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Commentary

Surgical treatment of metastatic pheochromocytomas of the spine: a systematic review

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Metastatic pheochromocytoma of the spine (MPS) represents an extremely rare and challenging entity. While retrospective studies and case series make the body of the current literature and case reports, no systematic reviews have been conducted so far. This systematic review aims to perform a systematic review of the literature on this topic to clarify the status of the art regarding the surgical management of MPS. A systematic review according to PRISMA criteria has been performed, including all studies written in English and involving human participants. 15 papers for a total of 44 patients were finally included in the analysis. The median follow-up was 26.6 months. The most common localization was the thoracic spine (54%). In 30 out of 44 patients (68%), preoperative medications were administered. Open surgery was performed as the first step in 37 cases (84%). Neoadjuvant treatments, including preoperative embolization were reported in 18 (41%) cases, while adjuvant treatments were administered in 23 (52%) patients. Among those patients who underwent primary aggressive tumor removal and instrumentation, 16 out of 25 patients (64%) showed stable disease with no progression at the final follow-up. However, the outcome was not reported in 14 patients. Gross total resection of the tumor and spinal reconstruction appear to offer good long-term outcomes in selected patients. Preoperative alpha-blockers and embolization appear to be useful to enhance hemodynamic stability, avoiding potential detrimental complications.

Keywords

Pheochromocytoma; Spinal metastasis; Spine surgery; Neurosurgical oncology

1. Introduction

Pheochromocytomas are rare neuroendocrine tumors with metabolic activity. They arise from the chromaffin cells primarily located in the adrenal glands, and their reported incidence ranges from 0.2 to 0.9 per 100,000 per year [1, 2].

According to their endocrine activity, the most reported clinical presentation is palpitations, paroxysmal hypertension, and tachycardia.

This consists of the secretion of catecholamines, such as norepinephrine and epinephrine, producing vasoactive effects on blood vessels. Therefore, elevated urinary levels of vanillylmandelic acid (236 g/24 hrs) and metanephrine (30,000 g/ng creatinine) are commonly found in these patients.

The 5-year survival rate of benign pheochromocytoma is reported to be between 84% and 96%, while in malignant forms, it is as low as 40% [3, 4]. Common metastatic sites include the liver, lungs, and bones, while the spine is considered an uncommon localization.

Spinal metastases from pheochromocytoma (MPS) may represent clinical and surgical challenges since they affect the segmental biomechanical stability and influence endocrine homeostasis. Biomechanical complications may consist of bone erosion or vertebral fractures, spinal deformity, neurological impairment, and back pain. On the other hand, the endocrine activity can cause hemodynamic instability or paroxysmal hypertension, which is reported in up to 90% of these patients. Other symptoms may include pallor, flushing, weight loss, weakness, fever, chest or abdominal pain, anxiety and psychiatric disorders; fatal complications such as myocardial infarction, arrhythmia, and stroke may occur as the result of severe hemodynamic instability in cases of high catecholamine concentration [1, 2].

Because of these peculiar features, MPS should be differentiated by other metastatic tumors. However, according to the relative rarity of the disease, pheochromocytoma is still not included as a separate entity in the current oncological staging protocols. Therefore, there are no dedicated scales or scores for prognosis estimation or treatment selection to be preferred in these cases.

The optimal management of MPS consists of the surgical resection of the spinal lesions, the correction of spinal deformity, the decompression of the neural structures, and the medical control of the endocrine and cardiovascular disorders.

Different surgical strategies have been reported, such as open surgery with "en bloc" resection, vertebroplasty, embolization, or simple biopsy, which can also be combined with adjuvant chemo-radiotherapeutic treatments; however, clinical-radiological outcomes of these treatments have been not adequately investigated or compared yet.

We have performed a systematic review on surgical treatments for spinal metastasis from pheochromocytomas, aiming to collect the proposed surgical approaches and techniques and compare their clinical-radiological outcomes.

2. Methods

We performed a systematic review of the literature, according to the PRISMA statement guidelines.

Inclusion criteria: English written papers including human participants diagnosed for MPS; availability of clinical, demographic and surgical data of the included patients.

Exclusion Criteria: incomplete data; oncological diagnosis other than pheochromocytoma; editorials, commentaries, and review papers.

Three different medical databases were selected for conducting the present systematic review (PubMed; Medline; Cochrane Library; Embase). We used as keywords "spinal pheochromocytoma", "spinal paraganglioma", "metastasis", "spine", "spine surgery", "spinal tumor", "tumor embolization" [MeSH Terms], combined using the Boolean operators. The last search was launched in October 2020.

A double cross-reference check of papers considered for eligibility (forward search) was performed to include supplementary papers erroneously undetected in the first search round. In addition, data regarding intraoperative medical management, neoadjuvant and adjuvant treatments, surgical techniques, preoperative embolization, clinical and functional outcomes, preoperative and intraoperative medications, reoperation rate and procedures-related complications were analyzed.

3. Results

From the first literature research, we retrieved 32 articles. After duplicates removal and titles/abstract screening, 17 papers were considered for eligibility. Two papers were then excluded with reasons: other reviews (1), unclear outcomes (1). Finally, 15 studies (44 patients) matched the inclusion criteria and were included in the present review (Fig. 1).

We collected 44 patients treated for 73 pheochromocytomas and paragangliomas: 34 males and 10 females. The median age was 42 years (range 21–69). The median follow-up was 26.6 months (3 months to 13 years). The most common localization of MPSs was the thoracic spine with 39 out of the 73 lesions (54%), 9 (12%) lesions were located in the cervical spine, 16 (22%) in the lumbar spine, and 9 (12%) in the sacrum (Appendix Table 1, Ref. [5–19]).

The primary tumor was located in the adrenal glands in 35 cases and in mediastinum in 5 cases. In the heart, carotid and sacrum, respectively in 1 case each, the primary site was lacking in one patient.

In 38 patients, the surgical resection of the primary pheochromocytoma was performed before diagnosing spinal metastasis.

The most frequently reported symptom was back pain (20 patients, 42%), while cardiovascular symptoms, consisting of refractory hypertension, palpitations and tremor, were reported in 13 (29%) cases. Radicular pain was reported in 3 (6%) cases, a progressive motor deficit in 14 (31%), while sensory disturbances in 3 cases (7%). In two cases (4.5%), bladder dysfunction was reported as the primary symptom.

Diagnostic workup includes traditional imaging modalities and dosage of blood and urine concentration of epinephrine, norepinephrine and vanyllilmandelic acid. While CT scan and/or MRI was performed in all cases, the dosage of epinephrine and its metabolites was reported in two cases (4.5%) only. Bone scans (including FDG, PET, and CT scans) were performed in 30 cases (68%). Needle biopsy leading to histological diagnosis was performed in 19 cases (43%). In six cases (13%), the description of diagnostic workup was unclear, but the history of previously resected adrenal pheochromocytoma was the major clue leading to the final diagnosis.

In 30 out of the 44 patients (68%), preoperative medications were reported: alpha blockers were administered in 26 cases and in all the reported cases, phenoxybenzamine was used at a dosage ranging from 10 to 45 mg daily; in four cases (14%) a combination of alpha and beta-blockers was reported; in three cases no drugs were administered, and in the remaining 11 cases (25%) data regarding preoperative medications were not reported.

Neoadjuvant treatments including preoperative embolization were reported in 18 (41%) cases, including 13 cases of embolization alone and 5 cases of preoperative embolization combined with other treatments such as chemotherapy and radiotherapy. No treatment-related adverse events were reported.

Adjuvant treatments were reported in 23 (52%) patients: radiotherapy alone in 10 cases (23%), chemotherapy or I^{131}-meta-iodobenzylguanidine (MIBG) in 8 cases (18%), and their combination in the remaining 5 cases (11.4%).

Postoperative complications occurred in 10 patients (23%): hypotension and tachycardia were reported in 4 cases (9%), cardiac tamponade in 1 case, a pleural tear in 1 case (2%), and pulmonary edema in 1 case (2%). Two patients experienced transitory neurological worsening after the surgical resection of the spinal lesion. Two cases (4%) of cerebrospinal fluid leakage were documented, and one case (2%) of superficial wound infection was also recorded.

Minimally invasive treatments, consisting of selective vertebral body augmentation or percutaneous biopsy, were performed in 7 cases, followed by open surgery in 3 cases.

Open surgery was performed as the first treatment in 37 cases (84%): consisting of total gross removal and spinal instrumentation in 29 cases (78%) and spinal decompression with or without posterior instrumentation in 8 cases (22%).

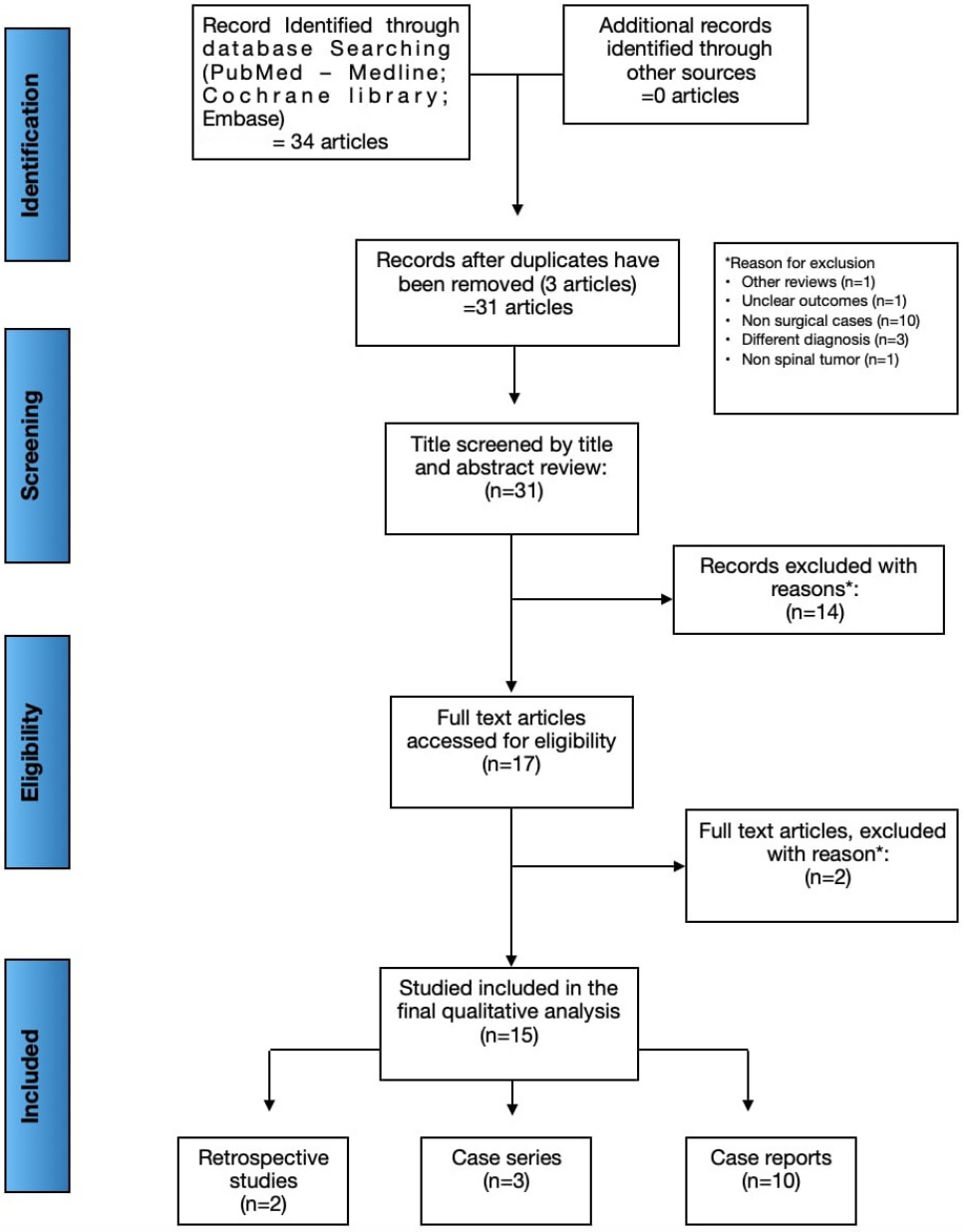

Fig. 1. Literature search process following PRISMA criteria. During the identification process based on title and abstract reading from Pubmed-Medline-Cochrane library—Embase databases, we retrieved 32 articles and removed three duplications. An accurate search of all manuscripts finally selected 15 papers for the literature search process.

The standard posterior approach was performed in 30 patients (81%), while a combined anterior-posterior approach in 7 (19%). In these cases, MPSs were located in the thoracic spine in 4 cases, in the lumbar spine in 2, and in the cervical spine in 1.

In patients who underwent total gross removal of the MPS and instrumentation, 16 out of 25 (64%) showed stable disease with no progression at the final follow up, 4 cases (16%) showed progression of the disease, and 3 patients (12%) died during follow up. In the remaining 5 patients (20%), it was not possible to retrieve data regarding disease progression. Nineteen patients out of the total 44 (43%) underwent biopsy, surgical decompression, and augmentation: 3 of them showed stable disease (15%), 6 showed progression (32%), and 3 died during the follow-up; in the remaining 10 cases, data regarding outcome were not available.

4. Discussion

Treating patients suffering from spinal metastases represents one of the most common, challenging clinical issues that clinicians and spine surgeons have to deal with.

Metastatic spinal pheochromocytomas are a relatively rare diagnosis, and they may represent clinical and surgical challenges for clinicians and spine surgeons. MPS endocrine activity may determine hemodynamic instability, and spinal stability can be severely affected.Therefore, surgery primar-

ily aims to decompress the neurological structures, restores spinal stability, and obtain tissue specimens for histological diagnosis.

The management of MPS and paragangliomas is not included in the most adopted classification systems, such as the revised version of Tokuhashi and Tomita's one [20, 21]; therefore, there is a lack of reliable tools for evaluating their prognosis. Accordingly, we designed the present systematic review to guide clinicians in choosing the medical-surgical treatment.

4.1 General features

Our results show that MPS occur more frequently in adults (mean age 42.4 years), while they are rare in the first three decades. The most involved spinal segment is the thoracic one (54%), followed by the lumbar (23%), the cervical (12%), and the sacrum (10%).

Clinical presentation of MPS comprises endocrine and systemic disturbances, such as refractory or paroxysmal hypertension, headache, palpitations, fatigue, flushing, and sweating. Neurological symptoms are due to the loss of spinal stability and the compression of the neural structures.

Due to the extremely low incidence of MPS, there is no consensus on their preferred treatment. In addition, spinal metastases may occur at the primary diagnosis or up to 85 months later than [5, 6]. Therefore, a long-term follow-up should be observed in these patients.

4.2 Diagnostic workup

MPS does not present pathognomonic features on CT scans, MRIs, and PET-CT. Therefore, radiological imaging maybe not effective in distinguishing these lesions from other metastases. In addition, a description of the diagnostic workup was missing in the majority of the reported series. However, several authors [6–14] considered the previous history of resected adrenal pheochromocytoma as a sufficient criterion to diagnose MPS.

In other cases, the dosage of catecholamines and their metabolites from blood and urinary samples have been helpful for differential diagnosis [8–12]. Needle biopsies are also proposed as a safe and valuable diagnostic tool [6, 7], although risks of bleeding and tumor spreading should be considered. Accordingly, we believe that the need for biopsy might be avoided in the case of previous pheochromocytoma surgery or high level of catecholamine or their catabolites in blood or urinary samples.

4.3 Preoperative treatments

In preoperative management, adrenergic receptor blockers should be used to control blood pressure and heart rate. The goal of blood pressure control is below 140/90 mmHg to ensure hemodynamic stability and to reduce the risk of perioperative complications [10]. In most reported series, phenoxybenzamine (10 to 45 mg per day) has been used [5–10]. Unfortunately, due to the non-homogeneity of the patients' sample sizes and surgical procedures, it was not possible to compare the status of the patients receiving preoperative adrenergic blockers with those in where these were not administered. Nevertheless, endocrinologist consultation should be carefully considered for these patients, and the use of adrenergic receptor blockers has been shown as advisable in refractory hypertension.

Some authors have advocated preoperative embolization. Kaloostian *et al.* [5, 6] reported the embolization of T10 MPS before performing vertebrectomy; T9 and T10 intersegmental arteries were embolized using glue and coils, significantly decreasing blood supply. The authors achieved intraoperative hemodynamic stability while preventing life-threatening intraoperative bleeding. However, they also reported one case in which massive intraoperative hemorrhage occurred regardless of the preoperative embolization. No adverse events following preoperative embolization were reported.

Therefore, preoperative embolization appears to be safe, and it should be considered when tumor resection and spinal instrumentation are planned to minimize intraoperative blood loss while improving hemodynamic stability.

4.4 Surgical treatment

Both minimally invasive procedures were reported, such as vertebroplasty, and open surgeries, such as decompressive laminectomies or multiple vertebral resection and reconstruction. Seven out of the 13 cases treated with radical resection and reconstruction achieved adequate disease control with no radiological progression at the final follow-up. On the other hand, progression was always reported after minimally invasive treatments. Kaloostian *et al.* [5] published the most extensive series on MPS management with radical surgical resection. They highlighted that even if a satisfactory control of the disease can be achieved with gross total resection, severe complications may occur intra- and postoperatively [5].

Total excision and reconstruction appear as promising approaches in well-selected patients. Most cases achieved reasonable control of the disease, and progression has been reported only in 2 cases. It has been postulated that mechanical stimulation and manipulation during resection can cause sudden catecholamine release, eventually influencing hemodynamics. Accordingly, en bloc resection of the vertebral body should be preferred to piecemeal removal.

The optimal treatment should be tailored to single patient characteristics, such as the functional status, number and localization of metastasis, and symptoms. For example, surgical resection can be achieved in single metastases, while laminectomy or tumor debulking should be considered in patients with multiple metastases or a poor oncological prognosis. Vertebral instrumentation may be required to preserve the segmental stability. Tumor mass debulking and segmental stabilization can alleviate neurological symptoms, prevent the development of secondary spinal deformities, and determine some grade of relief from mechanical and neuropathic pain. On the other hand, minimally invasive treatments, such as vertebral augmentation and percutaneous biopsy, seem to be effective for the symptomatic treatments of MPS, especially in the case of systemic disease.

4.5 Limitations

Non-homogeneous and poorly reported data represent the main limitation. In addition, the majority of the included studies present relatively short follow-up, and clinical outcomes were not reported. Lastly, data on tumor progression were not reported in almost half of the included patients.

5. Conclusions

Data on MPS are non-homogeneously reported, and the level of evidence of the available clinical reports is generally low. Preoperative embolization appears as a safe procedure, and it should be considered to reduce the intraoperative blood loss in gross total resections. Alpha blockade is generally recommended, especially in patients with refractory hypertension. Minimally invasive palliative treatments should be reserved for multi-metastatic patients or in case of poor prognosis, while radical resection has to be preferred in properly selected cases. Further clinical investigation is recommended, properly focusing on recurrence rates and clinical-radiological outcomes after the different available surgical treatments.

Abbreviations

CT, computed tomography; MPS, Spinal metastases from pheochromocytoma; Mri, magnetic resonance imaging; PET, positron emission tomography.

Author contributions

JV, LM and AS designed the research, JV and LM have collected the data, FC, LC and GL have analyzed the data, PBD and AS critically revised the manuscript.

Ethics approval and consent to participate

Since the manuscript is a systematic review of the literature and does not involve human participants, specifical ethical approval and informed consent are not required.

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Conflict of interest

The authors declare no conflict of interest.

Appendix

See Table 1.

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Table 1. Summary of the papers selected for the review, including demographics, treatment and outcomes.

Authors	Study	Age	Sex	Histology	Segments	Simptoms	Resection of primary lesion	Medications	Neo-adjuvant	Primary surgery	Further surgery	Complication	Adjuvant	Outcome	FU (months)
Kaloostian *et al.* [5]	Case report	23	M	pheochromocytoma	D10	back pain, hypertension	Yes	atenolol 12.5 mg/die. Phenoxibenzamine 10 mg/die	radiotherapy chemiotherapy embolization	En bloc resection (sec. Tomita) + thoracic cage positioning and T7–L1 instrumentation	None	Hypotension, transient paraparesis	None	NP	12
Kaloostian *et al.* [6]	Case series	28	M	pheochromocytoma	L3–L4	abdominal and low back pain.	Yes	atenolol Phenoxibenzamine	chemiotherapy embolization vertebroplasty	D5–D7 Posterior intralesional verterbrectomy and T3–T10 instrumentation	None	Tachycardia. marked blood loss	None	NP	48
		41	M	pheochromocytoma	D1–D5–D7	hypertention back pain	Yes	atenolol Phenoxibenzamine	Radiotherapy Embolization	D5–7: posterior intralesional vertebrectomy T1: two stage with sternotomy	None	Hypotension. Cardiac tamponade	None	DP	72
		21	F	pheochromocytoma	C7–D1–D2	hypertension	Yes	metoprolol Phenoxibenzamine	N/A	Posterior decompression and C3–T7 fusion	None	tachycardia	CT	DP	36
		62	F	pheochromocytoma	L1	hypertension, palpitation	Yes	Unreported	radiotherapy chemiotherapy embolization	Lateral single stage corpectomy and T12–L2 fusion	None	Unreported	RT + CT	NP	12
		23	M	pheochromocytoma	D10	back pain.	Yes	Phenoxibenzamine	radiotherapy chemiotherapy embolization	posterior en bloc resection + T7–L1 instrumentation	None	Hypotension, transient paraparesis	N/A	NP	156
Yamaguchi *et al.* [7]	Case report	27	M	pheochromocytoma	C2–C4–D10	nexk pain	No	Unreported	None	anterior C4 corpectomy	None	None	N/A	D	20
Yurt *et al.* [8]	Case report	47	M	pheochromocytoma	D8	hypertension, palpitation, paraparesis	Yes	Unreported	N/A	Posterior tumor resection	None	None	N/A	NP	24
Kheir *et al.* [9]	Case report	69	M	pheochromocytoma	C6–C7	back Pain, hypertension	Yes	Unreported	N/A	anterior C6–C7 corpectomy and C3–T4 fusion	None	None	RT	N/A	N/A

Table 1. Continued.

Authors	Study	Age	Sex	Histology	Segments	Simptoms	Resection of primary lesion	Medications	Neo-adjuvant	Primary surgery	Further surgery	Complication	Adjuvant	Outcome	FU (months)
Liu *et al.* [10]	Retrospective	31	W	pheochromocytoma	S	back Pain, hypertension	Yes	Phenoxibenzamine 30 mg/d	N/A	Dorsal instrumentation	None	None	None	N/A	3
		58	M	pheochromocytoma	S	pain, numbness	Yes	Phenoxibenzamine 10 mg/d	N/A	Dorsal instrumentation and augmentation	Posterior de-compression	None	None	N/A	3
		26	F	pheochromocytoma	D8–D11–D12	acute incomplete paralysis	No	Phenoxibenzamine 30 mg/d	N/A	Dorsal instrumentation	None	None	RT + CT + MIBG	N/A	3
		32	M	pheochromocytoma	D4	progressive paraplegia	Yes	None	N/A	Tumor resection and D3–D8 instrumentation	None	None	None	N/A	3
		59	M	pheochromocytoma	D9–D10	progressive paraparesis	Yes	Phenoxibenzamine 20 mg/d	N/A	Posterior resection and instrumentation	None	None	RT + MIBG	N/A	3
		63	M	pheochromocytoma	D2–D4–D7–L1–L3	back Pain, hypertension	Yes	Phenoxibenzamine 30 mg/d	N/A	Vertebroplasty	Vertebroplasty	None	MIGB	N/A	3
		27	M	pheochromocytoma	L1–L4	back Pain, hypertension	Yes	Phenoxibenzamine 30 mg/d	N/A	Vertebroplasty	None	None	None	N/A	3
		22	F	pheochromocytoma	D5	back pain.	Yes	Phenoxibenzamine 45 mg/d	N/A	Vertebroplasty	Posterior resection and instrumenta-tion	None	None	N/A	3
		60	M	pheochromocytoma	D11–L1–L3	progressive paraparesis	Yes	Phenoxibenzamine 30 mg/d	N/A	Vertebroplasty	None	None	RT	N/A	3
		38	M	pheochromocytoma	S	back pain, headache	No	None	N/A	Biopsy	None	None	MIGB	N/A	3
Cai *et al.* [11]	Case series	31	F	pheochromocytoma	L3	hypertension	Yes	alpha-beta blokers	N/A	tumor resection and fixation	None	None	None	N/A	24
		58	M	pheochromocytoma	S	back pain.	Yes	alpha-beta blokers	N/A	Biopsy, decompression, augmentation	None	None	None	N/A	6
Kasliwal *et al.* [12]	Case report	47	M	pheochromocytoma	D2	hypertension, bladder disfunction	Yes	Unreported	N/A	Posterior decompression	Anterior corpectomy and fusion	Unreported	RT	DP	12
Liu *et al.* [13]	Case report	58	M	pheochromocytoma	S	back pain, leg numbness	Yes	Phenoxibenzamine 20 mg/d	Embolization	Augmentation	Posterior de-compression and instru-mentation	None	N/A	NP	36

Table 1. Continued.

Authors	Study	Age	Sex	Histology	Segments	Simptoms	Resection of primary lesion	Medications	Neo-adjuvant	Primary surgery	Further surgery	Complication	Adjuvant	Outcome	FU (months)
Rittirsh *et al.* [14]	Case report	48	F	pheochromocytoma	D1–D5–D10–D12	hypertension, headache, tremor	Yes	Unreported	N/A	Posterior stabilization and augmentation T8–T12	None	None	RT + CT	N/A	N/A
Bodkey *et al.* [15]	Case series	54	M	Paraganglioma	C2	neck pain	Yes	Unreported	None	transoral resection	Occipitocervical fusion	Unreported	None	NP	30
		32	M	Paraganglioma	D10–D12	radiating pain	Yes	Unreported	Embolization	lateral corpectomy	None	None	RT	NP	24
Cybulsky *et al.* [16]	Case report	34	M	Paraganglioma	D8	back pain, numbness	No	Unreported	Embolization	Laminectomy	Posterior resection and instrumentation	None	None	DP	18
Laufer *et al.* [17]	Case report	69	F	Paraganglioma	S	back pain, leg weakness	No	Unreported	Embolization	Open biopsy	Decompression and instrumentation	None	RT	NP	N/A
Jia *et al.* [18]	Retrospective	34	M	Paraganglioma	D8	paraparesis	Yes	None	N/A	Posterior total piecemeal resection	N/A	None	RT	NP	27
		54	M	Paraganglioma	C2	neck pain	Yes	None	Embolization	Posterior total piecemeal resection	N/A	None	RT	NP	48
		32	M	Paraganglioma	D10–D12	back pain	Yes	None	N/A	Posterior en bloc resection	N/A	Pleural tear	None	NP	42
		34	M	Paraganglioma	D2	back pain, sphincter disturbances	Yes	None	N/A	Posterior en bloc resection	N/A	None	RT	NP	54
		47	M	Paraganglioma	D10–D12	back pain, headache	Yes	Alpha-blockers	N/A	Posterior total piecemeal resection	N/A	Wound infection	RT	NP	12
		47	M	Paraganglioma	D3	paraparesis	Yes	None	Embolization	Partial resection	N/A	None	CT	D	6
		58	F	Paraganglioma	S1	arm weakness	Yes	None	N/A	Partial resection	N/A	None	CT	D	35
		23	M	Paraganglioma	D2	paraparesis	Yes	None	Embolization	Partial resection	N/A	None	CT	NP	9

Table 1. Continued.

Authors	Study	Age	Sex	Histology	Segments	Simptoms	Resection of primary lesion	Medications	Neo-adjuvant	Primary surgery	Further surgery	Complication	Adjuvant	Outcome	FU (months)
		24	M	Paraganglioma	D2, L3, S1	paraparesis	Yes	None	Embolization	Posterior total piecemeal resection	N/A	None	RT	D	118
		29	M	Paraganglioma	C2–L2–L4	paraplegia	Yes	None	Embolization	Posterior total piecemeal resection	N/A	CSF leack	RT + CT	D	8
		58	F	paraganglioma	L4	paraparesis	Yes	None	Embolization	Posterior total piecemeal resection	N/A	CSF leack	RT	NP	21
		37	M	paraganglioma	D10–D12	back pain	Yes	None	N/A	Posterior total piecemeal resection	N/A	None	RT	NP	30
		25	M	paraganglioma	D7	paraparesis	Yes	None	N/A	Posterior total piecemeal resection	N/A	None	None	NP	46
		37	M	paraganglioma	D7–D8	back pain	Yes	None	Embolization	Partial resection	N/A	Pulmonry edema	CT	D	24
		64	M	paraganglioma	C3–C4	back pain	Yes	None	Embolization	Posterior total piecemeal resection	N/A	None	RT	NP	50
Kwan *et al.* [19]	Case report	46	M	paraganglioma	D5	Hypertension, progressive paraparesis	No	Unreported	Embolization	Corpectomy and fusion	None	None	N/A	N/A	3

Legend: NP, No progression; DP, Disease progression; D, Death; N/A, Not reported; CT, Chemotherapy; RT, Radiotherapy.