Filum terminale paraganglioma with leptomeningeal dissemination: a case report

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Abstract

Leptomeningeal dissemination of a paraganglioma is an extraordinarily rare phenomenon described in a small number of cases worldwide. Here, we report a case of filum terminale paraganglioma characterized by an indolent, insidious nature even in the setting of leptomeningeal dissemination.

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Purpose:

Leptomeningeal dissemination of a paraganglioma is an extraordinarily rare phenomenon described in a small number of cases worldwide. Here, we report a case of filum terminale paraganglioma characterized by an indolent, insidious nature even in the setting of leptomeningeal dissemination.

Methods:

A 52-year-old man with a one-year history of low back pain, presented with worsening pain accompanied by new onset bilateral lower extremity paraesthesia, gait disturbance and dermatomal pain (L2-L3 dermatomes). Magnetic resonance imaging detected an intradural filum terminal lesion.

Results:

The patient underwent L5 and S1-S2 posterior laminectomy and complete excision of lesion followed by post-operative radiotherapy from L4- to S3. After surgery, the patient demonstrated gradual improvement in neurologic deficits.

At 10 years of initial diagnosis spinal magnetic resonance evaluation detected leptomeningeal enhancement at the level of T9 and L2. Surgery with L2 posterior laminectomy and complete resection of the L2 lesion was performed.

Magnetic resonance and positron emission tomography scans after surgery were indicative of slowly progressing leptomeningeal enhancement at the T9, T12 and L3 level. No detectable extraspinal disease was present.

The patient remains presently asymptomatic and under regular follow up at our institution.

Conclusion:

Documentation of rare cases such as this one is important for enhancing clinical awareness, stimulation of novel research into biomarkers of malignant potential and development of treatment protocols.

Keyword:

Filum terminale; Paraganglioma; Leptomeningeal dissemination; Spinal Neoplasm; Neuroendocrine Tumor;

Introduction

Paragangliomas (PG) are catecholamine-secreting neuroendocrine tumours that arise from neuroendocrine cells of the extra-adrenal autonomic paraganglia. Most PG are benign, however up to 35% have malignant potential.[1]

Although some PG, particularly those arising in the skull base and neck, do not present with symptoms of catecholamine excess, intratumoral metabolism of catecholamines to metanephrines occurs independently of catecholamine release. As a result, biochemical testing is indicated in every patient with a paraganglioma even if the patient does not present with a clinical picture of catecholamine hypersecretion. [2]

Primary PG of the spine are extremely rare neoplasms. Classified as *World Health Organization (WHO)* Grade I tumors [3], due to their slow growth and histologically benign appearance. Data on prevalence and epidemiology is incomplete due to its rarity. The classical anatomical site is the *cauda equina* and *filum terminale* . Although the source of spinal PG as primary site remains somewhat unclear, some have suggested an origin in the sympathetic neurons in the thoracic and lumbar lateral horns of the spinal cord or heterotopic neurons, which lie along these branches proximal to the sympathetic trunk [3,4].

Primary treatment remains complete surgical resection, with preservation of the surrounding nerve roots[5]. However, in the current literature, there is a gap of knowledge with regards to several aspects, namely the role of radiotherapy and preoperative embolization, as well as therapeutic strategies at recurrence and in the case of leptomeningeal dissemination.

Leptomeningeal dissemination of a PG is an extraordinarily rare phenomenon described in a small number of cases worldwide [6,7,8].

Case report

A 52-year-old man with a one-year history of low back pain, presented with worsening pain accompanied by new onset bilateral lower extremity paraesthesia, gait disturbance and dermatomal pain (L2-L3 dermatomes).

Workup with spinal MRI detected an intradural filum terminal lesion. No other detectable suspicious lesions were present. The patient was referenced for neurosurgery with a clinical and imagiological suspicion of ependymoma.

Surgery with L5 and S1-S2 posterior laminectomy and complete excision of suspect lesion was performed. Progressive clinical resolution of the low back pain and neurological symptoms.

Pathological report described adenocarcinoma cells with papillary and trabecular pattern. Immunohistochemically positive for AE1/AE3, CAM 5.2, synaptophysin and negative for cytokeratin 7 and 20, EMA, TTF1, PSA, S100 and GFAP.

The histopathologically characteristics were compatible with metastasis of adenocarcinoma with neuroendocrine differentiation.

The patient underwent post-operative radiotherapy from L4- to S3 (45Gy in 18 fractions).

Investigative work up for primary neuroendocrine carcinoma with CT, PET scan and Otreoscan was conducted without evidence of active disease. No tumour cells were detected on cerebrospinal fluid cytology.

Follow up with regular appointments and imagiological surveillance on our institution for 10 years without evidence of recurrence. At 10 years of initial diagnosis spinal MRI evaluation with leptomeningeal enhancement at the level of T9 and L2. The patient remained asymptomatic. No tumour cells were detected on cerebrospinal fluid citology.

Histopathologically review of the first specimen was performed. Tumour cells with a nest pattern, separated by septae and constituted by monomorphic epithelial cells without major atypia. Immunohistochemically

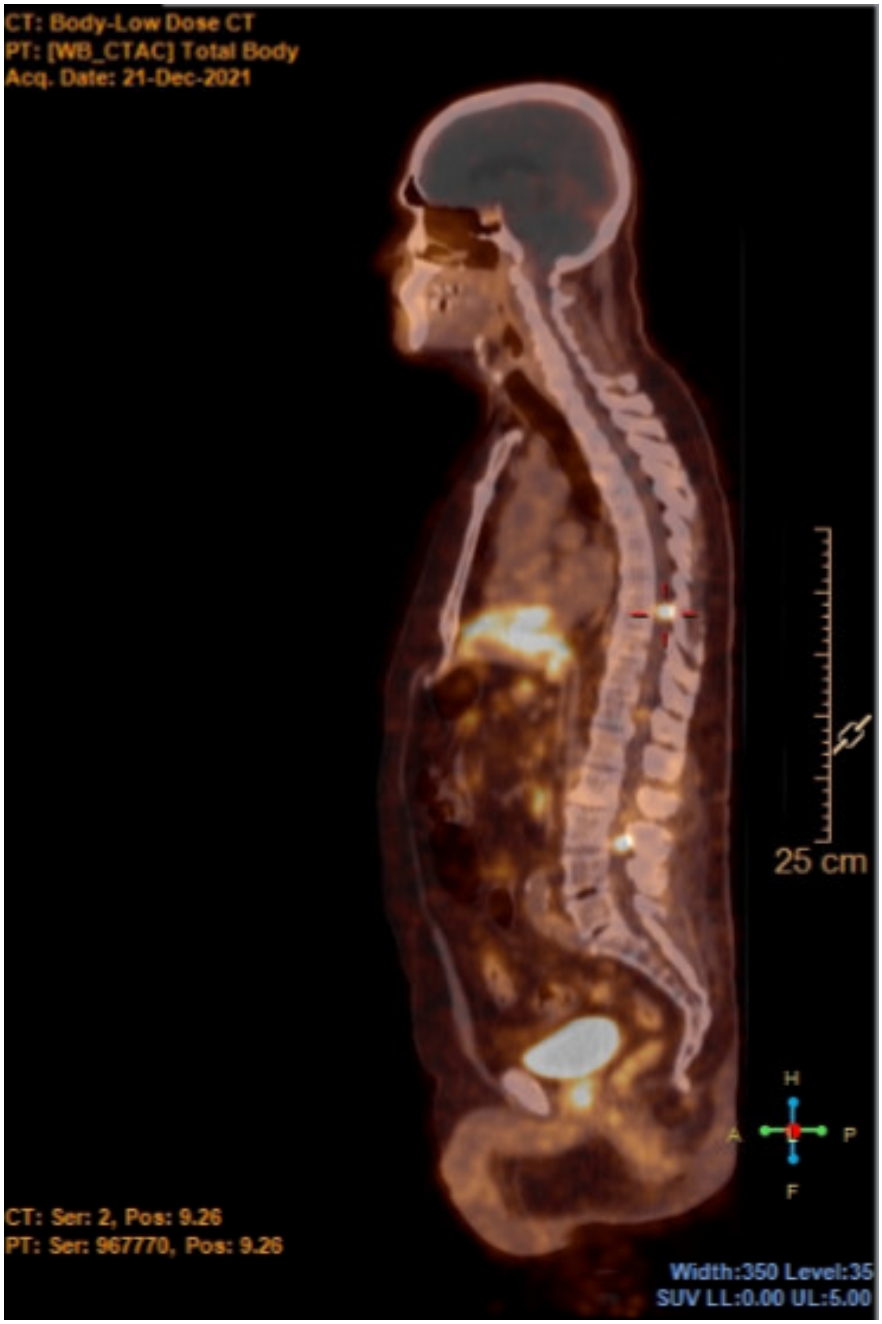
positive for AE1/AE3, CAM5.2, synaptophysin, CD56. Weakly positive for chromogranin. Negative for TTF1, SATB2, CDX2, calcitonin, GATA3, GFAP. Estimated proliferative index Ki67 of 5%.

From this pathological review the tumour was reclassified as a paraganglioma of the filum terminal with leptomeningeal dissemination.

Surgery with L2 posterior laminectomy and complete resection of the L2 lesion was performed. Pathology review presented similar characteristics as the first specimen and was compatible with the diagnosis of paraganglioma.

Genetic studies were performed without detections of pathogenic or likely pathogenic mutations.

Imagiologic surveillance with MRI (*Fig 1)* and PET scans after surgery indicative of slowly progressing leptomeningeal enhancement at the T9, T12 and L3 level. No detectable extraspinal disease.



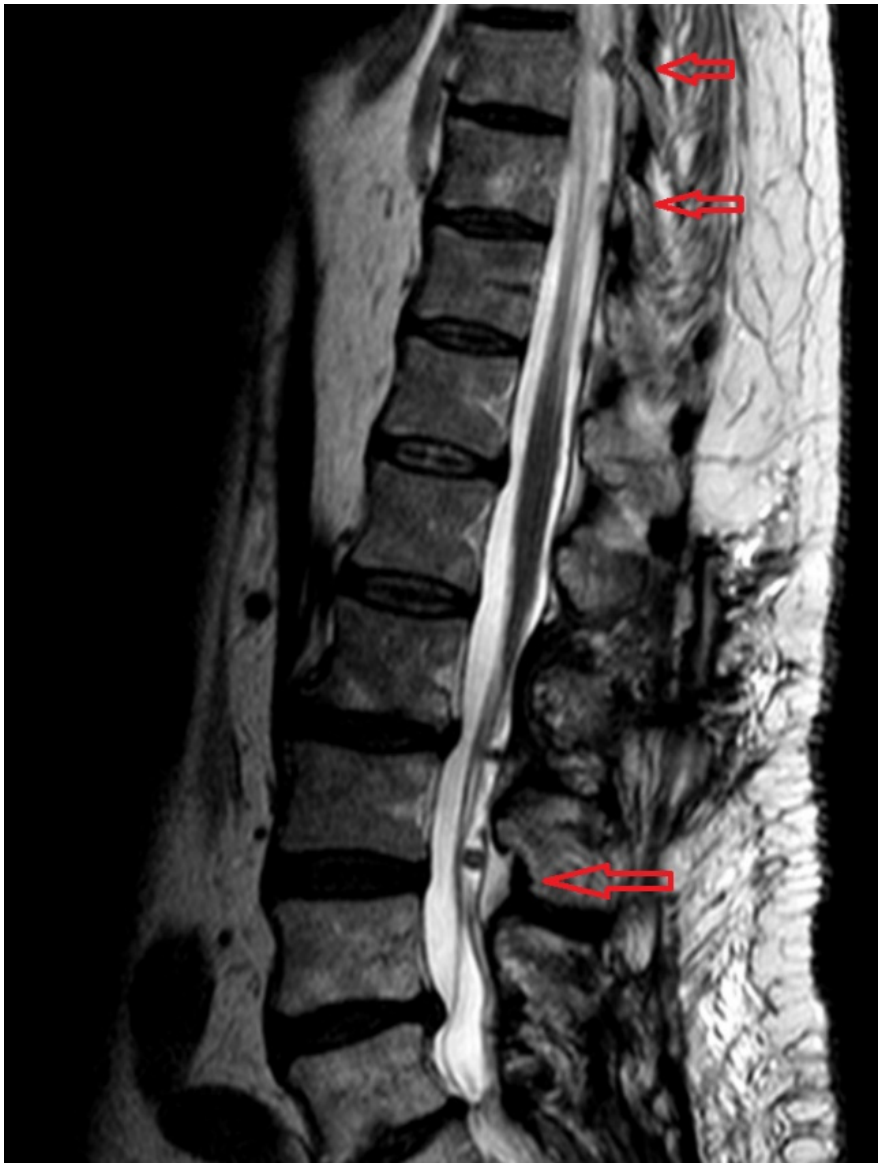


Fig1- *MRI after surgery showing* leptomeningeal enhancement at the T9, T12 and L3 level.

The patient remains presently asymptomatic and will maintain clinical and imagiological surveillance

Discussion

Our case presented and continues to present significant challenges to the attending physicians.

Firstly, the diagnosis was challenging. Clinical signs and symptoms were nonspecific and were all associated with local compression, with no symptoms due to catecholamine excess. Preoperative MRI can be diagnostic, however is frequently confounded, as it was in our case, with schwannoma, meningioma or ependymoma. The initial histopathological diagnosis was also incorrect, having the review of the specimen changed the initial diagnosis.

Secondly, as is described in the literature[,9, 10,11,12,]., spinal PG disease recurrence can occur decades after surgical resection, which highlights the need for long follow up periods with regular imagiological surveillance.

Thirdly, the optimal therapeutic strategies after primary resection remain unknow. Adjuvant radiation was performed after the first resection, however solid evidence in the literature for this approach is lacking. A second surgery with complete resection was performed after the first recurrence. There is some evidence of superiority of this approach *versus* radiation therapy.

Lastly the very small number of reported cases of PG where leptomeningeal dissemination has occurred means that treatment must be determined on an individual basis. Our review of the literature identified 6 described cases [6,7]. [Taken together these cases seem to suggest an indolent, insidious nature of the disease, even in the setting of dissemination.

Therapeutic options are limited as somatostatin analogs do not cross the blood-brain barrier. Radiotherapy and alkylating agents that penetrate the CNS can produce disease stability and their role in the management of leptomingeal dissemination warrants further investigation [5,8, 9,13]

Documentation of rare cases such as this one is important for enhancing clinical awareness, stimulation of novel research into biomarkers of malignant potential and development of treatment protocols.

References

1. William F Young, Jr, MD, MSc. Paragangliomas: Epidemiology, clinical presentation, diagnosis, and histology In: *UpToDate* , Post TW (Ed), UpToDate, Waltham, MA. (Accessed on April 16, 2022.)
2. Amar L, Servais A, et al. Year of diagnosis, features at presentation, and risk of recurrence in patients with pheochromocytoma or secreting paraganglioma. J Clin Endocrinol Metab. 2005; 90(4):2110. [PubMed: 15644401
3. Scheithauer BW, Brandner S, Soffer D. Spinal paraganglioma. In: Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, editors. WHO Classification of Tumours of the Central Nervous System. Lyon: IARC; 2007. pp. 117–9.
4. [4] G.C. Miliaras, A.P. Kyritsis, K.S. Polyzoidis, Cauda equina paraganglioma: a review, J. Neurooncol. 65 (2003) 177–190.
5. Ia Q, Yin H, Yang J, Wu Z, Yan W, Zhou W, Yang X, Xiao J (2018) Treatment and outcome of metastatic paraganglioma of the spine. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society 27:859-867
6. Nick Thomson, MDa, Karel Pacak, MD, PhD, DScb, Cheryl A. Palmer, MD, et al., Leptomeningeal Dissemination of a Low-Grade Lumbar Paraganglioma: Case Report and Review of the Literature ,J Neurosurg Spine. 2017 April ; 26(4): 501–506. doi:10.3171/2016.10.SPINE16948.
7. Constantin Tuleasca, Ahmed Salim Al-Risi, Philippe David, Clovis Adam, Nozar Aghakhani, et al.. Paragangliomas of the spine: a retrospective case series in a national reference French center.. Acta Neurochirurgica, Springer Verlag, In press, ff10.1007/s00701-019-04186-8ff. ffhal-02433449f
8. J.R. Anderson, R.W. Gullan, Paraganglioma of the cauda equina: a case report, J. Neurol. Neurosurg. Psychiatr. 50 (1987) 100–103, http://dx.doi.org/10.1136/ jnnp.50.1.100
9. Landi, R. Tarantino, N. Marotta, et al., Paraganglioma of the filum terminale: case report, World J. Surg. Oncol. 7 (2009) 95,*http://dx.doi.org/10.1186/1477- 7819-7-95*
10. Sousa J, O'Brien D, Crooks D. Paraganglioma of the filum terminale. J clin Neurosci. 2005;12(5):584–585. doi: 10.1016/j.jocn.2004.07.017.
11. Caruso R, Wierzbicki V, Marrocco L, Salvati M (2006) Paragangliomas of the cauda equina. Report of one case and review of the literature. Journal of experimental & clinical cancer research : CR 25:269-27
12. Corinaldesi R, Novegno F, Giovenali P, Lunardi T, Floris R, Lunardi P (2015) Paraganglioma of the cauda equina region. The spine journal : official journal of the North American Spine Society 15:e1-8
13. Mishra T, Goel NA, Goel AH (2014) Primary paraganglioma of the spine: A clinicopathological study of eight cases. Journal of craniovertebral junction & spine 5:20- 24