"Drop metastasis:" a rare diagnosis. A case report and review of literature

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Introduction

"Drop metastasis", also known as intramedullary spinal cord metastasis (ISCM), is a rare complication of cancer, affecting 0.1%-0.4% of all cancer patients.^{1,2}

It is the rarest type of central nervous system (CNS) involvement by systemic malignant tumours, and it accounts for 2%–8.5% of CNS metastasis and 0.9%–5% of all spinal cord metastasis. Before MRI being available, most cases of "Drop metastasis" were diagnosed only upon autopsy.^{1,2}

Allthough this rare complication is most commonly secondary to small-cell lung cancer, it can also be seen in non– small-cell lung cancer, breast cancer, kidney cancer, melanoma, and lymphoma.³ The clinical diagnosis of ISCM should be raised in the presence of rapidly progressive neurologic deficit. ^{2,3}

The incidence of "drop metastasis" is supposed to go on increasing due to the longer survival of cancer patients as well as the widespread use of magnetic resonance imaging (MRI) in the diagnosis of neurologic syndromes. As clinicians and medical oncologists we should consider the issues that will be raised by the need of diagnosing and managing these patients.⁴

We report a case of "drop metastasis" diagnosed by MRI in a patient with advanced small cell lung cancer.

Case presentation

We present a case of a previously healthy 58 year old male who was diagnosed a metastatic small cell lung cancer in january 2013. He had osteoblastic, cervical and lumbar vertebrae, bone metastasis.

He completed six cycles of chemotherapy with etoposide and carboplatin, with stable disease at the end of the treatment.

In January 2014 he presented with a two month history of intense somatic lower back pain (reported by the patient as visual numeric pain scale of 5 and breakthrough pain as 9), irradiated to the left knee. The pain interfered with sleep and daily living activities.

The CT scan showed a metastatic lesion in the 11th dorsal, 4th (with an associated fracture) and 5th lumbar vertebrae and acetabulum.

Palliative antalgic radiotherapy (5 fractions of a total of 20 Gray) to the lumbar column and left acetabulum was performed, with no relief from pain.

He was sent to our Pain clinic in March 2014 with severe pain associated with progressive paraparesis. He had no bowel or urinary complaints (either incontinence or retention).

He was on Fentanyl patch 50 ug every 3 days, fentanyl lollipop (dose 200mcg) for breakthrough pain (wich he took 6 times per day), gabapentin 300 mg per day, prednisolone 40 mg per day, esomeprazole 40 mg per day, 1 sachet of macrogol per day.

On examination he had a paraparesis, mainly of the tight abductors and flexors.

A CT was performed and a sigmoid distension and a very large bladder with thickened wall were reported without an obvious cause.

In order to rule out a cauda equine syndrome, an MRI (fig. 1,2) – cervical, dorsal, lumbar, sacral and medullary was requested. The MRI showed a metastatic lesion in the 11th dorsal, 4th (with an associated fracture) and 5th lombar vertebrae (as previous CT scan) as well as two "drop metastasis" in the dorsal segment D1 and D2. The CNS had multiple parenchymal lesions.

The patient was kept on opioids and started steroids; he also had cerebral and dorsal radiotherapy (5 fractions of a total of 20 Gray). He achieved pain control (described as numeric pain scale 2) but neurological deficits didn't reverse; his condition deteriorated progressively, and he died on April 2014 (4 months after the beginning of present complaints and 1 month after the radiological diagnosis of "drop metastasis".

Discussion

The majority of primary tumours in cases of "drop metastasis" are lung or breast cancers, which are also the two most common primary tumours in patients with vertebral metastasis. This case of "drop metastasis" is consistent with the reported literature as to the tumour topography; however most of the reported cases in lung cancer are in small cell lung carcinomas^{1,4} this entity is considered a rare event in non-small cell carcinoma of the lung.^{2,7}

The clinical picture will depend on the spinal level affected; in the literature the cervical cord is the most common site and a possible explanation may be its greater bulk and richer vascular supply.^{3,4,5,6}

The diagnosis of "drop metastasis" is a difficult one if based only on the primary tumour.⁶ The clues that may help in differentiating between "drop metastasis" versus vertebral metastases are the presence of a rapid progressive neurological deficit associated with pain.

The literature reports that the average time between the patient's initially diagnosed tumour and "drop metastasis" clinical presentation varies from 13 to 17 months and in the present report the time lag was 1 year.³

The diagnosis of "drop metastasis" synchronous with the initial diagnosis is not usual; the reported percentage is 22.5% to 39%. $^{4.8}$

In the case reported, the time from clinical presentation of "drop metastasis" until diagnosis was 5 months, significantly longer than the 28 days described in literature.^{2,3,4,8} This may be due to the fact that the patient had concomitant osseous metastasis that were misinterpreted as the cause of pain.

The most frequent clinical presentation is limb weakness (91% of the cases); sensory loss, urinary incontinence, pain,

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Fig.1. Spine magnetic resonance imaging showing solitary intramedullary nodular lesion at the D1 level

Brown-Sequard syndrome are other frequent symptoms. Our patient had only limb weakness and did not complain about urinary or bowel incontinence or retention, although he had bladder wall abnormalities and colon distention detected on CT scan.

Radicular pain is the presenting symptom in 25 to 33% of patients. As the clinical features of cord compression and cord invasion are similar, distinguishing an intramedullary metastasis from an extradural spinal metastasis only by clinical presentation is difficult. An asymmetrical neurological deficit is more frequent in this entity than in spinal cord compression (32–45% *versus* 1–8%), however this is not considered as pathognomonic for the diagnosis of "drop metastasis".^{2,3,4,8,}

Once an extramedullary lesion is excluded by the MRI, the differential diagnosis of "drop metastasis" in a patient with known cancer should include radiating myelopathy, paraneoplastic myelopathy, or a simultaneous (comorbid) nutritional, demyelinative, inflammatory, or vascular myelopathy. Before the routine use of MRI, the diagnosis of "drop metastasis" was difficult; many of the reported cases had the diagnosis established after post-mortem examinations (only 5% were recognized before death). Gadolinium MRI has a high sensitivity in identifying this type of lesions.^{8,9,10}

Patients with "drop metastasis" also have disease deposits at other levels of the CNS. A majority of patients (nearly half) are known to have brain metastasis. Since patients may have asymptomatic brain metastasis, brain imaging should be considered for all patients with this diagnosis.^{1,11} We performed brain imaging on our patient, and the he had multiple brain metastasis.

Cerebrospinal fluid 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.

Positron emission tomography (PET) has a role in supporting the diagnosis of ISCM by providing information on metabolic activity and eliminating other diagnostic considerations.^{1,12,13} The outcome of patients with "drop metastasis" remains poor, with a median survival time of 3-4 months. The survival

time of patients treated with surgical resection was reported to more than double when compared to other patients.^{2,4,5}

Optimal treatment after diagnosis remains controversial, and treatment decision should be made case by case. Due to the rarity of this diagnosis, no controlled studies comparing surgery and radiotherapy, either alone or in combination are available and no recommendation can be strongly made.³

Radiation therapy has been, so far, the treatment of choice, as it can slow down the progression of neurological deficits. Best responses are achieved in radiosensitive cases especially if implemented very early in the course of clinical presentation. Treatment with steroids offered no additional survival benefit when combined with radiation. However corticosteroids are known to relieve the progression of neurologic symptoms and decrease pain.^{1,4,5} Our patient achieved

Fig.2. Fig 1 enhanced



pain control with the combination of Radiotherapy plus steroids added on to opioids.

Chemotherapy has been used in conjunction with radiation therapy or surgery in some chemotherapy sensitive tumours like small-cell carcinoma and haematological malignancies.^{1,14,15}

In patients treated with conservatively, 50% improve, 28% exhibit no change and 22% deteriorate. In patients who undergo a surgical resection, improvement is seen in 77% of the cases and no change in 23%. Steroid therapy has no additional survival benefit, however, in patients with rapid-ly-progressive symptoms of cord compression, it may decrease pain and neurological dysfunction.^{2,6,14}

Aggressive surgery has been considered in selected patients, especially those presenting with previously undiagnosed or limited primary tumours, since it may improve the length and quality of survival.^{1,14,15}Surgery as performed in 34% of published cases, could be considered as the optimal therapeutic approach but obviously carried high risks of postoperative functional impairment. Given the inherent risks of operating on the spinal cord and the usual state of advanced cancer, surgeons are reluctant to perform aggressive surgery.^{1,14,15}

The majority of patients with "drop metastasis" have a poor life expectancy due to synchronous brain metastases and a poor performance status secondary to neurological deficits, with a median survival of 3 to 4 months from the time of diagnosis.^{1,8} Our patient had a 1 month survival since the diagnosis.

Conclusion

"Drop metastasis" is a rare entity, but its diagnosis may be rising as cancer patients survive longer and as we use MRI for clinical diagnosis more often. Early suspicion of "drop metastasis" and early start of treatment is required to improve neurologic deficit and survival of these patients.

There are no data about the best treatment option for these patients; RT is still the most used modality but in due time surgical treatment may come as an option.

For the time being prognosis remains poor; as such, one of our primary objectives still is maintaining quality of life of these patients, using adequate supportive care.

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