



Intradural extramedullary metastasis: a review of literature and case report

Charles F. Land¹ · Blake D. Bowden¹ · Brice G. Morpeth¹ · John G. DeVine¹

Received: 25 February 2019 / Accepted: 28 March 2019
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Abstract

Introduction Intradural extramedullary (IDEM) metastatic disease is infrequently encountered by spine surgeons and consequently poorly understood. Discovery often corresponds with the onset of neurologic symptoms and no consensus exists regarding the importance of complete resection or anticipated postoperative outcome. We aim to elucidate treatment methodologies that exist in the literature.

Case presentation We present a unique case of a 57-year-old male with a known history of esophageal adenocarcinoma, including brain and visceral metastases, who presented with cauda equina syndrome. An IDEM metastatic esophageal adenocarcinoma lesion was identified on advanced imaging and biopsy. This was treated operatively without return of neurologic function.

Discussion We reviewed and summarized the existing literature. Trends are highlighted to further guide surgeons treating this unusual metastatic phenomenon.

Conclusion Intradural metastasis is a harbinger of advanced disease with a poor prognosis regardless of the etiology of the primary lesion. There are a number of proposed mechanisms for metastatic spread with little available literature for surgeon guidance. Most authors are advocates of a palliative, decompressive approach.

Introduction

IDEM is a rare entity—uncommon enough to preclude general recommendations for surgical management and an understanding of the underlying pathophysiology. A review of the literature reveals a heterogeneous group of primary malignancies that have demonstrated metastatic potential to the intradural extramedullary space, including lung, renal, thyroid, and primary bone, among others. Much of the literature is devoted to mention the number of documented cases of each primary malignant etiology, with authors often noting that their case is the only documented case, or one of few. Given the lack of guidance in our case, it was clear that a comprehensive review of how these cases are managed is what was needed. As such, we set out to identify the differences and commonalities in how patients

were treated, how they performed postoperatively, and their surgeons' theories for pathogenesis.

We begin by presenting a unique case report of esophageal adenocarcinoma metastatic to the IDEM space which is the first reported case of its kind in the literature. Esophageal carcinoma is an aggressive malignancy when discovered in its advanced stages, and it has become increasingly prevalent in past decades [1]. The survival rate for esophageal carcinoma is poor, and when metastatic disease is present, the 5-year survival rate is less than 5% [2]. Common sites of metastasis for esophageal carcinoma include lymph node, liver, lung, bone, and brain with known dissemination via contiguous spread, lymphatics, and the blood stream [3]. Although metastasis to the vertebral column occurs in ~3–5% of all cancers, it has been rarely reported in the case of a primary esophageal neoplasm [4]. When lesions of any malignancy are present in the vertebral column, intradural lesions are only seen in 6% of these cases, further emphasizing the rarity of intradural metastatic pathology in general [5–7].

✉ Charles F. Land, MD
cland@augusta.edu

¹ Department of Orthopaedic Surgery, Medical College of Georgia at Augusta University, Augusta, GA 30912, USA

Case presentation

A 57-year-old male with a known history esophageal carcinoma, including brain and visceral metastases, presented to our emergency department with sudden onset of bilateral lower extremity weakness and saddle anesthesia. He stated that he was ambulatory without assistive device the evening prior to his presentation and endorsed a history of deep venous thrombosis for which he was maintained on rivaroxaban. He reported a prior surgical history of gamma knife radiation for cerebral metastases. Despite the strong association of esophageal malignancy with tobacco and alcohol, the patient's social history was negative for alcohol and tobacco.

Upon examination, the patient demonstrated a normal neurologic exam in his upper extremities and abnormal exam in his lower extremities consistent with acute cauda equina syndrome. Motor power was 1/5 bilaterally at the level of L2, and 0/5 bilaterally at L3 and below. Examination also demonstrated absent sensation in the perineum, absent rectal tone, and absent reflexes. Computed tomography imaging was performed in the emergency department which identified numerous bony metastases throughout the neural axis, and no notable space occupying lesion that accounted for his symptoms of acute cauda equina syndrome. A magnetic resonance imaging study of the lumbar spine was performed which revealed an IDEM lesion at the level of the L2 vertebral body with displacement of the nerve rootlets (Figs. 1 and 2). With this imaging study completed, the diagnosis of cauda equina syndrome secondary to tumor metastasis was confirmed. A discussion about the patient's prognosis and treatment options took place and both the primary surgeon and the patient deemed that surgery would be best treatment option to improve neurologic function.

A standard posterior approach was carried out overlying the L2 vertebral body and the sub-periosteal dissection was performed to expose the laminae of L1, L2, and L3. A complete laminectomy was performed at L2 with partial laminectomies performed at L1 and L3, as well as resection of the ligamentum flavum in order to expose the dura mater. The dura was incised longitudinally exposing the intradural lesion and rootlets. The lesion was then removed and a specimen was sent to pathology (Fig. 3). The durotomy was primarily repaired followed by the closure of the surgical wound in standard fashion. Upon evaluation by pathology, the tumor was reported as a metastatic poorly differentiated non-small cell adenocarcinoma, which was consistent with the primary esophageal neoplasm.

Post-operatively the patient's bilateral lower extremity motor and sensory deficits persisted, while the overall health of the patient continued to deteriorate. Eleven days post operation the patient and the patient's family decided



Fig. 1 Sagittal views of a T1 weighted MRI demonstrating an intradural, extramedullary lesion posterior to the L2 vertebral body

to pursue palliative care. Due to the advanced stage of the esophageal carcinoma and extensive metastasis, the patient expired 2 weeks after the procedure.

Discussion and literature review

Mechanism of metastasis

The discussion regarding mechanism of metastasis for intradural lesions continues to evolve as more case series and reports are published; however, most authors propose one or a combination of 5 mechanisms for neoplastic cells reaching the IDEM space. These include spread from Batson's venous plexus, perineural lymphatics, seeding from local invasion adjacent to the dura, spread from the sub-arachnoid space in so called "drop metastasis" or leptomeningeal fashion, and hematogenous spread via the arterial system [8]. It is unclear which route was utilized in our case, but given our patient's known and documented intracranial metastatic lesions, we propose that the lesion was the result of spread from the sub-arachnoid space. In fact, the most commonly advocated mechanism in the literature reviewed was leptomeningeal spread [7, 9–13]. It

follows that concurrent intracranial disease is likely to create metastatic disease given the fact that >50% of cases with an intracranial malignancy will demonstrate neoplastic cells in the CSF [9].

Kotil et al. describes a case in which an intradural metastatic lesion from small cell carcinoma of the lung presents as cauda equina syndrome [14]. As lung cancer is predisposed to spread via the hematogenous route and the authors identified no bony, visceral, or cerebral metastatic

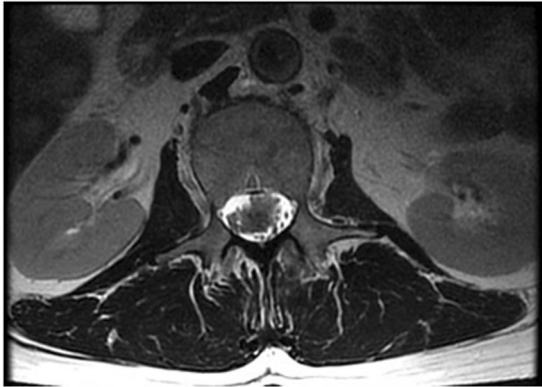


Fig. 2 Axial views of a T1 weighted MRI demonstrating an intradural, extramedullary lesion with displacement of adjacent nerve rootlets

lesions, they surmised that hematogenous spread was most

likely. This proposition is consistent among case reports with a known lung primary malignancy [5]. Other, more complex routes have also been described which include renal cell carcinoma spreading along the autonomic nerves to the aorticorenal, celiac, and mesenteric ganglia and then along the thoracic and lumbar splanchnic nerves to the corresponding spinal nerves to the intradural, extra-medullary space [13].

Only one case was noted to mention direct invasion, because the majority of cases of intradural extramedullary metastatic disease demonstrate no extradural or bony involvement. Hematogenous spread via Batson's plexus is an attractive proposition given the bidirectional flow and extensive network of this system—it has been implicated in a large fraction of case reports as well.

Numerous factors play roles in the routes of spread for intradural lesions and further research is warranted in identifying factors that predispose neoplasms to metastasize via specific routes to the intradural space. As an example, mutations in the (ALK) gene in non-small cell lung cancer have been shown to exhibit a propensity for CNS involvement [15]. Further advances in understanding the tropism of these neoplasms and their respective pathways for metastasis might be found in future studies exploring tumor genetics.

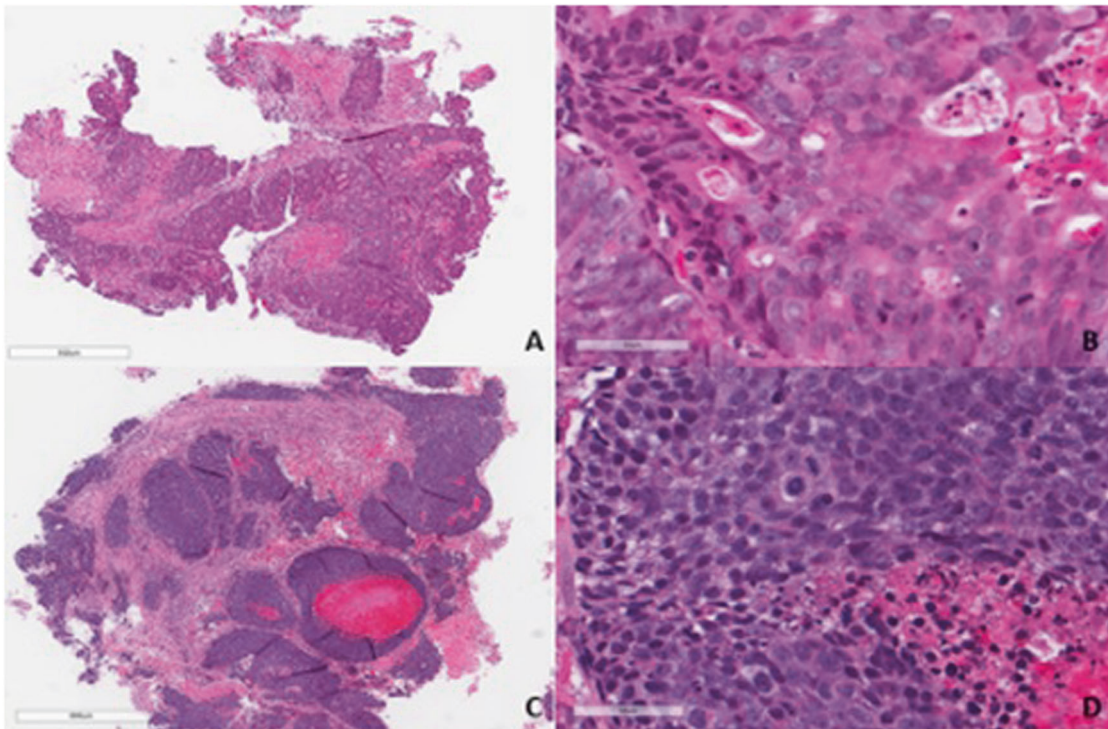


Fig. 3 a H&E; Patient's primary esophageal mass—invasive moderately to poorly differentiated adenocarcinoma (×100). Note the dysplastic glands underlying the squamous epithelium. **b** H&E; High power view of primary esophageal mass (×400). Note the enlarged, hyperchromatic nuclei with frequent mitoses and necrosis. **c** H&E;

Spinal intradural tumor—metastatic poorly differentiated adenocarcinoma (×100). **d** H&E; High power view of spinal tumor (×400). Note the similar cytological features—enlarged, hyperchromatic nuclei, increased mitoses and necrosis, to the esophageal primary

Surgical considerations

IDEM spinal metastasis originating from a primary tumor outside the central nervous system is exceedingly rare and usually discovered secondary to symptoms of compression of nerve root(s), the cord, conus, or cauda equina [16]. Compression of the cauda equina presents with very noticeable, predictable symptoms, and in patients with a compressive neoplastic lesion of the cauda equina, such lesions are typically extradural. Patients with an IDEM metastatic lesion involving the cauda equina have been mostly associated with primary lesions of the prostate, kidney, thyroid, lung, and breast [17]. Nonetheless, surgical treatment for intradural lesions appears to be the mainstay for tumors that present acutely with neurological deficits. As was in our case, cauda equina syndrome is universally treated surgically as it constitutes a surgical emergency.

In most cases, complete resection of the IDEM lesion seems desirable to decompress the neural elements and relieve the compressive pathology. A review of the literature, however, suggests that complete resection may be unnecessary. In the vast majority of cases, patients exhibit some subjective improvement in pain relief and or motor power post-operatively even when simple debulking or sub-total resection is performed [5–7, 10, 12, 14, 18–26]. Furthermore, it is unclear preoperatively which types of metastases will be amenable to complete resection. In some case reports, tumor resection was reported as en block [14, 19, 21, 27, 28], whereas others convey adherence of the tumor to neural elements precluding subtotal resection [7, 10, 18, 20, 22, 23, 26]. Our case was consistent with the latter—intimately associated with the intradural rootlets of the cauda equina. One author, in keeping with a palliation pain control strategy, promotes transection of the affected nerve rootlets in the event that metastatic disease is firmly adhered precluding complete resection [25].

Return of normal neurologic function, although generally improved following surgical decompression, is never guaranteed. A case report of IDEM metastatic follicular thyroid carcinoma exhibited post-operative improvement of 2/5 motor power in the affected segments to 3/5 motor power despite complete resection without intraoperative changes on neuro-monitoring [21]. Given the variable origin of these metastases, prognoses and therefore the goals of surgery are paramount in discussions with the patient preoperatively.

Adjuvant therapy

Fortunately, a number of treatment modalities exist for intradural metastatic lesions aside from surgery. Nearly

every case report reviewed utilized some combination of surgery and chemotherapy or radiation therapy (RT), all of which have been described for intradural tumors with varying degrees of success. The type of primary disease that ultimately leads to intradural metastatic lesions also plays a role in treatment. Marotta et al. describe a metastatic intradural thymoma that underwent RT following surgical treatment. As is well documented in the tumor literature, this primary malignancy is radiosensitive and incomplete surgical excision is adequate given the patient's improvement in symptoms and lesion size following a course of RT. The use of chemotherapeutics has also been employed in treatment strategies for intradural metastatic lesions [29]. Again, primary malignancy etiology and possible genetic variations are likely to play a role in whether chemotherapy is effective or not—we advocate early involvement of a multidisciplinary team including oncologic specialists in all cases of IDEM metastatic disease given its late presentation.

Prognosis

Irrespective of the etiology of the primary malignancy, the finding of IDEM metastasis portends a grim prognosis given the late nature of disease on presentation [7] and as such, most authors recommend surgery from a palliative approach [12, 21, 25, 28, 30]. Intradural metastatic lesions with a carcinoma primary are indicators of advanced disease and presence of a pre-surgical neurological deficit is an independent overall negative predictor of survival with one study reporting a hazard ratio of 10.2 [9]. Tumor morphology and physiology may also play a role in neurological recovery following intradural tumor resection. Further research is needed to identify factors of specific primary malignancies that make tumors more or less likely to be adherent to other intradural structures, as this information may have important prognostic implications.

Treatment strategies include curative, functional, and palliative and vary widely because of specific treatment goals tailored to individual patients. Much of the decision regarding surgical approach involves both the extent of neoplastic burden and the wishes of the patient. In the case report by Petterwood et al., the authors contend that despite the number of surgical options available for treatment of metastatic lesions, surgical treatment is futile for overall survival and efforts of palliation may be in the patients' best interest in order to provide improved pain, function, and quality of life. The literature reviewed seem to suggest that pre-operative counseling for patients with intradural lesions should indicate that no significant difference in survival is to be expected, and surgery is aimed primarily at improvement in quality of life.

Conclusion

IDEM metastasis is a harbinger of advanced disease with a poor prognosis regardless of the etiology of the primary lesion. As such, patient counseling should reflect a palliative approach without anticipated improvement in survivorship with surgical efforts aimed at debulking compressive disease combined with appropriate multidisciplinary adjuvant therapy. Future research might target detection of IDEM metastasis prior to symptomatic neural compression and further investigate the genetic features that drive neoplastic tropism to the IDEM space.

Acknowledgements We thank the patient and the patient's family for providing informed consent for inclusion in this case report, as well as Dr. Mara Banks of the Medical College of Georgia Department of Pathology.

Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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