



Intra-Medullary Spinal Cord Metastasis of Ovarian Carcinoma: A Rare Case Report

Authors

Dr Milap Shah¹, Dr Ambreen Aman², Dr Bharat Vaswani³, Dr B J Rajesh⁴
Dr CN Sreekanth⁴

¹MD (Pathology), Senior Consultant Pathologist, Yashoda Hospital, Secunderabad

²Resident, (DNB) Pathology, Yashoda Hospital, Secunderabad

³DM Oncology, Consultant Oncologist, Yashoda Hospital, Secunderabad

⁴MCh Neurosurgery, Consultant Neurosurgeon, Yashoda Hospital, Secunderabad

⁵MCh Oncosurgery, Consultant Oncosurgeon, Yashoda Hospital, Secunderabad

Abstract

Ovarian carcinomas metastasizing to the spinal cord are infrequent. Incidences of isolated metastatic deposits of ovarian carcinoma to spinal medulla have rarely been reported. We present a case of a 74 year old woman who was previously diagnosed with and treated for ovarian adenocarcinoma. She was disease-free for a period of 8 years after which she presented with complaints of low back pain and numbness in both lower limbs. On PET evaluation she was found to have an isolated space occupying intra-medullary lesion at D-7 level. Biopsy from the lesion revealed features of metastatic ovarian papillary adenocarcinoma. Spinal metastasis from ovarian carcinoma indicates a poor prognosis with a survival of 10 months to 3 years. Recognizing intramedullary metastatic deposits is essential as timely intervention may prevent permanent neurological sequelae.

Keywords: intra-medullary spinal cord metastasis, ovarian adenocarcinoma.

Introduction

The spinal cord is a common site of osseous metastasis of systemic cancers. Most of these metastases involve the leptomeninges, epidural space and vertebrae. Intramedullary seeding of tumor deposits is uncommon and accounts for about 0.5-1% of spinal metastasis. It occurs in the setting of an advanced disease and is rarely the first manifestation of an underlying carcinoma².

The incidence of spinal metastatic disease is slightly higher in males and is often seen in adults aged 40-60 years. The most common primary sources are the lung and breast; other

malignancies known to cause intramedullary metastases are melanoma, lymphoma, leukemia, renal cell carcinoma and colorectal cancer.

Ovarian carcinoma causing isolated intramedullary spinal metastasis after a prolonged symptom-free interval is extremely rare. To the best of our knowledge, there are only 9 reported cases of isolated, intra-medullary metastasis of ovarian carcinoma.

Case Report

This is a case of a 74 year old woman who was diagnosed with serous papillary adenocarcinoma

of the ovary in the year 2009 and underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy, followed by adjuvant chemotherapy. Her follow up investigations showed no evidence of residual disease. She presented 8 years later, in April 2017 with complaints of low back pain and numbness of bilateral lower limbs.

MRI done elsewhere suggested astrocytoma of the spinal cord. Considering prior history of carcinoma of ovary, whole body PET scan was performed which showed a hypermetabolic, focal, ill defined enhancing lesion in the spinal cord at the level of D-7 vertebra with no evidence of vertebral body erosion (SUV MAX 10). The lesion was confined to the spinal cord with no other metabolically active lesions in the body.

MRI with contrast imaging of the thoraco-lumbar spine was performed. The dorsal spinal cord at the level of D7 vertebral body revealed a well defined oblong shaped intramedullary enhancing lesion measuring 2.5x1.2 cm with diffuse perilesional edema extending superiorly and inferiorly along the spinal cord.

The radiological findings suggested a neoplastic intramedullary space occupying lesion of dorsal spinal cord.

An intra-operative biopsy from the space occupying lesion was sent for frozen section analysis. Squash preparation of the biopsy revealed a malignant tumour with elongated tumor

cells in vague papillaroid pattern. A differential diagnosis of papillary ependymoma and metastatic adenocarcinoma was conveyed to the surgeon who proceeded to perform spinal laminectomy at the level of D6-D8 vertebral bodies.

Histopathological analysis of the excised lesion revealed a tumor with pleomorphic cuboidal to low columnar cells having hyperchromatic nuclei in clusters and in vague papillary and acinar patterns. On microscopy, papillary ependymoma shows cuboidal to elongated tumor cells around vascularised myxoid cores with a myxopapillary appearance and low mitotic activity. Papillary adenocarcinoma also shows similar papillary fronds with complex glands lined by cells with oval, elongated nuclei. Stroma may have a myxoid appearance. Both high grade ependymoma and papillary adenocarcinoma will exhibit marked nuclear atypia and frequent abnormal mitosis. A diagnosis of Metastatic Adenocarcinoma with papillary pattern was preferred due to previous history of ovarian carcinoma. Immunohistochemistry (IHC) was performed; tumor cells were immunoreactive for ER, PR, PAX 8, and WT1 while they were negative for TTF1 and CDX2.

The histological features and immune profile favoured a diagnosis of adenocarcinoma of Mullerian origin, likely to be metastasis from ovarian papillary serous adenocarcinoma.

Table 1: A brief review of previously published case reports on intra-medullary spinal cord metastasis.

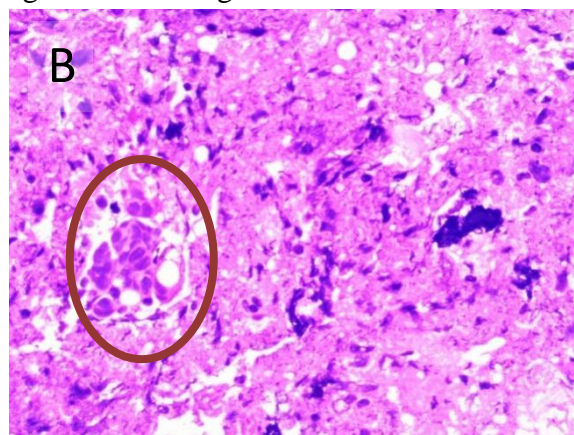
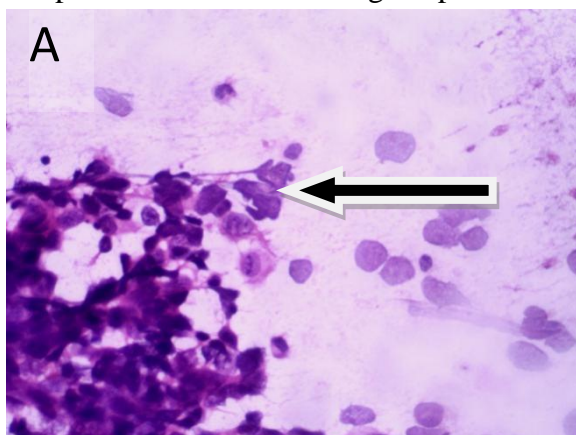
Reference Number	Author	Year	Age	Vertebral Level
9	Cormio et al	2001	58	C5 – C6
7	Isoya et al	2004	59	T10
6	Rastelli et al	2005	73	T11
8	Bakshi et al	2006	40	Conus medullaris and cauda equine
4	Miranpuri et al	2011	65	C2 – C5
1	Peyer et al	2014	79	C4 – C7
13	Sarah Safadi	2016	78	T11 – T12
14	Jon Huang	2017	50	C7 – T1

Legend 1: MRI with contrast of dorsal spinal cord, at D7 level showing a well defined, oblong, intra-medullary, enhancing lesion with diffuse perilesional edema, extending both superiorly and inferiorly

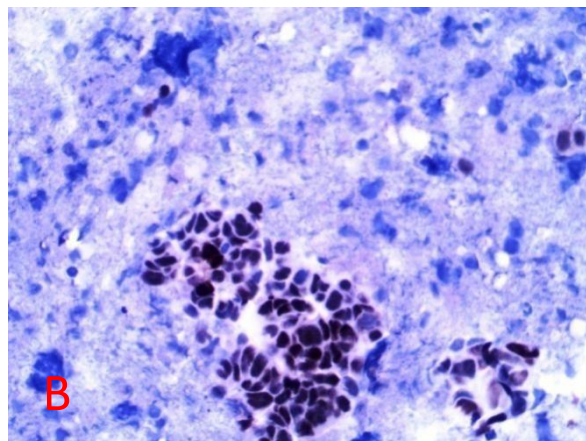
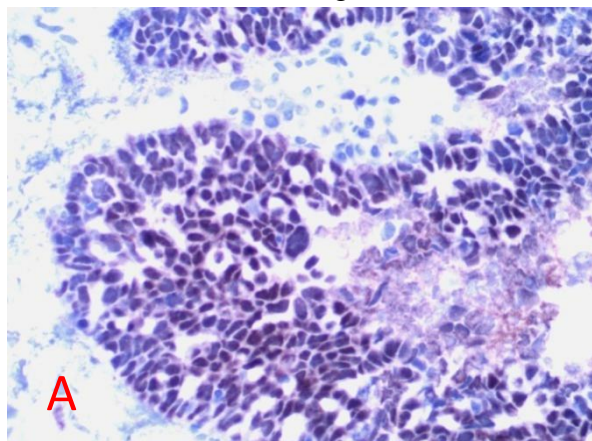


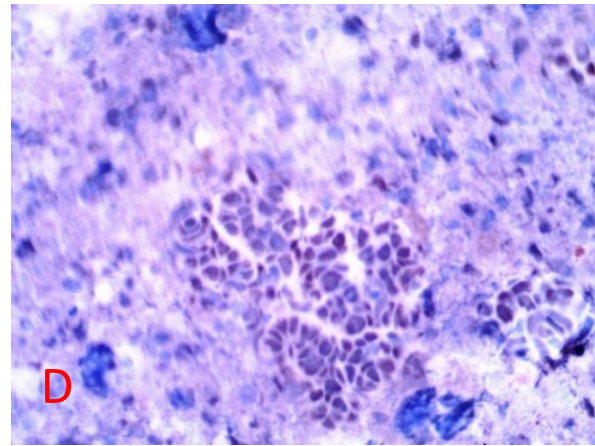
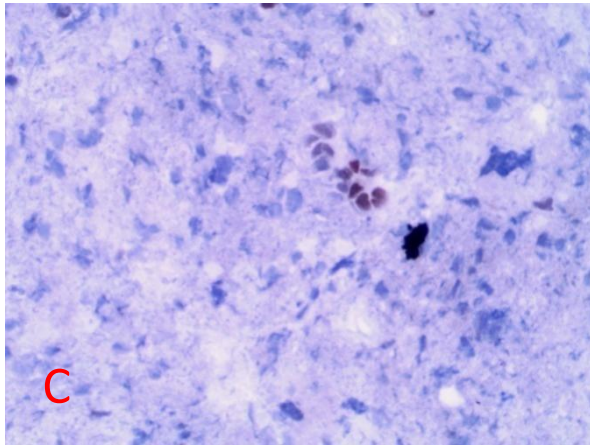
Legend 2

- A. H&E stained squash preparation showing tumor cells with high grade nuclear atypia in a vague papillary pattern.
- B. Routine paraffin sections showing neoplastic cells in a glandular arrangement.



Legend 3: IHC immunostaining for (A) ER, (B) PAX 8, (C) PR, (D) WT1





Discussion

Tremendous advancements in the detection and treatment of ovarian carcinomas have resulted in prolonged survival of patients. Highly effective chemotherapy and radiotherapy combined with aggressive surgery has ensured successful treatment with long-term disease free survival. But high grade epithelial ovarian cancers usually recur and present with extensive intra-abdominal metastasis. Most commonly involved distant organs are the lung and liver. The CNS is an unusual site of metastasis of ovarian tumors. Whenever it occurs, it is a part of widespread systemic dissemination⁸. The common sites of CNS involvement are the brain parenchyma, leptomeninges and very rarely, the spinal cord⁹. Intramedullary spinal cord involvement occurs in 0.5% -1% of patients with cancer and in 8.5% of all patients with metastasis to CNS⁶. These recurrences are being detected with increasing frequency due to the availability of highly sensitive imaging techniques.

The mechanism of metastatic spread of ovarian cancer is not clear, most probable routes are hematogenous dissemination, spread through Virchow-Robin spaces, or direct extension from leptomeninges. Another mechanism, by which ovarian cancer can metastasize, as hypothesized by Lengel.E et al, is by direct seeding of detached tumor cells singly or in clusters from the primary tumor through the peritoneal fluid into peritoneum, omentum and other organs³.

Patients with intramedullary spinal cord metastasis commonly present with radicular pain

(83%-95%) and sensory deficits (40%-90%). Motor weakness (60%-85%) and autonomic dysfunction (40%-57%) are less common⁵. A high index of suspicion is necessary for an early detection of these lesions which can otherwise result in lasting neurological sequelae. MRI is a sensitive imaging technique for detecting the location and nature of the lesion. Measurement of Ca 125 levels and CSF analysis may give indirect evidence of the disease. But a definitive diagnosis can only be made on histopathological evaluation of the resected tissue.

An intra-operative frozen section evaluation of the excised tumor helps in deciding the extent of neurosurgical resection. The type of tumor, as confirmed by histopathology and immunohistochemistry, aids in deciding the role of chemotherapy and radiotherapy.

Immunohistochemistry helps in resolving diagnostic dilemma and confirms the tissue of origin. 80%-95% of all ovarian carcinomas, across all subtypes express estrogen and progesterone receptors (ER, PR)^{10,12}. PAX 8 is a sensitive and relatively specific marker for Mullerian tumors¹¹. WT1 reactivity is seen in more than 50% of the cells of all serous ovarian carcinomas¹². TTF1 and CDX2 are used to rule out primary malignancies of the lung and GIT respectively. In our case, the tumor cells expressed ER, PR, PAX8 and WT1 while they did not demonstrate expression of TTF1 and CDX2. This characteristic antigen expression pattern favoured a diagnosis of metastatic adenocarcinoma of Mullerian origin,

more likely to be from previous ovarian serous papillary adenocarcinoma.

An extensive search of previously published literature revealed nine cases of intramedullary spinal cord metastasis of ovarian adenocarcinoma. Four cases involved the cervical spinal cord; four others involved the thoracic spine, and one case involved conus medullaris and cauda equina. To the best of our knowledge, ours is the 10th reported case of tissue-confirmed, intramedullary spinal cord metastasis of ovarian adenocarcinoma. Data from previous studies has been briefly summarized in Table 1.

The mainstay of treatment of spinal metastatic deposits is surgical resection, although this may greatly increase the risk of morbidity to the patient and worsening of neurological sequelae. Indications for surgery include pathological diagnosis, restoration of neurological function by decompression of mass effect and spinal stabilization.⁴ Radiotherapy is beneficial in patients without neurological symptoms and is used for post surgical palliative therapy as well¹. Steroids are used in combination with radiotherapy to reduce the perilesional edema. Systemic chemotherapy with platin compounds is an excellent adjuvant especially in patients with extensive metastatic disease⁴.

Conclusion

Patients who present with intramedullary metastases usually have limited life expectancy. But early detection and treatment of these metastatic deposits becomes necessary to relieve the patient of severe disabilities caused by these deposits and to preserve neurological functions. A thorough histopathological evaluation not only confirms the diagnosis but also identifies the tissue of origin and predicts response to treatment. In general, the prognosis of metastatic ovarian carcinoma is poor. Treatment is mainly aimed at palliation of symptoms and to improve the quality of life of the patient. Complete surgical excision followed by irradiation and chemotherapy may increase the prospects of long term survival and

possible cure for patients with advanced metastatic disease.

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