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# Paragangliomas of the spinal canal

**P. Sundgren**
**M. Annertz**
**E. Englund**
**L. G. Strömblad**
**Ś. Holtås**

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P. Sundgren (✉) · M. Annertz · Ś. Holtås
Department of Diagnostic Radiology,
University Hospital of Lund,
S-22185 Lund, Sweden
Fax: +46-46-12 18 37

E. Englund
Department of Pathology,
University Hospital of Lund, Sweden

L. G. Strömblad
Department of Neurosurgery,
University Hospital of Lund, Sweden

**Abstract** We report the clinical MRI and histopathological features of five consecutive cases of spinal paraganglioma. Three intradural tumours were found in the typical location (two at the L4, one at the S2 level); one intradural extramedullary tumour arose at an unusual level, from the ventral C2 root, and one extradural tumour growing along the L5 nerve root sheath had an aggressive growth pattern with early, local paraspinal recurrence and, eventually, intradural metastatic spread. This type of growth pattern has not been described previously. Paragangliomas of the spinal canal are more common than previously thought and can be located anywhere along the spine, although the lumbosacral level is the most common. Their appearance on MRI can not disinguish them from other tumours in the spinal canal. Even though paragangliomas in general are benign and slowly growing their growth pattern can vary and be more aggressive, to the point of metastatic spread.

**Key words** Paraganglioma spinal · Magnetic resonance imaging

## Introduction

Extra-adrenal paragangliomas are rare tumours, usually benign histologically, derived from paraganglion cells of neural crest origin. The tumours occur within or near the carotid body or glomus jugulare in 80–90 % of cases [1]. A few cases of paraganglioma in the pineal region, sella turcica and suprasellar region have been described [2, 3]. A spinal location is also rare; tumours have been found in the intradural, extramedullary compartment, predominantly in the lumbar region [4–10] and rarely in the cervical or thoracic regions [11–13].

We report the clinical MRI and histopathological features, of five consecutive cases of spinal paraganglioma found in a 1.5 million population within a 5-year period.

## Case reports

Case 1

A 64-year-old woman presented with a 1 year history of lumbar pain and left S1 sciatica. MRI revealed a 2 × 2 × 5 cm intradural tumour dorsal to the L4 vertebral body, with intermediate signal on T1- and T2-weighted images, and homogeneous contrast enhancement (Fig. 1 a, b, c). The tumour was surgically removed, with subsequent radiotherapy.

Histological examination revealed a richly vascular paraganglioma with a regular growth pattern, homogeneous cellular structure without atypia and a distinct capsule (Fig. 1 d, e). Immunohistochemical staining for chromogranin A showed strong, general tumour cell positivity.

Because of lumbar pain MRI was performed 1 year after surgery. It revealed no residual tumour. The findings were unchanged 3 years later.

Case 2

A 41-year-old man presented with 8 months of low-back pain radiating into the left leg. MRI revealed a 3 × 2 cm well-circum-

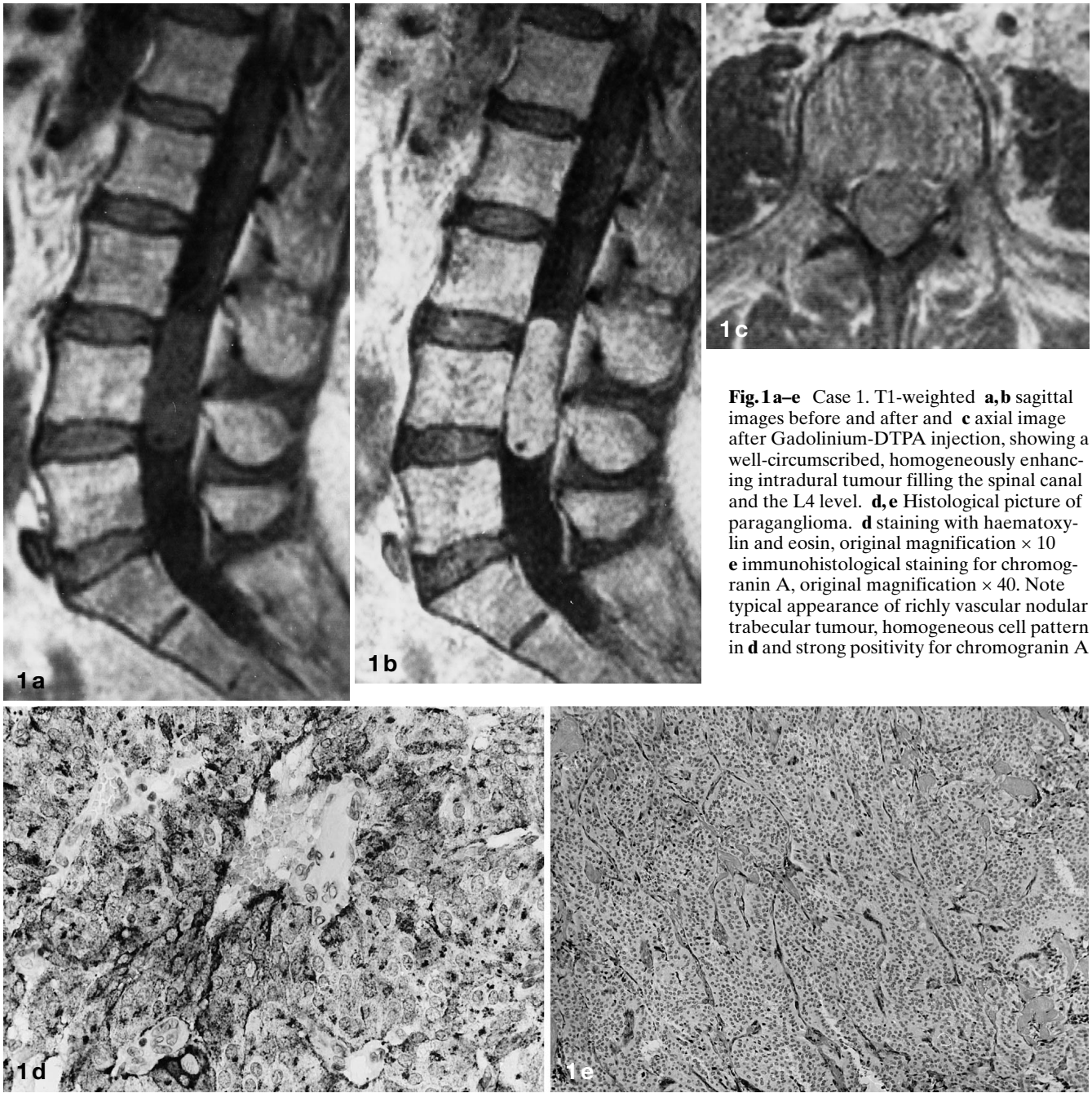



**Fig. 1 a–e** Case 1. T1-weighted **a, b** sagittal images before and after and **c** axial image after Gadolinium-DTPA injection, showing a well-circumscribed, homogeneously enhancing intradural tumour filling the spinal canal and the L4 level. **d, e** Histological picture of paraganglioma. **d** staining with haematoxylin and eosin, original magnification × 10 **e** immunohistological staining for chromogranin A, original magnification × 40. Note typical appearance of richly vascular nodular trabecular tumour, homogeneous cell pattern in **d** and strong positivity for chromogranin A

scribed intradural tumour at the L4–L5 level. The patient was operated upon. The histological findings were consistent with a paraganglioma enclosed in a thin fibrous capsule, but structurally similar to a syncytial meningioma. There was no marked cellular atypia or pleomorphism Chromogranin A staining showed moderate, diffuse positivity.

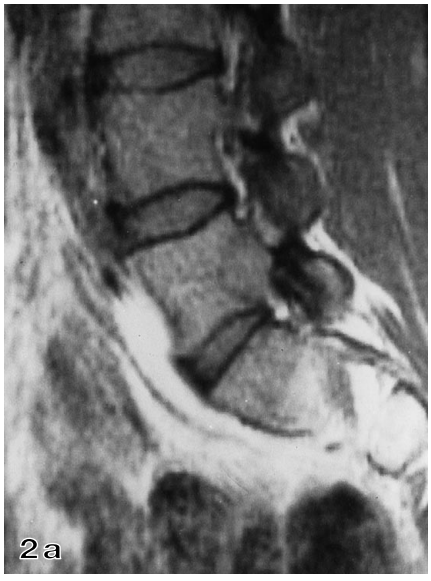
Postoperatively the patient's pain disappeared and there were no signs of recurrence after 4 years of follow-up.

Case 3

A 43-year-old man presented with 2 months of sacral pain, right sciatica and paresis of the right leg.

CT revealed a 6 × 6 × 6 cm tumour with partial destruction of the S1 vertebral body, and paravertebral growth. MRI showed an infiltrative tumour in the S1 vertebral body with extension into the spinal canal and to the presacral soft tissues.

An open biopsy was performed and the histological examination showed a solid tumour composed of large clear cells, with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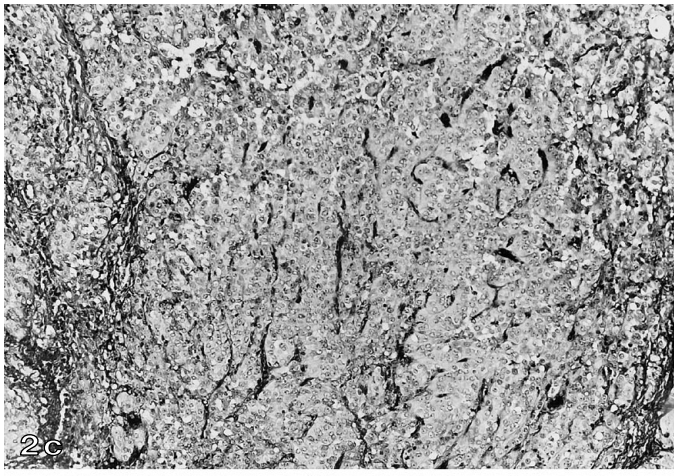
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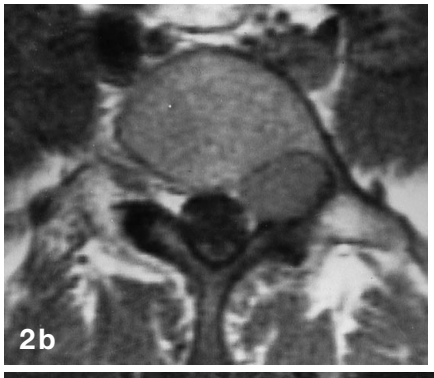
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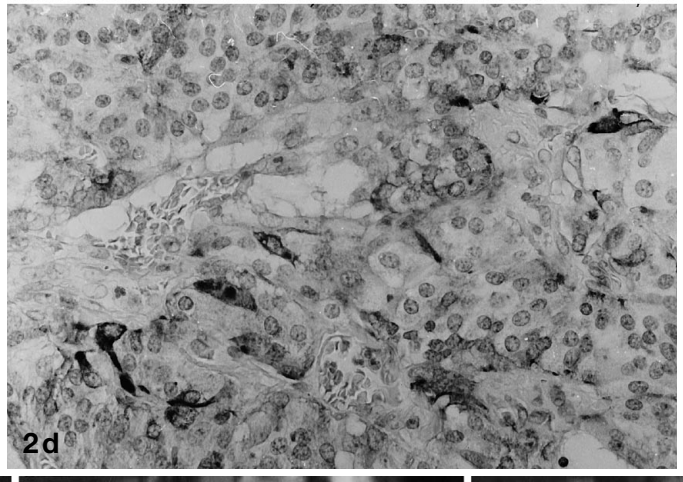
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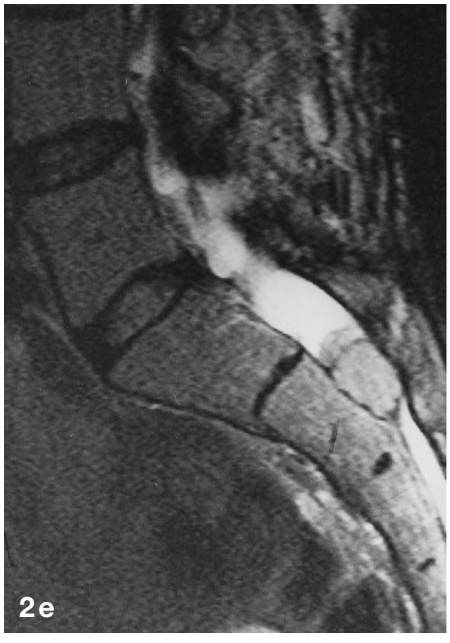
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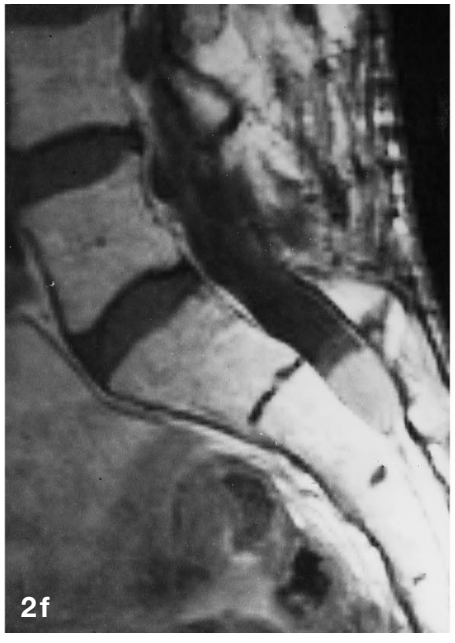
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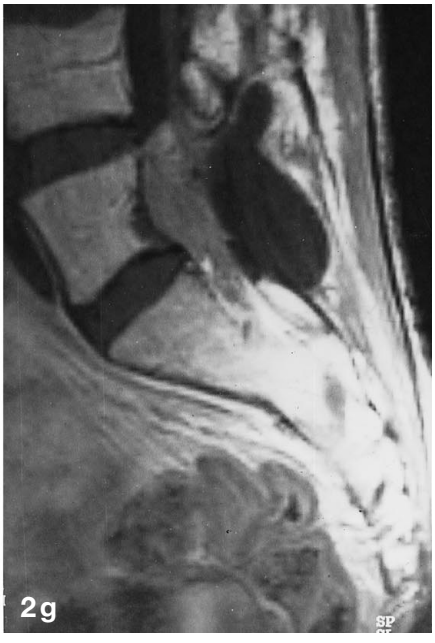
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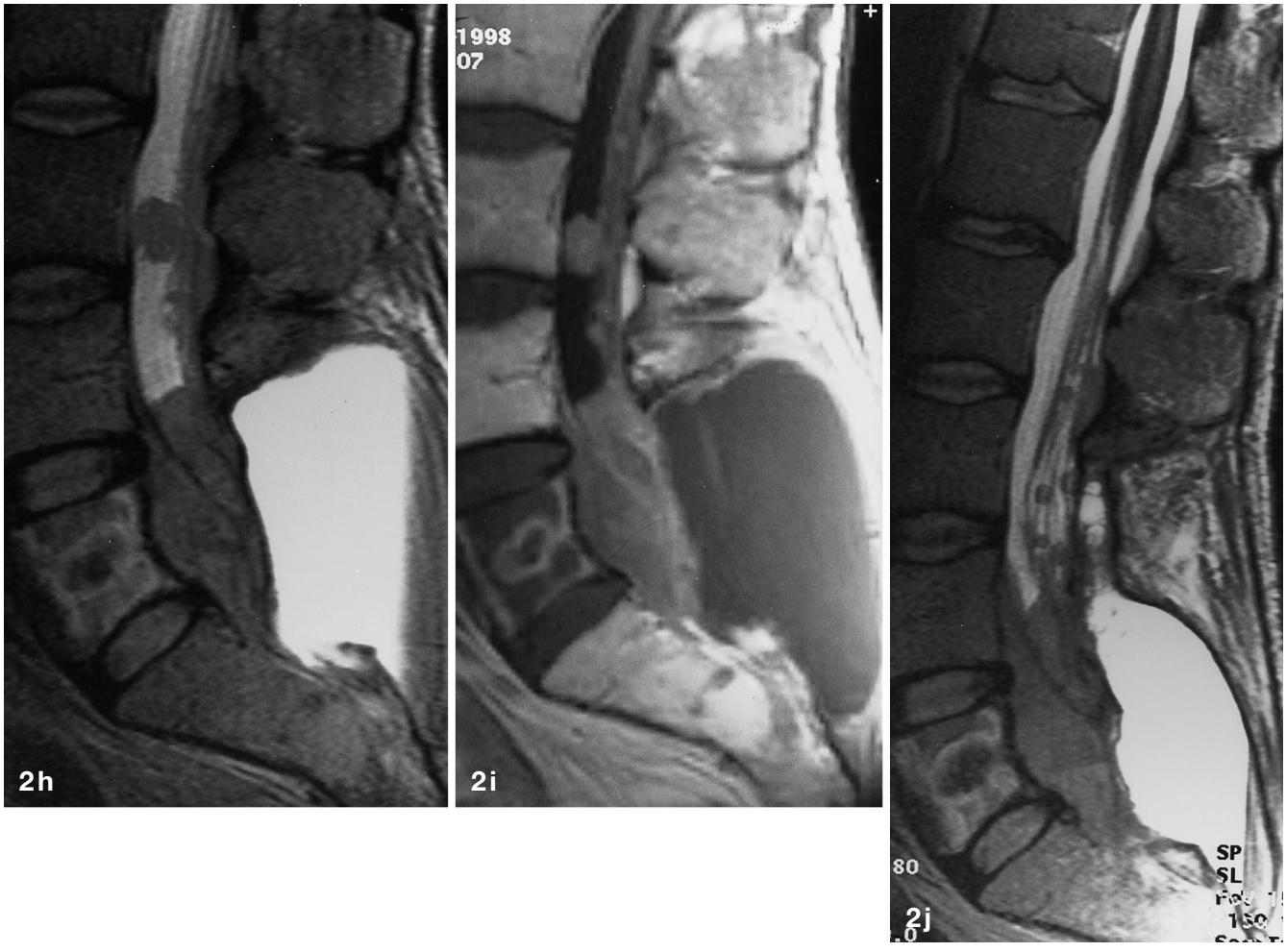


**Fig. 2 a–j** Case 4. **a, b** Original tumour: T1-weighted sagittal and axial images showing a 20 × 10 mm well-circumscribed extradural tumour in the left L5-S1 intervertebral foramen, remodelling the left L5 peduncle. The tumour is isointense with spinal cord. **c, d** Microphotography of paraganglioma at time of second tumour recurrence. **c** Staining with haematoxylin and eosin, **d** immunohistological staining for chromogranin A. The pattern is irregularly nodular, with some cytological pleomorphism and mild atypia in **d**. Focal, weak immunopositivity for chromogranin A. **e, f** Recurrent and a new intradural tumour. **e** T2-weighted **f** contrast-enhanced T1-weighted parasaggital images showing a new well-circumscribed, homogeneously enhancing intradural tumour dorsal to S2. **g** The recurrent contrast-enhancing epidural tumour in the intervertebral foramen, a postoperative fluid-filled cavity dorsally, and decreased signal intensity in the L5 vertebral body are evident on a midsagittal contrast-enhanced T1-weighted image. **h, i** Recurrent tumour and a further new intradural tumour **h** sagittal T2-weighted and **i** contrast-enhanced T1-weighted images demonstrate the large, lobulated, diffusely contrast-enhancing residual tumour at L5, changes in the vertebral body of L5, postoperative fluid-filled cavity, a new 8-mm intradural tumour at L3, and multiple small intradural nodules. **j** Residual tumour and additional intradural tumours: T2-weighted sagittal image showing new multiple small intradural tumours at L2–L4, some of them already visible on the previous examination (**h, i**)

some nuclear pleomorphism and atypia, and occasional mitoses. Chromogranin A staining showed intense positivity. These findings were consistent with a paraganglioma.

The patient had external radiotherapy (60 Gy) but no further surgery. The tumour increased slightly in size and the patient had I-131 MIBG (metaiodobenzylquanidine) at two separate therapeutic sessions within 14 months of the first examination. CT, yearly over 5 years, showed no increase in skeletal involvement or tumour extension.

Case 4

A 35-year-old man presented with a 4 month history of lumbar pain and left L5 sciatica.

CT showed a 25 × 13 mm contrast-enhancing lesion in the left L5-S1 intervertebral foramen. MRI revealed a 20 × 10 mm extradural tumour, with high signal on T2-weighted images (Fig. 2 a, b). An L5-S1 laminectomy was performed and the tumour was subtotally removed. Histological examination showed a compact tumour mass of small, densely packed nodules of pale cells, rich in cytoplasm. The stroma was scanty and there were areas of more trabecular tumour growth, suggesting a slightly biphasic growth pattern. There was, however, neither marked atypia, nor increased mitotic activity. Chromogranin A staining was negative at this

stage but became positive later. Staining for neurone-specific enolase was focally positive, as were markers for cytokeratins. These findings were consistent with a paraganglioma.

Due to progressive left-sided symptoms CT was performed 18 months postoperatively, showing a slightly enhancing 12 × 12 mm lesion adjacent to the L5 root sheath, with a caudal-lateral extension through the left L5-S1 intervertebral foramen, and faintly enhancing epidural scar tissue. Because of the recurrent tumour the patient was again operated upon with complete extirpation of the tumour. Histological examination showed a pattern similar to that of the first tumour.

Two years later the patient developed a left L5 radiculopathy. MRI demonstrated, besides a fluid-filled postoperative cavity, a new 3 × 3 cm lobulated contrast-enhancing tumour in the left L5 intervertebral foramen, with a ventral paravertebral extension, measuring 2 × 2 cm, and, a 3 × 2 cm epidural component. The patient was operated upon for a third time and was given radiotherapy. Microscopically, there was a similar dense neuroendocrine tumour mass, now with slight cellular pleomorphism and mild scattered atypia (Fig. 2c,d). Chromogranin A staining was weakly and focally positive.

MRI 18 months later again revealed a recurrent paravertebral and epidural tumour in the left L5 intervertebral foramen, and an intradural tumour at S2, which was clearly separate from the recurrent epidural tumour (Fig. 2e–g). Signal intensity was decreased on the T1-weighted images in the L5 vertebral body. The intradural tumour at S2 was removed surgically. Histological examination showed no further progress towards a higher degree of atypia, but rich fibrous admixture in the infiltrating tumour. MRI 8 months later showed residual tumour extending through both L5 intervertebral foramina and infiltrating the L5 vertebra, a new 8-mm intradural tumour at L3, and multiple small intradural nodules (Fig. 2h,i). The patient received chemotherapy.

A further study 9 months later revealed progression: the spinal canal between L5 and S2 was filled with tumour, extending through the foramina and surrounding the L3, L4, and L5 vertebral bodies, and three new small intradural tumours had appeared at the L2–L3 level (Fig. 2j).

Case 5

A 30-year-old woman presented with 6 months of pain in her neck and both arms. Examination revealed motor and sensory radiculopathy including the left ulnar, median and radial nerves. MRI showed a large intradural extramedullary tumour growing caudally from the foramen magnum to the C2–C3 disc space. It was isointense with the spinal cord on T1- and slightly inhomogeneous on T2-weighted images, and showed intense homogeneous contrast enhancement (Fig. 3). The spinal canal was filled with tumour and the upper cervical spinal was markedly compressed and displaced dorsally. The tumour was completely removed through a C1–C4 laminectomy and occipital craniectomy. At surgery, the tumour was thought to arise from the ventral left C2 nerve root.

Histological examination showed a well-demarcated, slightly lobulated tumour with large clear cells enclosed in a thin fibrous capsule. No cellular atypia or mitoses was identified. Chromogranin A staining was positive but weak. These findings were consistent with a paraganglioma.

MRI performed 2 months after surgery because of continuous pain showed a fluid-filled postoperative cavity dorsal to the spinal canal from foramen magnum to C4 level. No cord compression was seen, nor was there evidence of blood or tumour recurrence. The patient continued to have some pain and neurological deficits in the right arm, but MRI 7 months postoperatively showed no change. There have been no signs of recurrence after 5 years follow-up.

**Table 1** Patient data

| Case | Sex | Age (years) | Site of tumour | Follow-up |
|---|---|---|---|---|
| 1 | F | 64 | L4, intradural | 3 years, no recurrence |
| 2 | M | 41 | L4–5, intradural | 4 years, no recurrence |
| 3 | M | 43 | S1, intradural | 6 years, stationary |
| 4 | M | 35 | L5-S1, extradural | 7 years, local recurrence, new intradural tumours |
| 5 | F | 30 | C2, intradural, extramedullary | 5 years, no recurrence |

## Discussion

The majority (80–90 %) of extra-adrenal paragangliomas of the parasympathetic type, generally corresponding to the designation chemodectomas, occur in the carotid and jugular bodies [1, 6]. Paragangliomas in the spinal canal, believed to be rare, are predominantly of the sympathetic type. To date, approximately 80 spinal cases have been reported. During an 18-year period (1980–1997) the Department of Pathology at Lund University Hospital, the referral hospital for the south of Sweden (approximately 1.5 million people), has received 30 cases of extra-adrenal paraganglioma. No spinal tumours occurred among the 17 paragangliomas seen in the first 11 years, whereas in the last 7 years, five of 13 paragangliomas were spinal. This rather high proportion (17 % over 18 years, almost 40 % of extra-adrenal paragangliomas in the last 7 years) indicates that their prevalence might not be as low as previously expected. Histological rather than radiological or surgical underestimation may, besides chance, explain the absence of spinal paragangliomas diagnosed in the first 11 years. The histological methods that may differentiate paragangliomas from, for example, meningiomas have been employed more frequently recently, when awareness of the possibility of spinal paragangliomas has increased. The overall incidence of extra-adrenal paragangliomas is unknown; in an autopsy study of 19 610 patients it was found to be 0.01 % [14]. From our material the following figures can be calculated: 0.019/100 000/year in the whole 18-year period or 0.07/100 000/year in the last 7 years.

The primary histological features of paraganglioma are the “zellballen”, a nesting or clustering of cell groups, and the trabecular cords of cells within thin compartments of connective tissue stroma [15, 16], whereas the main lesion in the differential diagnosis, the

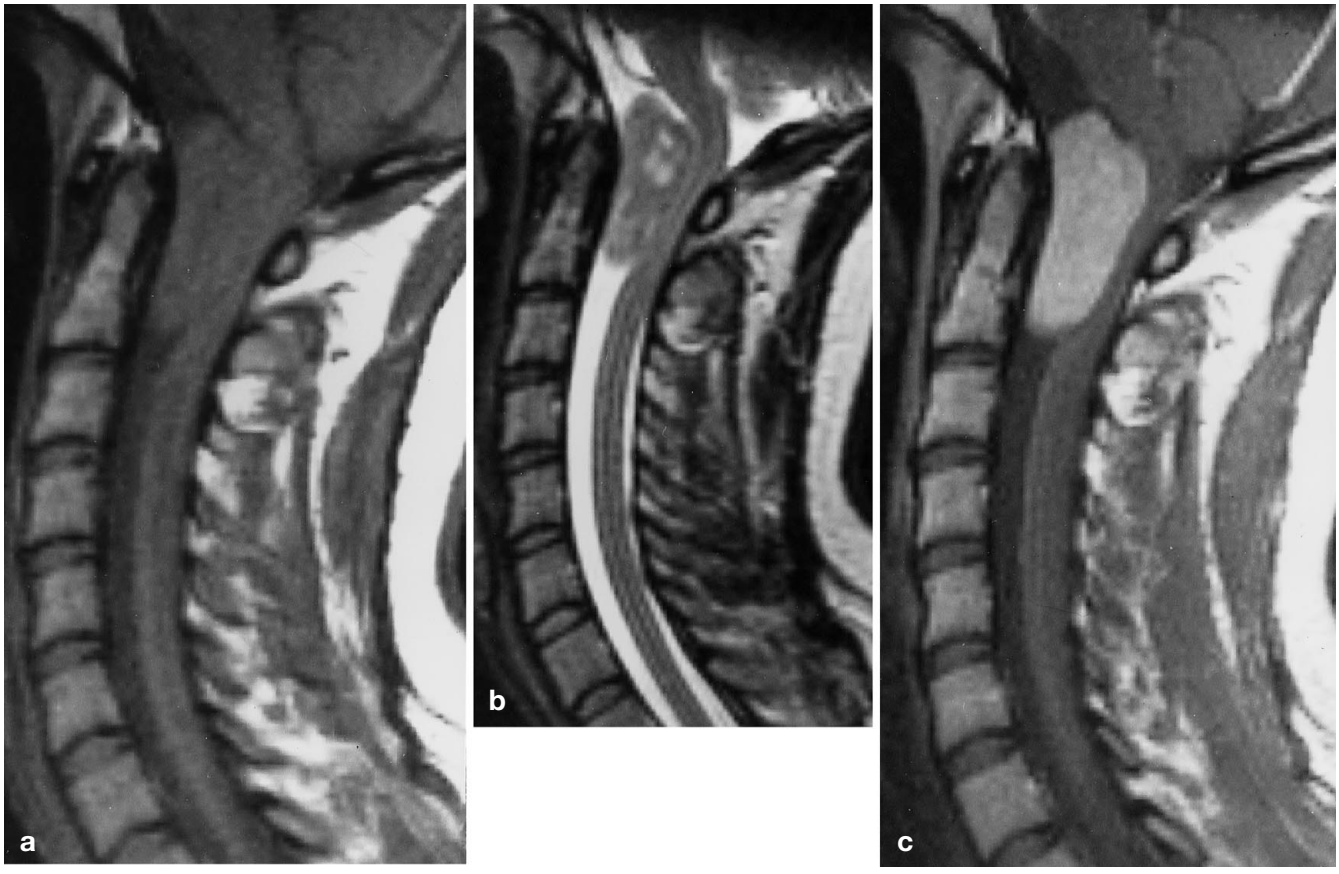


**Fig. 3 a–c** Case 5. **a** T1-weighted sagittal image showing a large well-circumscribed intradural extramedullar tumour isointense with spinal cord. **b** It gives slightly inhomogeneous signal on T2-weighting and **c** shows intense homogeneous contrast enhancement

myxopapillary ependymoma, is characterised by perivascular pseudorosettes, radially oriented cell groups surrounding small vessels [15]. The histological differentiation of paragangliomas from ependymomas on routine staining can be very difficult when none of the above "classical patterns" is seen or when surgical artefacts are present. Most commonly used for differential diagnosis is immunohistochemical staining for chromogranin, neurone-specific enolase and synaptophysin, which is positive for paraganglioma, whereas negativity for glial fibrillary acidic protein readily excludes an ependymoma. More rarely, investigation with electron microscopy is required.

Spinal paragangliomas are found most commonly in the intradural extramedullary compartment at the level of the cauda equina [1, 2, 4–9, 17]. It has been suggested that paragangliomas in the spinal canal represent a distinct subtype of extra-adrenal paraganglioma. Since paraganglionic tissue is not normally found in this region various hypotheses about the origin of the tumour have been proposed [4, 18, 19]. As none of these can be proved by contemporary investigation methods, the pathogenesis of these tumours remains unknown.

We suggest that spinal paragangliomas may originate from sympathetic neurones in the thoracic and lumbar lateral horns of the spinal cord, sending their axons to the sympathetic trunk through the communicating branches. It may also be possible that heterotopic neurones lie along these branches proximal to the sympathetic trunk and, in this site, may be the original locus of tumour formation.

The tumours present with symptoms due to spinal cord or nerve root compression, and there are no clinical features to distinguish them from other masses. The MRI findings are also nonspecific the tumours are often lobulated or ellipsoid, encapsulated and contrast-enhancing, impossible to differentiate from the myxopapillary ependymoma, the most common tumour in this region. Other differential diagnoses are neuroma, meningioma, dermoid tumour or lipoma; the latter two are easily excluded by their signal pattern.

In one of our patients (case 4), the primarily extradural tumour along the left L5 nerve root sheath demonstrated a very unusual aggressive growth pattern with

early local recurrence, paravertebral tumour extension, tumour infiltration of the L5 vertebra and, finally, intradural spread. Varying degrees of anaplasticity, albeit uncommon, have been reported [1, 17, 20]. There have been a few reports of local recurrence after macroscopically total [7, 8, 21] or subtotal [22] extirpation, implying a recurrence rate of approximately 4–10%. Four cases of metastatic spread have recently been reported [11, 12, 21, 23], all following surgical resection. In one case [11] the spread was probably due to CSF dissemination of a surgically created fragment. However, to our knowledge there has been no previous report of intradural metastatic spread or tumour extension of an extradural tumour prior to surgery. In our case the first three surgical procedures were confined to the extradural space, with no evidence of damage to the dura mater. Different explanations for intradural spread of a tumour primarily in the extradural space are possible. Apart from intraoperative tumour seeding, which could be excluded in the first three operations in this case, there is also a possibility of haematogeneous or lymphatic spread. More likely is that this is a case of multiple spinal paragangliomas, possibly occurring over a period of time. Primary multiplicity of extra-adrenal paragangliomas has been reported [2, 24, 25], also along the sympathetic trunk [26]. We thus suggest that this particular case represents a primarily multifocal tumour, occuring in different sites within and proximal to the sympathetic trunk.

Paraganglioma in the spinal canal, will seldom be considered in the presurgical differential diagnosis due to its rarity and nonspecific imaging features. The frequency of follow-up studies should be determined not only by the postoperative clinical course but also by the histological nature of the tumour.

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