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Prescribing and adverse event reporting information can be found on page 5.

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Breakthrough pain due to multiple bone metastases in lung cancer: pain that is difficult to control

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Introduction

Bone metastases secondary to lung carcinomas present with a high incidence, as well as having a serious functional impact. Due to this, they require constant study and progress in evaluation, diagnosis and treatment methods.[1] Pain is a common presenting symptom, sometimes with multiple associated complications such as pathological fractures, local neuropathic and muscular infiltration or spinal compression. The traditional tests for detection and evaluation of growth in metastatic disease, simple radiology and scintigraphy,[1] are complemented by computed tomography (CT) and magnetic resonance imaging (MRI), which improves information on the characteristics of the lesion, as well as positron emission tomography (PET).

Sometimes, the major functional impact and the major alteration in quality of life that bone metastases cause means a worsening of the initial prognosis of patients and even a limitation when it comes to being able to administer cancer treatments, thereby reducing the expected survival of these patients.[1-3]

The treatment of bone pain is multidisciplinary and includes analgesic and adjuvant drugs, chemotherapy, hormones, steroids, bisphosphonates, surgery, radiotherapy, as well as invasive local infiltration techniques. It must be preceded by a meticulous evaluation of the bone pain characteristics, intensity and frequency, as well as its most probable aetiopathogenic mechanism.[1-3]

We present a case of bone pain that was difficult to control, requiring less common drug administration routes such as the epidural route, leading to complications and multidisciplinary patient management.

Case study

A 74-year-old man, who smoked 30 cigarettes/day for 30 years before quitting in 2004, with a personal history of arterial hypertension, dyslipidaemia, type 2 diabetes mellitus and emphysema-type COPD. He was diagnosed with a non-small cell lung carcinoma, squamous type, stage 4, T2N1M1, with multiple bone metastases.

Staging PET-CT revealed (Figure 1):
- A lung mass in the middle lobe with pathological uptake of FDG, compatible with a primary tumour
- Small bilateral pulmonary nodules without FDG uptake
- Multiple mixed bone lesions in the axial and appendicular skeleton, the vast majority with pathological uptake of FDG, some with a small soft tissue lesion associated with left costal arches, in relation to metastatic involvement

He was evaluated in the Medical Oncology office where it was decided to administer chemotherapy with a carboplatin-gemcitabine regimen (days 1 and 8, every 21 days) and treatment with denosumab every 28 days.

Since diagnosis, the patient had pain associated with bone metastases in the left posterior costal region, left scapular, lower dorsal region, as well as lumbar region. He had continuous pain at baseline with VAS 7-8 and breakthrough pain peaks at VAS 9 more than 5 times a day. Third-step analgesic treatment with fentanyl patch 25 µg every 72 hours and dexamethasone 4 mg every 12 hours as adjuvant treatment was commenced in the first oncology consultation. Rescue treatment for breakthrough pain was prescribed in the form of 100 µg transmucosal sublingual fentanyl.

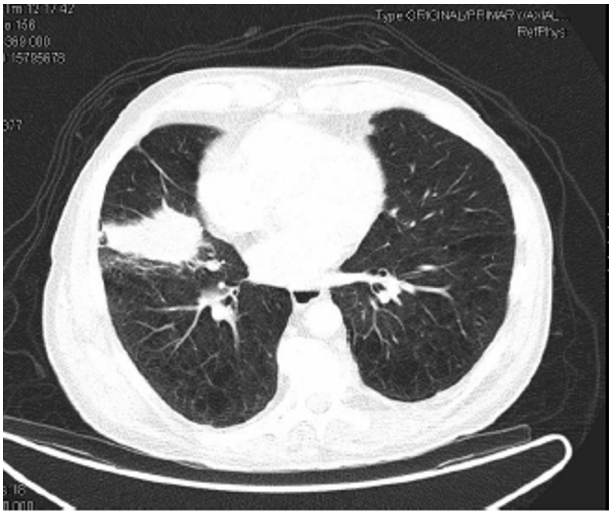


Figure 1.

Despite the prescribed analgesic treatment, the patient continued to experience poor pain control in all the regions mentioned, which required multiple visits to casualty and the need to increase the dose of treatment for baseline and breakthrough pain. Despite the adjustments, when the patient came to the consultation for the 2nd chemotherapy cycle, the pain was uncontrolled; at that time with a dose of 125 µg fentanyl patch every 72 hours, rescue for breakthrough pain with sublingual fast-acting fentanyl 200 µg and dexamethasone 4 mg every 8 hours.

Dorsolumbar MRI was requested to rule out complications associated with bone metastases. Dorsolumbar bone metastatic dissemination was observed, with involvement of posterior elements in D10 and D11 and signs of meningeal infiltration due to contiguity. There were also signs of degenerative disc disease with posterior bulging of the discs at L3-L4 and L4-L5 (Figure 2).

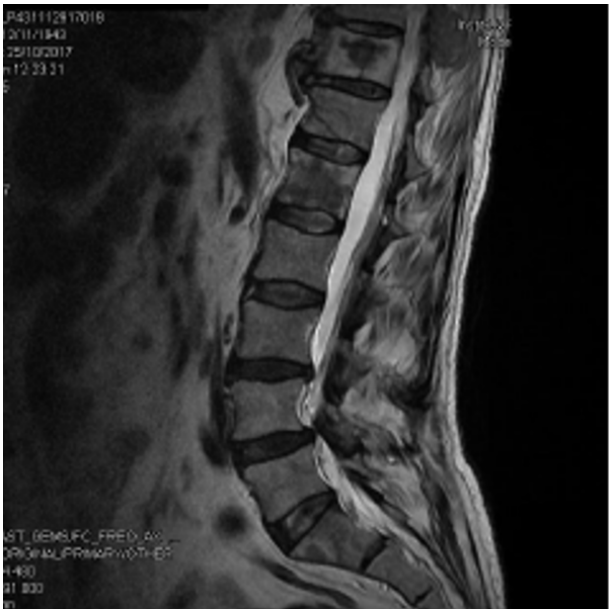


Figure 2.

Despite the attempt to control pain on an outpatient basis, the patient required hospital admission due to significant functional deterioration, with persistence of left scapular pain, mainly posterior dorsal left rib and lumbar pain.

At this time, a CT scan was requested to re-evaluate the disease. We observed a slight decrease in the size of the left main (LM) lesion, with progression of the number of millimetric pulmonary nodules. With a bone window, metastatic bone involvement was observed in practice in the entire axial skeleton, right scapula, lateral arch of the left 9th rib, lesion with fracture of the left posterior 10th arch, and growth of the lesion in the second left rib with a soft tissue component, in the right clavicle and right iliac bone (Figures 3 and 4).

Figure 3.

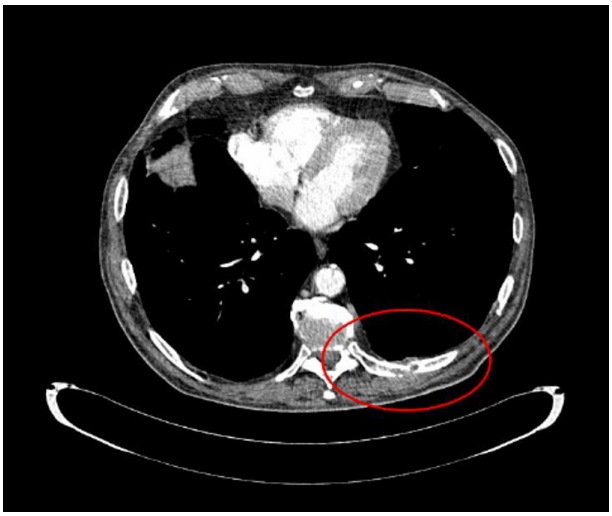
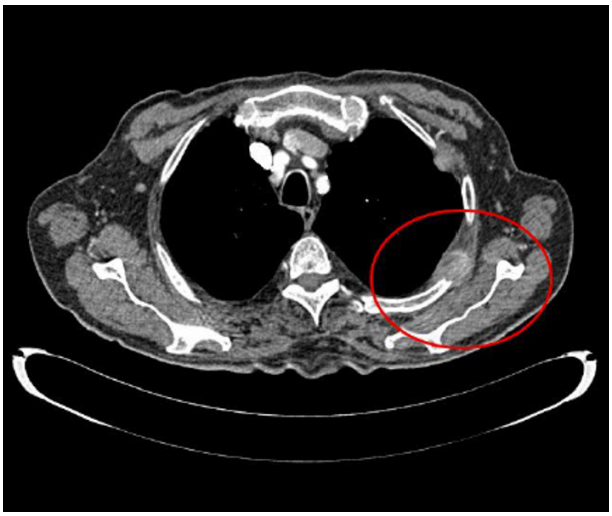


Figure 4.



During admission, the first action for pain control was to switch opioids to 1% morphic chloride in continuous intravenous infusion for analgesic titration of the necessary dose, with rescue treatment for breakthrough pain performed with 0.5 mg of the same drug intravenously. Dexamethasone was increased to 4 mg every 6 hours and the Radiation Oncology service was contacted, which after evaluating the case and presenting pain and lesions at multiple levels, ruled out treatment on their part.

Intravenous morphic chloride infusion attained a dose of 200 mg in 24 hours with virtually no pain control, despite 72 hours' treatment. It was then decided to contact the Pain Unit service, deciding to place an epidural catheter with an elastomeric pump, with 20 mg of morphic chloride in 200 mL at 2 mL/h.

The patient's clinical course in terms of analgesic control was slow, with a gradual increase in the epidural pump dose for about 14 days. Good analgesic control was achieved with an elastomeric pump at 9 mL/h with intravenous morphic chloride of 10 mg for initial doses and subsequent rescues. Given the high doses of drugs, the patient experienced drowsiness, without other side effects. Due to immobility and prolonged hospitalisation, there was a manifest functional deterioration with bed-chair life and ECOG 3. The possibility of continuing treatment at home with the epidural catheter connected to a preloaded hospital preparation elastomer was evaluated, which the patient and family accepted.

At that time, he had a fever peak of 38.5ºC, with no apparent focus and blood cultures (x 2) were extracted peripherally. Broad spectrum antibiotic treatment was established covering nosocomial infections. After 48 hours, *streptococcus epidermidis* grew in both blood cultures. Faced with a possible focus on the epidural catheter, the examination revealed redness at the entrance of the catheter with an exit of crystalline material, which appeared to correspond to the exit of the analgesic perfusion. It was then decided to withdraw it and contact the Pain Unit again. Given the patient's situation, with major deterioration and derived complications, it was agreed with them to try to evaluate a change of opioids to another administration route and not to perform invasive procedures if the patient was controlled in this way. After removal of the epidural catheter, the patient remained afebrile and the antibiotic treatment was completed.

Due to the drowsiness experienced by the patient when receiving 1% morphic chloride pain control via the epidural route, the administration route was changed to an intravenous continuous infusion pump, with a morphic chloride 1% starting dose of 250 mg/day (25 x 10 mg ampoules in 500 mL at 21 mL/h) and rescues for breakthrough pain with morphic chloride 1% 10 mg intravenously. After several days of dose titration with an increased perfusion rate, without new side effects and with an improvement in drowsiness, the patient maintained an acceptable level of pain control, with a baseline VAS of 3-4 and 2 x morphic chloride rescues a day for breakthrough pain. It was then decided to change the administration route to oral for outpatient management, switching opioids to prolonged-release oral morphine sulphate every 12 hours. Equianalgesic doses were gradually established and acceptable pain control was achieved with morphine sulfate 460 mg every 12 hours and rescue medication of 400 µg fast-acting sublingual fentanyl as required. Dexamethasone treatment was maintained in a down-titration regimen at home.

With this, the patient was discharged with a home care support team and oral analgesic treatment at high doses, with mild drowsiness as the only side effect.

Conclusions

- Pain due to bone metastases causes significant functional deterioration in patients that require complex and often multidisciplinary management.[1-3] In cases like the one described above, unusual routes need to be used, such as the epidural, to attain rapid and adequate pain control, although with the risk of associated complications, as in our case, in which a catheter infection occurred.
- The individualised management of each patient, evaluating the general condition, baseline situation and survival expectations, should guide actions regarding the best treatment and administration route.[3]
- The complications associated with the treatment and the functional deterioration produced by the pain due to bone metastases can lead to a worsening of these patients' baseline situation and a decrease in their prognosis.[1]

Bibliography

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3. Liu WC, Zheng ZX, Tan KH, et al. Multidimensional Treatment of Cancer Pain. Curr Oncol Rep. 2017;19(2):10.

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