



Paraganglioma in the cauda equina A Case Report

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Paraganglioma of the cauda equina is rare, and diagnosis is difficult. A 47-year-old woman presented with backache, with a 2-year history of pain radiating in her right lower extremity. Initial neurologic examination revealed mild hypaesthesia in the L4 dermatome on both sides. Spine MRI showed a well-delimited intradural extramedullary mass compressing the spinal cord. It extended from L2 to L4, with anterior compression of the spinal cord which was displaced posteriorly. Clinical and radiological findings suggested an ependymoma. Surgical decompression was performed from L2 to L4 through lumbar laminectomy under microscope. Intraoperatively, the patient experienced unexplained paroxysmal hypertension while manipulating the tumour, which was not relieved by hypotensive medication but resolved immediately after resection of the mass. Postoperatively, the neurologic status improved and the radiating pain was relieved. Histopathologic examination showed cellular perivascular arrangement which looked like 'pseudorosettes'. Taken together, these histologic and radiologic findings suggested a benign myxopapillary ependymoma. However, immunohistochemical examination showed reactivity with synaptophysin and chromogranin. Finally, histological examination of the specimen revealed a 'Zellballen' pattern of paraganglioma, and the final diagnosis of paraganglioma with secreting function was confirmed. Paraganglioma is a rare tumour that can exhibit a secreting function causing paroxysmal hypertension which may be life threatening. Therefore, the differential diagnosis is important. The diagnosis is based on close examination of the clinical, radiologic and pathologic findings.

Keywords : paraganglioma ; cauda equina ; paroxysmal hypertension ; recurrence.

INTRODUCTION

Paraganglioma is a benign slow-growing neuroectodermal tumour commonly found in the adrenal medulla. Extra-adrenal paraganglioma is rare ; it can occur throughout the body. It occurs most commonly in the carotid bodies and in the jugular glomus of the head and neck. It also occurs in other locations such as the liver, urethra, larynx, duodenum, orbit, adventia of the abdominal aorta and the

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para-aortic space (1). However, paraganglioma of the central nervous system is very rare, and occurs almost exclusively in the cauda equina region. Lerman *et al* (12) first reported paraganglioma of the cauda equina in 1972 and several cases have been reported since then (1,3,5,7,15,17,21).

Paraganglioma is a solid, highly vascularized, slowly growing and well encapsulated tumour, which usually originates from the proximal filum terminale. Paraganglioma of the cauda equina generally shows features resembling those of other tumours arising in the spinal cord; clinical symptoms are non-specific. For these reasons, spinal paraganglioma is hardly ever diagnosed or is misdiagnosed before the pathological confirmation. However, there were some cases of paraganglioma with functional hormonal activity which can induce perioperative vital instability (5,23). Complete surgical resection is curative; subtotal resection often leads to recurrence, and postoperative radiation therapy for patients with incomplete resection has no effect on prevention of recurrences (18,21). For these reasons differential diagnosis of the tumour is important.

We report a case of spinal paraganglioma that was initially misdiagnosed as ependymoma in spite of intraoperative clues for the diagnosis. The aim of this report is to warn about the possibility of a paraganglioma causing paroxysmal hypertension,

which can be life threatening and may result in incomplete removal of the tumour, but is hardly diagnosed.

CASE REPORT

A 47-year-old woman presented with backache, with a 2-year history of pain radiating in her right lower extremity. Initial neurologic examination revealed mild hypaesthesia in the L4 dermatome on both sides. Plain radiographs of the spine did not reveal any abnormality. Spinal MRI was performed showing a well-encapsulated intradural extramedullary mass compressing the spinal cord. The mass was isointense on T1 and hyperintense on T2 sequences with uniform contrast enhancement. The lesion was extending from L2 to L4 level, with anterior compression of the spinal cord backward displaced (Fig. 1).

Surgical decompression was performed from L2 to L4 through lumbar laminectomy. An encapsulated intradural extramedullary mass was found, displacing the spinal cord without infiltration. The mass was highly vascular, well encapsulated and attached to the filum terminale. There was no attachment to the dura mater, spinal cord and nerve roots. Complete removal of the lesion was done by gentle stripping of the mass under the operating microscope. Initially, the patient's vital signs were



Fig. 1. — Isointense signals with medullary tissue in T1 and hyperintense in T2 sequences with uniform contrast enhancement

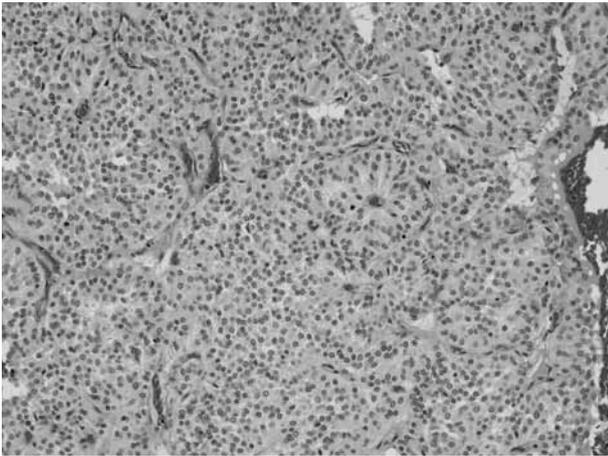


Fig. 2. — Cellular perivascular arrangement of papillary and epithelial cells which looks like a 'pseudorosettes' (H & E $\times 200$).

stable and blood pressure was in a normal range. However, during manipulation and resection of the tumour, the patient repeatedly experienced unexplained paroxysmal hypertension (up to 180/100 mmHg), which was resistant to any hypotensive agents. Fortunately, the blood pressure normalized immediately after complete resection of the tumour. Postoperatively, the patient's neurologic condition was improved. Lower extremity radiating pain and hypaesthesia were completely cleared within 2 weeks. There was no abnormality in urine catecholamine concentration. Radiotherapy and chemotherapy were not performed. Magnetic resonance imaging at 2 years after surgery showed no residual mass and no recurrence. Cerebral magnetic resonance imaging did not show any abnormality.

On pathological examination, a perivascular arrangement of papillary and epithelial cells which looked like 'pseudorosettes' was seen microscopically (Fig. 2). No mitoses or anaplastic changes were present, however parietal hyalinization of vascular channels was noted. These pathologic and radiological findings suggested a benign myxopapillary ependymoma. However, immunohistochemical examination did not show immunopositivity with glial fibrillary acidic protein (GFAP). It exhibited widespread reactivity with

synaptophysin, chromogranin and equivocal results with S-100 (Fig. 3). Therefore, with the suspicion of a neuroectodermal tumour, microscopic examination was rechecked. Histological examination of the specimen revealed an encapsulated tumour with an alveolar pattern. It also displayed chief cells with granular amophilic cytoplasm and spheroidal nuclei, separated by fine fibrovascular septae and many dilated blood vessels, suggestive of the 'Zellballen' pattern of paraganglioma (Fig. 4). It was finally diagnosed as a paraganglioma with secreting function that can induce medication resistant paroxysmal hypertension.

DISCUSSION

Spinal paragangliomas are rare ; they exclusively occur in the cauda equina. The most frequent clinical presentation is lumbar pain and sciatica accompanied by sensory or motor deficit in the lower extremities (1,14). Radiologically, paraganglioma is usually hypo- or iso-intense on T1 sequences, hyperintense on T2 sequences with uniform contrast enhancement (6,11,13,23). Pathologically, the classic 'Zellballen' pattern predominates in paragangliomas, which exhibit a similar pattern of clusters of cells separated by vascular channels. The predominant cell types are the chief cell, which is round to oval in shape with abundant eosinophilic granular cytoplasm, and the sustentacular or supporting cell (21). Differential diagnosis of spinal paraganglioma in the cauda equina includes e.a. ependymoma, schwannoma, meningioma, and metastatic tumours. Complete surgical resection is the treatment of choice for paragangliomas. Although they are benign, paragangliomas were found to recur in about 10-12% of patients. All of these recurrent tumours had not been resected completely in the first operation (4,7,21). In extramedullary type tumours, total resection should be attempted whenever possible. The best treatment is en bloc resection, with or without adjuvant radiotherapy. Adjuvant treatment (radiotherapy, chemotherapy) of histologically confirmed paraganglioma still remains questionable. Adjuvant treatment may be reserved for incompletely excised lesions, although its effectiveness has not been

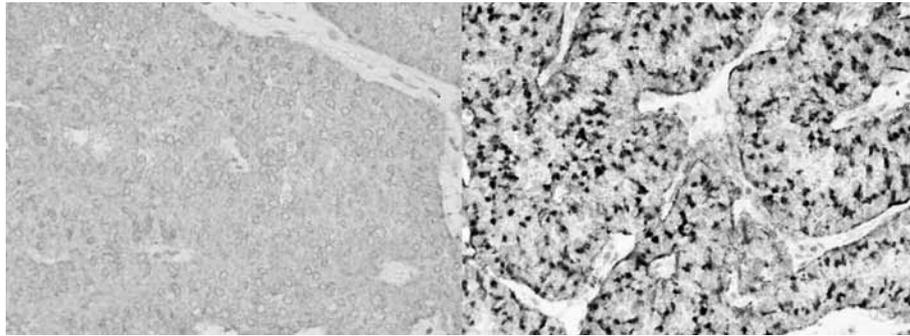


Fig. 3. — Widespread reactivity with synaptophysin, chromogranin ($\times 400$)

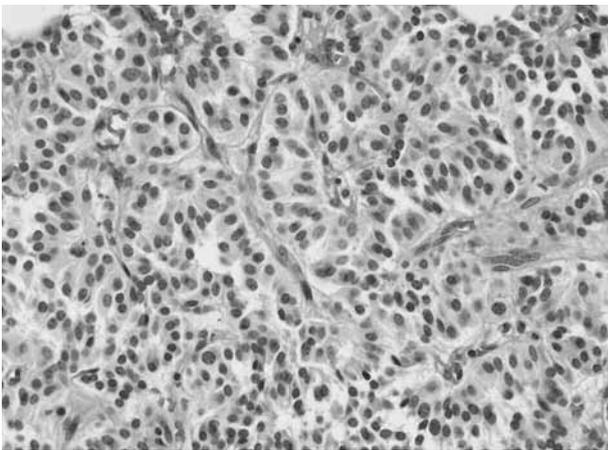


Fig. 4. — Main cells with granular amphiphilic cytoplasm and spheroidal nuclei separated by fine fibrovascular septa and many dilated blood vessels appears comparable to the 'Zellballen' pattern of paragangliomas (H & E $\times 400$).

established (18,21). Prediction of long term survival mainly depends on the extent of resection and the amount of tumour on postoperative imaging (7,15,18,21,22). Therefore, correct diagnosis and complete resection is important to prevent recurrence.

The common symptom of paragangliomas in the cauda equina is pain in the back, rectal area, or both lower legs. Despite their neuroendocrine origin, there were only few cases of paraganglioma of the cauda equina with functional hormonal activity reported in literature (5,23). One report showed flush like attacks without paroxysmal hypertension, with postoperative elevated urine noradrenaline concentration. The other report presented hyperadrenergic

symptoms while intraoperatively manipulating the tumour (23) in a 53-year-old man with a long history of low-back pain and motor and sensory deficit in a lower extremity. Intraoperatively, the patient experienced transient supraventricular tachycardia and paroxysmal hypertension during laminectomy. During tumour removal, each manipulation of the tumour produced a rapid rise in blood pressure. It was considered that this paraganglioma delivered vaso-active agents, probably catecholamines, into the systemic circulation. In our case, intraoperative paroxysmal hypertension was noted during manipulation of the tumour., and this was resistant to any hypotensive agent. Monitoring showed blood pressure up to 180/110 mmHg, which was difficult to control and caused intraoperative blood loss, and interfered with complete removal of the tumour. The blood pressure normalized immediately after resection of the tumour. In literature, some spinal paragangliomas presenting with symptoms of raised intracranial pressure have been reported (9,10,19) ; this may be related with the secretion of a large amount of fluid and catecholamines by the tumour. Biochemical analysis performed by Llena *et al* (11) suggested that the functional tumours predominantly contain noradrenaline, while non-functional tumours contain variable amounts of noradrenalin, dopamine and adrenaline. Pigott *et al* (17) reported a case that showed a very high level of serotonin. Although paraganglioma rarely shows secreting function, it can unexpectedly produce severe clinical symptoms, as in our case, and this may be fatal to the patient, and interfere with the complete removal of the tumour, thus encouraging

its recurrence. Therefore, the diagnosis of a paraganglioma should at best be made preoperatively, based on clinical, radiologic and pathologic clues.

However, spinal paraganglioma is seldom considered in the preoperative differential diagnosis because of its rarity and its non-specific features on MR imaging. Some findings are helpful in diagnosing a paraganglioma. With well-demarcated heterogeneously enhancing masses showing a hypointense tumour margin in the cauda equina, paraganglioma should be included in the differential diagnosis. Hypointense tumour margins on T2 weighted images, suggest paramagnetic effects from haemosiderin, and it is a specific MR finding in paragangliomas. It shows a salt and pepper appearance on T2 weighted images, which is considered a characteristic feature of paragangliomas of the head and neck, and has been described in lesions arising from the cauda equina (16). Unfortunately our case did not show these important characteristic features. Usually serpentine vessels are visible around the lesion. Serpiginous defects were found around the tumours, suggesting dilated serpentine vessels. Araki *et al* (2) suggested that this sign is important in diagnosing a highly vascular paraganglioma because it is unusual in ependymoma or schwannoma. The hypervascular nature of paraganglioma is often an important feature for the diagnosis.

In order to diagnose paraganglioma, pathological confirmation with immunohistochemical staining is necessary, because differential diagnosis from myxopapillary ependymoma is difficult. The latter is considered as a morphologically distinct variant of ependymoma, occurring almost exclusively in the cauda equina. In radiographic images it appears isointense on T1 and hyperintense on T2 sequences, demonstrating uniform contrast enhancement. The similarity between paraganglioma and ependymoma of the cauda equina has led to diagnostic confusion. Pathologically, myxopapillary ependymoma is characterized by perivascular 'pseudorosette', radially oriented cell groups surrounding small vessels (8,20). In our case, paraganglioma showed a pseudopapillary pattern with thick hyalinizing fibrous trabeculae like myxopapillary ependymoma. Histological differentiation of paragangliomas

from ependymomas on routine staining is very difficult. However, the immunohistochemical features of paraganglioma are quite clear, and distinguish it from other cord tumours (3,15). The characteristic immunohistochemical profile is a positive staining for various endocrine markers, especially synaptophysin, chromogranin and neuron-specific enolase (NSE), which may be positive in sustentacular cells. Therefore, immunohistochemical techniques must be used to achieve a correct diagnosis.

In conclusion, paragangliomas are benign but may recur after incomplete resection. They sometimes show secreting function which may result in life-threatening paroxysmal hypertension. However, the pre- and postoperative diagnosis of a paraganglioma is very difficult. Even though paraganglioma is a rare tumour, whenever unexplained paroxysmal hypertension is noted, the surgeon should consider the possibility of a paraganglioma. In order to avoid a paroxysmal hypertension and prevent a recurrence of the tumour, correct diagnosis is important, based on radiologic, pathologic and clinical findings.

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