Intramedullary Spinal Cord Metastasis in Spinal Ependymomas

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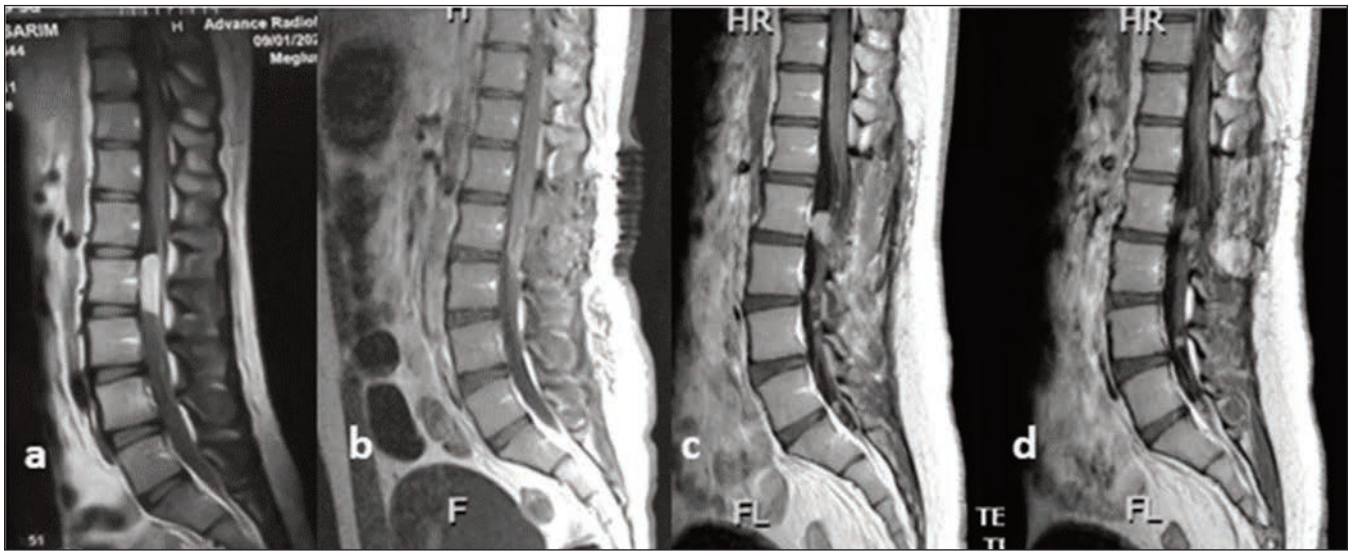

Figure: **a** shows preoperative sagittal T1 post contrast lumbar spine MRI displaying intradural enhancing lesion at L2. **b** shows the postoperative MRI with complete excision of ependymoma grade 2. **c** and **d** show multiple drop metastases at L2, L3 and L4, largest two at L2, four years later.

Abstract

Drop metastasis, or intramedullary spinal cord metastasis (ISCM), is a rare condition accounting 0.9%–5% of CNS or spinal metastases. It arises from tumour cell dissemination through cerebrospinal fluid (CSF), often affecting the thoracic and lumbar spine. Clinical features include rapidly progressive neurological deficits, limb weakness, sensory loss, and pain. Diagnosing drop metastasis is challenging and MRI with gadolinium remains the gold standard modality for investigation. Surgical resection followed by radiotherapy remains the primary treatment option, whereas chemotherapy serves a palliative role in cases of recurrence or disseminated metastases.

Keywords: Ependymomas, Drop metastases, Radiotherapy

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Introduction

Ependymoma are central nervous system tumours originating from the ependymal cell of the ventricle and the central canal of spinal cord, or ependymal cell nest in the white matter of the brain. It often occurs in children and accounts for only 2–9% of adult neuroepithelial cell tumours.[1] In 2021, World Health Organization (WHO) revised the classification of ependymoma to supratentorial ependymoma, posterior fossa ependymoma, spinal ependymoma, and subependymoma.[1] Drop metastasis, also known as intramedullary spinal cord metastasis (ISCM), is a rare occurrence which accounts for 0.9%–5% of 2%–8.5% of all CNS metastasis and spinal cord metastasis.2 This phenomenon is observed in about 18.8% in supratentorial anaplastic ependymoma.[1] ISCM should be clinically suspected in patients presenting with rapidly worsening neurological deficits.[2] Factors contributing to poor prognosis include incomplete tumour resection, high-grade histology, and extraventricular location. This review aims to explore the challenges of managing drop metastases in ependymomas, focussing on pathophysiology, clinical presentation, diagnostics, therapies and prognostic factors.

Literature Review

Genetically distinct subgroups of ependymoma have been identified by genomic studies based on locations in classic grade II and III ependymomas. They are supratentorial ependymomas with *C11orf95-RELA* fusion or *YAP1* fusion, infratentorial ependymomas with or without a hypermethylated phenotype (CIMP), and spinal cord ependymomas.[4] (Figure). The dissemination of tumour cells in cases of drop metastases is hypothesized to occur via the

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cerebrospinal fluid (CSF), particularly when the tumour invades the subarachnoid space.[5] Surgical intervention, by disrupting the tumour environment, may increase the probability of such metastases. However, it is noteworthy that drop metastases have also been documented in patients without history of surgery; at the time of diagnosis.[6] The distribution; of these metastatic lesions appears to be influenced by gravitational forces, with a predilection for the dorsal lower-thoracic and lumbar regions of the spine.[5] The occurrence of drop metastasis at the time of the initial diagnosis is uncommon, with reported rates ranging from 22.5% to 39%.[3]

Pathologically there are four types of ependymomas, mainly: typical, anaplastic, subependymoma and myxopapillary. Anaplastic ependymomas are known to spread to multiple sites in the spine and cranial cavity.[6] Metastatic spread of myxopapillary ependymoma (MPE) is infrequent and, when it does occur, the disease tends to spread in the rostral direction within the central nervous system. Intracranial metastasis is the most common site for MPE spread.[6] Metastases in MPE have been reported up to 20 years after initial treatment, emphasizing the role for extremely long-term follow up in these patients.[6]

The diagnosis of drop metastasis can be challenging and gadolinium-enhanced MRI with contrast is the gold standard for diagnosis. Cerebrospinal fluid (CSF) is of little value in the diagnosis of ISCM, and although it is often abnormal with high level of proteins, it infrequently contains detectable malignant cells.[7]

Management strategies for recurrent disease included salvage surgery and radiotherapy (RT). RT is highlighted as a cornerstone of metastatic management, especially in cases where GTR was unachievable. RT stabilized disease in over 70% of patients with drop metastases and provided significant symptomatic relief in half of these cases. The addition of RT to subtotal resection (STR) improved outcomes compared to STR alone, with combined therapy yielding a 10-year Progression Free Survival rate of 77%. Chemotherapy, although not a primary modality, was used in select cases for palliative purposes, offering modest benefits in slowing progression.[5]

In a focussed study on MPE, data from 19 patients treated surgically at a single centre between 2005 and 2015 emphasized the impact of gross total resection, adjuvant therapy, and close follow-up for metastases. The median age at diagnosis was 32 years, with 52.6% female and 47.4% male. Tumours were primarily located in the conus medullaris or cauda equina, with most spanning 1–3 vertebral levels. GTR was achieved in 78.9% of cases, significantly lowering local recurrence rates to 20% compared to 50% for STR. Median time to recurrence was 36 months. Metastasis was observed in 57.9% of patients, with 36.4% presenting metastases at diagnosis and 63.6% developing metastases during follow-up. The thoracic spine, sacral spine, and brain were common metastatic sites. The majority of metastases (72.7%) remained asymptomatic and stable over a median follow-up of 32 months, indicating that many metastatic lesions can be monitored without immediate intervention. Management of metastases included radiotherapy (RT) for stabilizing asymptomatic or mildly symptomatic metastases, achieving disease control in over 70% of cases with significant symptom relief in 50%. GTR of accessible metastatic lesions yielded local control rates of 85% and prevented further metastatic dissemination in most patients. Chemotherapy showed limited benefits, serving primarily as a palliative measure. Adjuvant RT was administered to 20% of GTR patients and 75% of STR patients, reducing local recurrence rates and stabilizing metastatic disease. Overall survival was 100% at the last follow-up, with 78.9% of patients having no or mild neurological deficits and 21.1% experiencing intermediate or severe deficits primarily due to advanced disease or tumour location.[8]

In a single institute study of a cohort of 72 patients with spinal MPE treated between 2011 and 2021, 29.2% presented with preoperative spinal drop metastases. Radiotherapy (RT) emerged as a critical adjunct in managing drop metastases. Among patients with preoperative metastases, RT significantly improved PFS (p=0.039) and stabilized disease progression when GTR was not feasible. The estimated 5-year and 10-year PFS rates for the entire cohort were 82% and 77%, respectively, with an overall recurrence rate of 18.8%. Notably, 58.3% of patients with recurrence had preoperative drop metastases.[9] Chemotherapy was selectively employed in cases of recurrence or disseminated metastases, often utilizing temozolomide. Though outcomes with chemotherapy were modest, the drug provided limited progression control and symptomatic relief. Despite the challenges posed by drop metastases, overall survival for the cohort was 100% at the last follow-up, with most patients maintaining stable or improved neurological function.[9]

These findings emphasize the importance of early and comprehensive management, including preoperative MRI of the entire craniospinal axis to detect metastases, aggressive surgical resection where feasible, and the strategic use of RT to stabilize residual disease or drop metastases. Chemotherapy, though limited in efficacy, remains a potential option for cases unresponsive to surgery and RT. Long-term follow-up and a

multidisciplinary approach are essential for optimizing outcomes in spinal myxopapillary ependymomas with drop metastases.[9]

Conclusion

Drop metastases in spinal myxopapillary ependymomas, while presenting significant management challenges, can be effectively addressed through a combination of surgical resection, radiotherapy, and strategic follow-up. Gross total resection (GTR) remains the cornerstone of treatment, significantly reducing recurrence and improving progression-free survival (PFS). Radiotherapy, particularly when combined with subtotal resection (STR), has emerged as a critical modality, stabilizing disease in over 70% of cases and providing symptomatic relief in nearly half. Chemotherapy, although limited in its effectiveness, offers modest benefits as a palliative approach in unresectable or recurrent metastatic disease.

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