodine-131 labelled meta-iodobenzylguanidine (I131-MIBG), a structural analogue of guanethidine with uptake independent of catecholamine secretion, has been proved to be a useful tool for identification of metastasis and improvement of remission rate for spinal paragangliomas.(Noorda et al.,1996;Khafagi et al.,1987) The major roles of I131-MIBG, however, are still limited in diagnosis and palliation instead of curing.(Hartley et al.,2001)

The previous therapy was total resection of the mass without radiotherapy and chemotherapy. It is difficult to differentiate malignant from benign paragangliomas. The case proved that some of paragangliomas have malignant tendency and a rapid aggressive tumor may predict a poor prognosis. So, clinical practitioners should pay more attention to how to differentiate malignant paragangliomas and a long-term follow-up shoud be necessary for spinal paragangliomas in order not to lose operation opportunity. In addition, it is difficult to differentiate between non-secreting and secreting tumors, according to previous documents, most of paragangliomas in cauda equina are non-secreting. And it is rather difficult for a clinical practitioner to resect secreting tumors and these tumors have high malignant tendency. But even the non-secreting tumors have rapid recurrent risk, clinical practitioners should not neglect these tumors. Although most paragangliomas are benign and slow growing, the risk of malignant transition in patients with paragangliomas is three times higher than that in the adrenal pheochromocytomas. According to Fitzgerald et al., for example, malignant paragangliomas were found in more than 6.5% of their patients and local recurrence rate in 12% of them.7 The diagnosis of malignant transition is mainly based on the presence of metastases and the local recurrence after total resection of the tumor, because it is difficult to differentiate benign from malignant paragangliomas only by histological or immunohistochemical staining. (Spector et al.,2003;Olson JJ et al.,1989) In our patient, local spinal mass recurred and proved to be paraganglioma for three times. The previous therapy was total resection of the mass without radiotherapy and chemotherapy. Surgical decompression combined with radiotherapy and chemotherapy was adopted at last but the results were not satisfactory. In a word, the recurrent paragangliomas may be more difficult in treatment and need further research.

Conclusion

We reported a patient with recurrent paragangliomas in cauda equina, including his clinical presentation, radiological findings and histopathological features. The successful treatment of paragangliomas may be based on the early diagnosis and total surgical resection of tumors. Although spinal paragangliomas are rare and difficult to diagnose, they should also be considered within the presurgical differential diagnosis of spinal tumors. In addition, a long-term follow-up should be necessary for spinal paragangliomas because of the relatively higher local recurrence and metastasis.

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