Clinical Case Report

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Surgical management of spinal metastases of thymic carcinoma

A case report and literature review

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Abstract

Rationale: Metastatic thymic carcinoma in the spine is a rare disease with no standard curative managements yet. The objective of this study is to report a very rare case of spinal metastases of thymic carcinoma successfully operated by combination of instrumentation and cement augmentation together with adjuvant treatment. The management of these unique cases has yet to be well-documented.

Patient concerns: A 57-year-old man presented with a 6-month history of continuous and progressive back pain. The patient, who had been diagnosed of thymic carcinoma (stage IV B) for 3 years, received surgical treatment of median sternotomy thymectomy, followed by 3 cycles of chemotherapy and 12 cycles of radiotherapy.

Diagnosis: Magnetic resonance imaging (MRI) of spine showed spinal cord compression secondary to the epidural component of the T4 mass, with increased metastatic marrow infiltration of the left T4 vetebral body, which presented as a solid tumor. Post-operative pathology confirmed the diagnosis of spinal metastases of thymic carcinoma.

Interventions: The patient underwent exploratory surgery, circumferential spinal cord decompression, cement augmentation and a stabilization procedure via a posterior approach.

Outcomes: The patient's neurological deficits improved significantly after the surgery, and the postoperative period was uneventful at the 3-month follow-up visit. There were no other complications associated with the operation during the follow-up period.

Lessons: Taken together, the lesion's clinical features, imaging results, and pathological characteristics are unique. Combined efforts of specialists from orthopedics, neurosurgery, thoracic surgery, and medical oncology led to the successful diagnosis and management of this patient. Metastatic thymic carcinoma of the spine, although rare, should be part of the differential diagnosis when the patient has a history of thymic carcinoma and presents with back pain and radiculopathy. We recommend the posterior approach for spinal decompression of the metastatic thymic carcinoma when the tumor has caused neurological deficits. Osteoplasty by cement augmentation is also a good choice for surgical treatment.

Abbreviations: MRI = magnetic resonance imaging, T1WI = T1-weighted image, T2WI = T2-weighted image, VAS = visual analogue scale.

Keywords: adjuvant therapy, cement augmentation, metastatic thymic carcinoma, stabilization, surgical treatment, thoracic spine

1. Introduction

Thymoma and thymic carcinoma are rare epithelial tumors that originate from the thymus gland. Extrathoracic metastases of thymic carcinomas are extremely rare entities and mainly occur in the lymph nodes, liver, and kidney.[1] Although thymoma and thymic carcinoma exhibit highly aggressive biological behavior, spinal metastasis is exceedingly rare. According to the World Health Organization, there are "organotypic" (types A, AB, B1,

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SL, XZ, and AS contributed equally to this work.

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B2, and B3) and "nonorganotypic" (type C, thymic carcinomas) thymomas.[2] Spinal metastases of thymic carcinomas are extremely rarely reported in literature, only very few patients with spinal metastasis have been documented, thus there is still short of imaging proof. Here, we are presenting an analysis of a rare case of spinal metastasis of thymic carcinoma treated with surgical management. We performed a surgical exploration, circumferential decompression, and stabilization surgery through a posterior approach. In the short term, the patient's conditions improved significantly postoperatively. After reviewing pertinent literature, we discussed common diagnosis and management considerations in patients with metastatic spinal thymic carcinomas.

2. Case report

In June of 2018, a 57-year-old man with progressive back pain was presented to our hospital. In his history of present illness, the patient stated he has been experiencing a paroxysmal and severe back pain for approximately 5 months. The pain in his back could reach 8 points using visual analog scale (VAS) and could not be alleviated with rest and hot compresses. Initially, the patient attributed the pain to his overwork and thus did not seek medical attention. The patient denied experiencing any other constitutional symptoms. Upon further questioning, he recalled a history of thymic carcinoma (Fig. 1A–H). The patient, who had been diagnosed of thymic carcinoma (stage IV B) for 3 years, received combined treatments including thymectomy in 2015, and subsequent 3 cycles of chemotherapy, and 12 cycles of radiotherapy. No pertinent family history was identified, including, hypertension, cancer, and congenital birth difficulties.

On physical examination, the patient showed decreased sensation to pin-prick and fine-touch of bilateral lower extremities and exhibited a 5-/5 strength in the lower extremities. Deep tendon reflexes revealed hyporeflexia, 1+, for both knee-jerk and Achilles tendon reflexes bilaterally. Ataxia was absent. Cranial nerves, mini-mental, and the rest of the neurological exam showed no abnormalities. Routine laboratory tests were ordered, including electrolytes, liver, and kidney function tests, tumor markers, and complete blood count. The results of the laboratory studies were almost within normal range, except that the tissue polypeptide specific antigen was significantly elevated to 165.81 U/L (normal: <80 U/L), serum neuron-specific enolase (NSE) elevated to 24.1 ng/mL (normal: <16.3 ng/mL), squamous cell carcinoma antigen elevated to 2.8 ng/mL (normal: <1.5 ng/mL), and carcinoembryonic antigen elevated to 5.3 ng/mL (normal: <5.0 ng/mL). Preoperative assessments included electrocardiogram, echocardiogram, and chest X-ray. Spinal magnetic resonance imaging (MRI) was ordered to visualize the metastatic lesions, to assess the stability of the vertebral column, and to aid in the formulation of a surgical approach. MRI of the thoracolumbar spine revealed widespread abnormal signal of multiple vertebras in keeping with diffuse metastatic infiltration. MRI of spine showed spinal cord compression secondary to the epidural component of the T4 mass, with increased metastatic marrow infiltration of the left T4 vertebral body, which presented as a solid tumor (Fig. 2A–D). Tumor infiltrated through the T4 vertebral body into the left pedicle and posterior elements. Extraosseous spread into the left lateral aspect of the epidural space extending posteriorly, resulting cord compression with the nerve root (Fig. 3A–G).

We performed a circumferential decompression procedure of the spinal metastasis to alleviate the symptoms caused by the spinal cord compression and subsequently stabilize the vertebral spine to prevent multiple vertebral bodies from collapse. Because of the size and location of the metastatic lesion and the extent of the metastases, the risk of surgical intervention is exceedingly high. Furthermore, extensive preoperative cardiovascular functions and intraoperative spinal cord function monitoring were also recommended.

In brief, posterior circumferential decompression from T2 to T6 internal fixation was performed. After general anesthesia induction and intubation, the patient was placed in a prone position for dorsal access to the thoracic spine. For the posterior approach, the paraspinal muscles were detached gently on each side after a midline longitudinal incision was made over the spinous processes. The pedicle entry points were exposed by step-by-step bilateral dissection. At first, left lateral transverse process of T4 and costal vertebra joint were removed, and the left part of vertebral body and paraspinal lesion at T4 was resected. The left nerve root of T4 was obviously compressed by the red and white fish-like tumor tissue. Then, the pedicle screws were placed bilaterally at T2 and T6, followed by pedicle screw insertion at T3 and T5. Because the patient did not exhibit hemodynamic instability to the placement of the pedicle screws, bone cement was filled with bone defect after excision of T4 vertebral body, and fixation using a Moss SI screw-rod system was employed. Visual inspection using the intraoperative fluoroscopy showed optimal position of all pedicle screws. The incision was closed. Intraoperative blood loss was approximately 400 mL, thus we

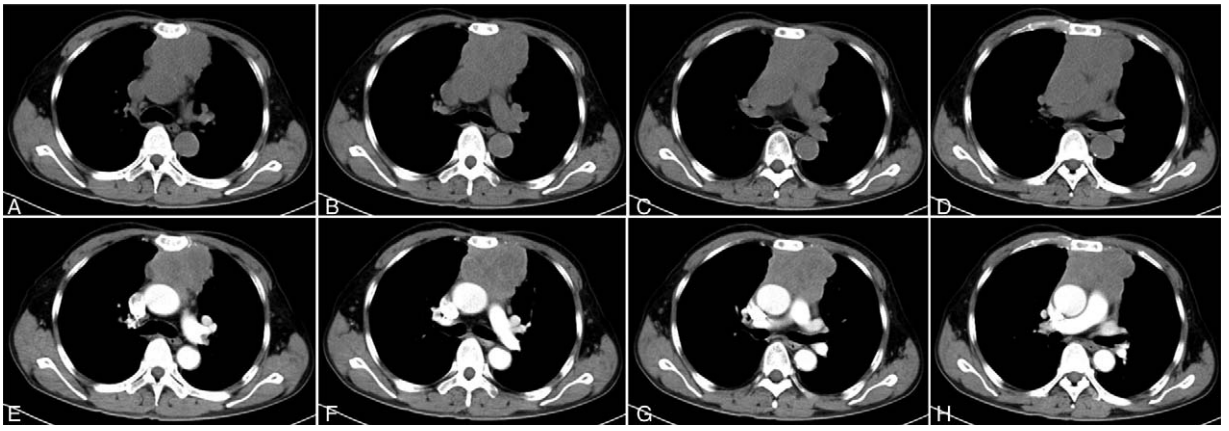

Figure 1. (A–H) Preoperative transverse computed tomography showing the primary thymic carcinoma in the anterior mediastinum.

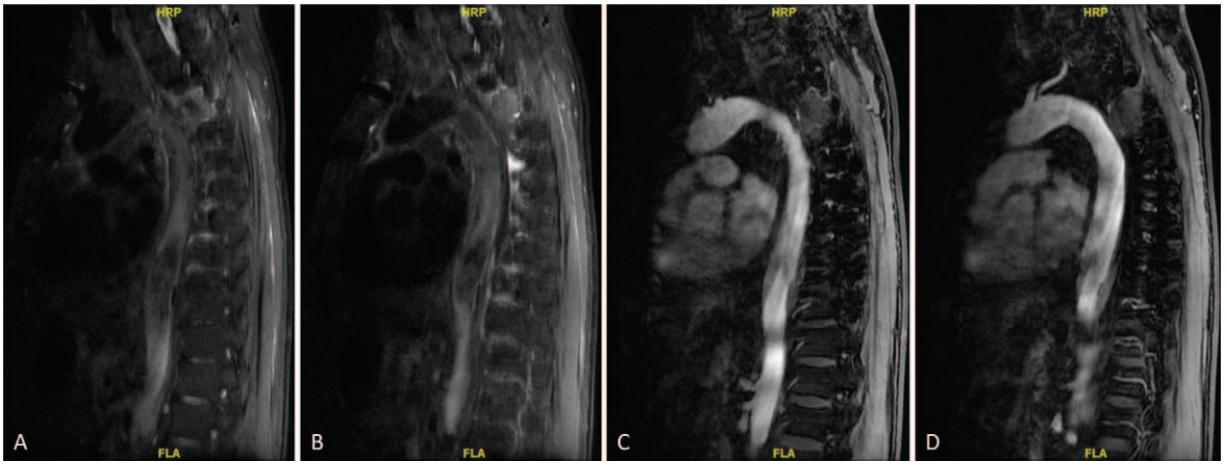

Figure 2. (A–D) Preoperative sagittal MRI scan revealing abnormal signal of T4 in keeping with diffuse metastatic infiltration caused by metastatic thymic carcinoma. MRI = magnetic resonance imaging.

used erythrocyte 4U. Postoperatively, the patient was referred to the regular ward. An X-ray after the surgery confirmed the correct positioning of the implants and no signs of displacement of the screws and rods (Fig. 4A and B). The postoperative pathology report confirmed thymic carcinoma. Pathological result was positive for AE1/AE3 indicating epithelial origin from thymus gland. Biopsy samples were positive for CD5, P40, P63 (Fig. 5A–F).

One week after the operation, the patient's bilateral lower extremities muscle strength improved to grade V compared to the preoperative status, grade V-, and the tendon reflex returned to normal. Moreover, VAS score of his back pain improved to 0 to 1 point compared to the preoperative status, 8 points. Following wound healing, the patient underwent rehabilitation therapy and was monitored as an outpatient. The postoperative 3-month follow-up visit showed no tumor progression and no new symptoms.

3. Discussion

Thymic tumors are amongst the most common mediastinal neoplasms. They comprise about 20% of all mediastinal tumors and up to half of all tumors in the anterior mediastinum in adults, and are typically slow-growing tumors that usually metastasize to the pleura, pericardium, or diaphragm. But spinal metastases are unusual.[1–3] Thymic carcinomas (TC) are invasive and classified as type C thymomas according to the classification from World Health Organization, and these rare tumors account for only about 0.06% of all thymic neoplasms.[1,3] However, unlike most thymomas that have indolent features, TC shows overt cytologic

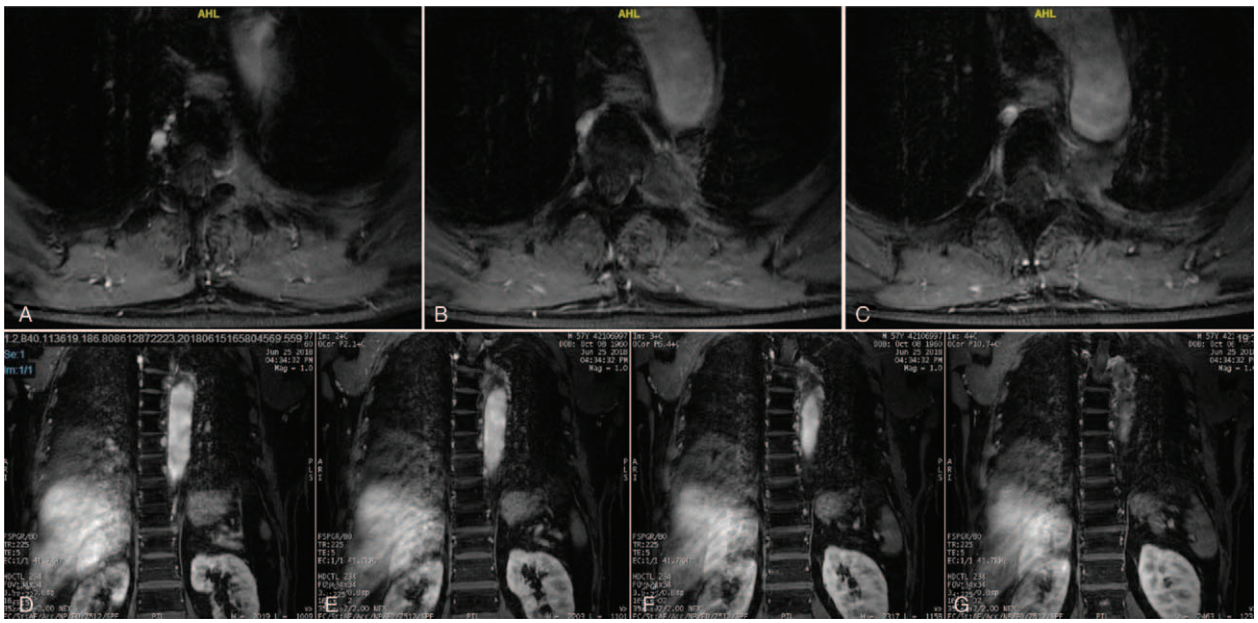

Figure 3. (A–G) Preoperative coronal and transverse MRI images revealing spinal cord compression secondary to the epidural component of the T4 mass, with increased metastatic marrow infiltration of the left T4 vetebral body, which presented as a solid tumor. Tumor infiltrated through the T4 vetebral body into the left pedicle and posterior elements causing significant compression of the nerve root. MRI = magnetic resonance imaging.

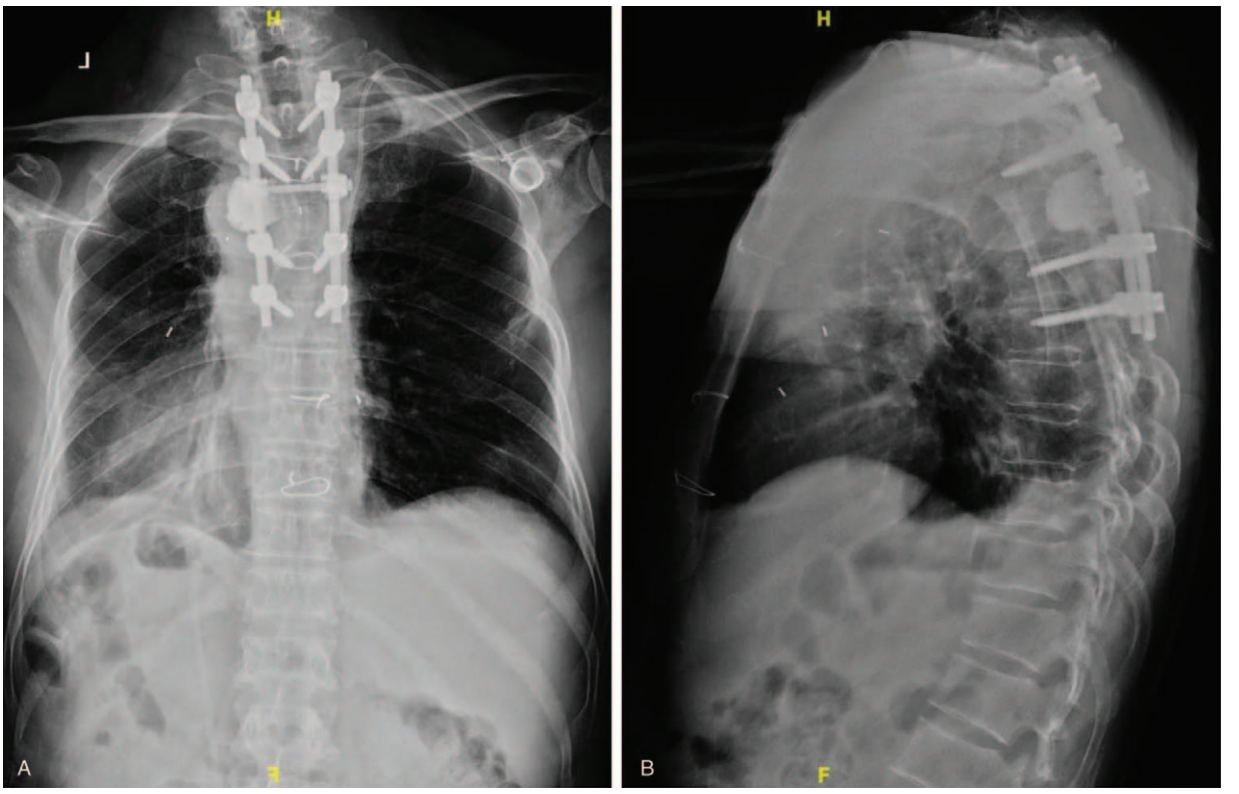

Figure 4. (A) PA X-ray image of the thoracic spine obtained postoperatively. (B) Lateral X-ray image of the thoracic spine obtained postoperatively. PA= posteroanterior.

features of malignancy and highly aggressive biological behavior with extrathoracic metastases to the liver, kidney, and bone in 1% to 15% of patients.[4] The characteristics of spinal metastatic thymic carcinomas have not yet been fully clarified. Moreover, there are still no defined treatment protocols for TC owing to the paucity of these patients.

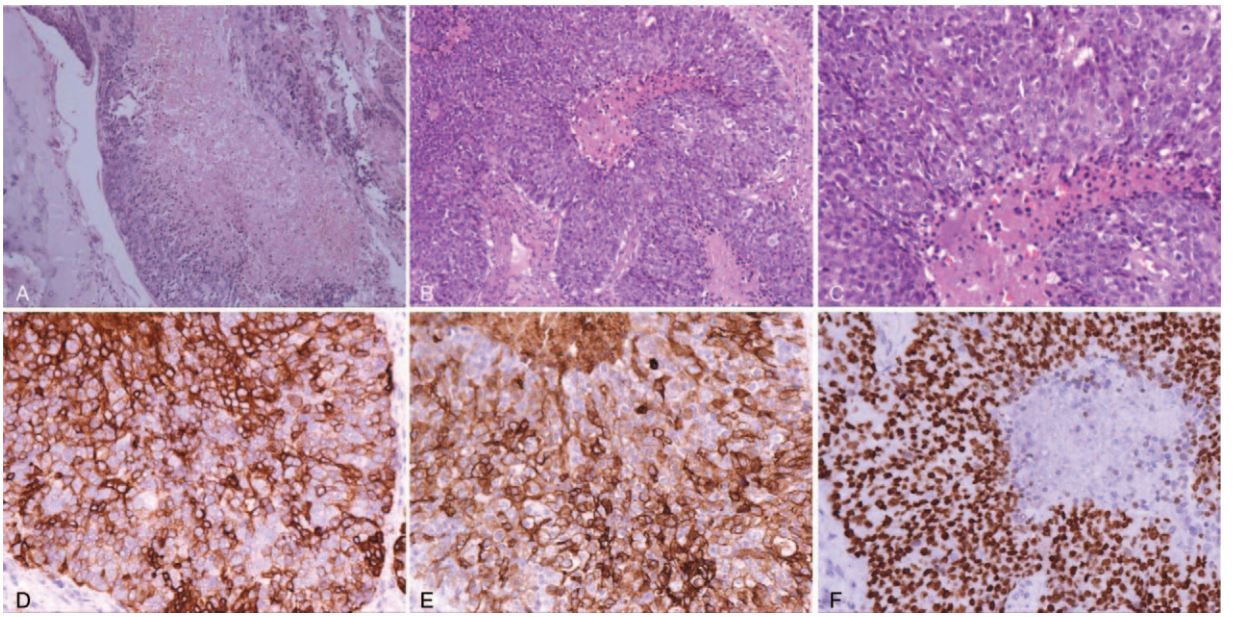

Figure 5. Pathologic histology of spinal metastases. (A–C) Microphotography showing characteristic nests of tumor cells separated by vascular septa (Zellballen) with cells showing significant nuclear pleomorphism with prominent nucleoli (H&E, original magnification 100x, 200x, and 200x). (D) AE1/AE3 immunostaining is strongly positive in the epithelial cells. (E) CD5 immunostaining shows strong, diffuse cytoplasmic staining in the tumor cells. (F) The sustentacular cells of the spinal metastases of TC showing characteristic staining of P63.

TC are rare tumors that were usually determined by the invasiveness into nearby tissues or distant metastasis. Most patients with TC have clinical symptoms such as chest pain, cough, weight loss and shortness of breath.[5,6] Like most metastases, TC metastasis to the spine may result in vertebral collapse, spinal instability, and progressive neurologic compromise, which may cause local, radicular, or axial pain in addition to neurologic deficits from mild radicular weakness to paraparesis. Back pain and radiculopathy can often mimic the most common cause of spinal diseases, making timely diagnosis of spinal metastatic thymic carcinomas difficult without a high level of suspicion.[7,8]

In literature, it is a rarity of metastatic thymic carcinomas of the thoracic spine presenting with back pain and radiculopathy. Clinical studies looking at metastatic thymic carcinomas to the spine is lacking due to the extremely low incidence rate. Based on our review of the 16 case reports on PubMed (Table 1),[1,3–5,9–11] metastatic thymic carcinomas of the spine is slightly more common in the thoracic region and are more commonly diagnosed during the fifth and the sixth decades of life for the sporadic form (mean age: 55.8 years; range: 36–78 years).[1,3–5,9–11]

The location of the spinal lesion determines the neurological deficits, and there is a great deal of variability.[12,13] Compression of the cervical vertebra often exhibit symptoms of paresthesia and weakness in the upper extremities, while those located in the thoracic and lumbar regions usually show symptoms of lower back pain, lower extremity paresthesia, weakness, and dysuria. In our case, the patient sought medical attention after experiencing serious back pain, lower extremity weakness, and numbness. To our knowledge, this is a less-documented case of thymic carcinoma with spinal metastases. Imaging studies including CT, MRI, and bone scan are non-specific, making it difficult to differentiate metastatic spinal thymic carcinoma from other common spinal lesions. However, imaging studies play a crucial role in the surgical intervention decision making. Imaging studies can demonstrate consecutive spinal stenosis, spinal cord or nerve root compression, and pathological vertebrae fractures. MRI images from previous case reports demonstrate inhomogeneous lesion of spine, isointense on T1-weighted image (T1WI) and iso-hyperintense on T2-weighted image (T2WI), indistinguishable from other metastatic spinal lesions.[3,14–17] Heterogeneous enhancement, calcification, and cystic changes are rarely observed.[18,19] Our patient's MRI showed isointense on T1WI and isointense lesion on T2WI, which is consistent with previous case reports.

Thymic carcinoma may become malignant via their metastatic tendency, and the metastases can help us diagnose a thymic carcinoma. The "gold-standard" diagnosis of thymic carcinoma relies on pathological findings. Histopathologically, metastatic spinal thymic carcinomas are characterized by architecture of nests of tumor epithelial cells separated by vascular septa with the cells showing significant nuclear pleomorphism with prominent nucleoli. Generally, metastatic thymic carcinomas are commonly immunoreactive for AE1/AE3, CD5, P40, P63.[20–23] A histological examination of our case was positive for AE1/AE3, CD5, P40, P63 indicating thymic carcinoma from epithelial cells of the thymic gland, which confirmed the diagnosis of metastatic thymic carcinoma.

Currently, no treatment guidelines exist because of the variability in treatment modalities and reported outcomes.[1–11] Surgical resection is the mainstay of treatment for thymic tumors and their metastatic lesions. We recommend surgical management of the spinal metastatic tumor when the tumor has caused neurological deficits, spinal cord compression or destruction of spinal stability. The best treatment for metastatic spinal thymic carcinomas causing acute partial paralysis and lower back pain is posterior decompression, tumor resection, and internal fixation.[1–3,24–28] This protocol accomplishes 2 objections: it alleviates the neurological deficits by decompressing the stenosis; and at the same time it provides histopathological specimens for diagnosis, which is valuable in cases where the patient presents with atypical clinical and radiological findings.[12] The objective of surgery is to maintain spinal stability and prevent neurological deficits. If possible, complete or grossly complete surgical resection of the primary tumor remains the treatment of the first choice. Adjuvant radiation therapy and chemotherapy after surgery may provide excellent local control and improve the long-term outcome.[1–3,29,30] The survival benefit of resection of spinal metastases is still unproven. However, such a procedure does have the benefit aiming at controlling residual tumor and is recommended for most patients.[1–11,24–28] This survival benefit of reducing the tumor burden, decompressing the spinal stenosis to alleviate radiculopathy, and facilitating subsequent chemotherapy and radiation therapy.

To date, surgical management of metastatic thymic carcinoma to the spine still remains under evaluation with no standard criteria. Vertebroplasty with cement augmentation might be a useful strategy to achieve rapid and sustained neurological improvements for patients with metastatic thymic carcinoma involving the spine.[12,13,31] Vertebroplasty by cement augmentation may be a proper treatment option for patients with spinal metastatic thymic carcinoma who cannot undergo appropriate surgery or decline open surgery.

Due to the paucity of patients, it can only be assumed that multimodality treatment including neoadjuvant chemotherapy and post-operative radiotherapy may offer improved survival rates in patients with unresectable spinal metastatic TC.[1–5,9] TCs are generally radiosensitive and chemosensitive tumors, with response rates ranging from 62% to 100% in literature.[1–5,9] Thus, higher-staged tumors are often treated by surgery combined with adjuvant chemoradiotherapy, although such adjuvant therapy is not standardized due to its rarity. Moreover, little is known about the natural history and prognosis of metastatic thymic carcinoma to the spine. The time intervals from primary diagnosis to spinal metastasis of TCs might be highly variable, Vladislav reported that the time interval until metastasis in 35 cases of TC averaged 3.6 years.[30] To date, studies have revealed that the most important determinants of long-term survival in thymic carcinoma are completeness of resection, Masaoka stage, and Mueller-Hermelink histologic classification.[1,3] In conclusion, we present an extremely unusual occurrence of spinal metastasis of thymic carcinoma that is successfully managed by surgical procedure and osteoplasty with cement, which has not been previously well reported. Our focus is to emphasize the importance of considering spinal metastasis of thymic carcinomas as a diagnosis and guiding the proper management strategy upon treatment.

4. Conclusion

Although uncommon, metastatic thymic carcinoma of the spine should be part of the differential diagnosis when the patient presents with neurological deficits and has a medical history of thymic carcinoma. We recommend the posterior approach for spinal decompression of the metastatic tumor when the tumor has caused neurological deficits. With a multidisciplinary team approach, proper planning, and adequate perioperative medical

Table 1

Clinical review of 16 previously published metastatic thymic carcinomas of spine.

Authors	Year	Age (y), sex	Symptoms and signs	Thymoma type (WHO)	Spinal metastases location	Intradural or extradural	Incomplete paralysis or paralysis	Myasthenia gravis	Years since initial diagnosis	Resection of primary lesion	Surgical Treatments	Adjuvant Treatment	Postop Complications and Outcome
Hentschel et al[10]	2004	60,F	Axial thoracic spinal pain with a severe radicular component	C	T7	Extradural	No	No	2	Thymectomy	Percutaneous vertebroplasty with cement augmentation	Radiation and chemotherapy	In the postoperative period, the patient had near complete relief of her axial and radicular pain
Oguri et al[9]	2004	64,F	Hoarseness; dysphagia	C, squamous cell	C3-C4	Extradural	No	No	0	CT-guided biopsy	No surgical intervention for spinal involvement	Chemotherapy	Multiple recurrences with rapid enlargement of tumor
Liu et al[4]	2011	57,M	Progressive cervicodorsal pain and decreased sensation in both hands; decreased grip strength	C, poorly differentiated squamous TC	C4–T1	Extradural	No	No	0	Not reported	C5-C7 laminectomies, tumor resection, and C3–C7 posterior internal fixation and fusion	Radiation and chemotherapy	Symptoms resolved; initially recovered well; died from respiratory failure 5 months after surgery
Hong et al[22]	2013	62,F	Segmental thoracic pain	C, well-differentiated thymic carcinoma	T9-T10	Extradural	No	No	13	6 surgical procedures for resection of a thymic carcinoma during a period of 13 years	A gross-total tumor resection was performed via a costotransversectomy and facetectomy T9–T10	Radiation and chemotherapy	No neurological deficits. The patient died 2 years later because of disease progression
Jee et al[3]	2014	61,M	Paraparesis	C	T4-T5	Extradural	No	No	0	Not reported	Decompression, tumor resection, and pedicle screw fixation	Radiation or chemotherapy	Died 3 years after surgery
	2014	42,M	Paraplegia	C	T3-T5	Extradural	Yes	No	2	Not reported	Decompression, tumor resection, and pedicle screw fixation	Radiation or chemotherapy	Recurrence of paraplegia; died <1 year postoperatively
	2014	36,M	Paraparesis	C	T2-T4	Extradural	No	No	5	Not reported	Decompression, tumor resection, and pedicle screw fixation	Radiation or chemotherapy	Died 2 weeks after surgery
	2014	68,M	Back pain	C	L1-L2	Extra-intradural	No	No	5	Not reported	STR of extradural component	Radiation or chemotherapy	Died 4 months after surgery
	2014	57,M	Paraplegia	C	T4-T6	Extradural	Yes	No	5	Not reported	Decompression, tumor resection, and pedicle screw fixation	Radiation or chemotherapy	Died 3.5 months after surgery
	2014	59,F	Back pain	C	T5	Extradural	No	No	0	Not reported	Pedicle screw fixation	Radiation or chemotherapy	Died 7 months after surgery
	2014	54,F	Back pain	C	T11	Extra-intradural	No	No	14	Not reported	STR of extradural component	Radiation and chemotherapy	Died 9 months after surgery
Sasaki et al[11]	2015	50,F	Back pain; weakness and numbness of left lower extremity	C, squamous cell	T3	Extradural	Yes	No	0	Thymectomy	T3 laminectomy with tumor resection	Radiation and chemotherapy	Improvement of symptoms
Kim et al[5]	2017	78,F	Weakness of the left wrist and grasp	C	C6-T1, intervertebral foramen	Extradural	No	No	7	Surgical resection	A nearly total resection preserving nerve roots was performed via a total C6-T1 laminectomy	None	Disease free at 6-month follow-up
Achey et al[1]	2018	63,M	Acute urinary incontinence; low back pain; right lower extremity radiculopathy	C	T8, L5-S1	Extradural	No	No	8	Not reported	L5-S1 decompression and GTR of the metastatic lesion at L5, along with stabilization	Radiation	Remained neurologically stable, symptoms of lower back pain and radiculopathy improved
	2018	38,F	Left flank pain radiating to the lower abdomen and groin and rapidly progressive myelopathy	B3 with cytologic atypia, mitoses and infiltrative growth concerning for type C thymic carcinoma	T12-L1	Extradural	No	No	2	Thymectomy	T12-L1 decompression with facetectomy; T11-L2 posterior instrumented fusion; GTR of T12-L1 tumor	Chemotherapy	Neurologically stable
	2018	44,F	Rapidly progressive myelopathy; neck pain	C	C7	Extradural	No	No	4	Mediastinotomy	Anterior C7 vertebrectomy for decompression and tumor resection, with the placement of a cage graft and plating from C5 to C7	None	Remained neurologically stable. Died 4 months after surgery

GTR = gross total resection, STR = subtotal resection.

management, metastatic thymic carcinoma in the spine can be managed much more effectively.

Author contributions

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Writing – review & editing: Shuzhong Liu, William A. Li, Radhika Rastogi, Yipeng Wang, Yong Liu.

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