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Research Article

Palliative Treatment of Multiple Level Painful Vertebral Metastases Employing O-Arm, Navigated Radiofrequency Ablation and Augmentation

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Abstract

Purpose: The aim of this study was to evaluate the benefit of the palliative treatment of multiple level painful vertebral metastases employing O-Arm navigated radiofrequency ablation (RFA) and augmentation.

Methods: Over a period of two years, the author of this paper additionally treated his patients with painful vertebral metastases on more than one level, using an O-Arm device and a navigator, to perform radiofrequency ablations with additional augmentation. In a few cases without obvious instabilities and if necessary, small microsurgical decompressions were also performed. The clinical effectiveness of this treatment was analysed by examining: 1) pain relief (standard 10-point visual analogue scale (VAS)), 2) follow up of the neurological condition and 3) procedure related morbidity (surgical bleeding, infections, and wound disorders). Radiological evaluations included: 1) MRI calculated percentage of tumour infiltration area on involved vertebra; 2) CT assessed morphological changes and the percentage cemented of the treated vertebra.

Results: Sixteen patients with painful metastases involving two to four levels were palliative treated during this period. Twelve patients had previously been irradiated and submitted to chemotherapy. All of them presented pain on more than one level. The mean age of the patients was 56 years (range 36 to 72); the mean time of onset of pain was 4 months; the surgeries lasted an average of 74 minutes. No neurological deterioration was observed in any of the treated patients. The mean VAS score decreased from a preoperative score of 8.3 to 3.2 at patient discharge ($p < .001$), and 4.1 ($p < .001$) 1 month later.

The mean percentage of vertebral bodies infiltrated by the tumor on MRI was 52% and the mean percentage of cemented vertebral bodies observed on computed tomography images was 46%. A good individual anatomical-radiological overlap between both areas was confirmed. In the postoperative period, a clear reduction in the use of narcotic drugs was observed. Pain relief was not related to the percentage of vertebral cementation, suggesting that thermal injury was the main mechanism involved in its resolution. In only one case there was a leakage of cement into the spinal canal, which was detected during the operation and immediately removed. One month later, no delayed radiological changes (new tumor growth, cement-induced tumor displacements, or vertebral instability) were found.

Conclusion: The palliative use of radiofrequency ablation and augmentation procedures coupled with intraoperative navigation performed with an O-Arm, reported several benefits in all patients treated with multiple-level vertebral metastases. These allowed to improve the accuracy of the procedures, achieve a prompt resolution of the pain suffered by the patients and reduce the time of surgical and X-ray exposure, with a very low complication rate.

Keywords: Radiofrequency Ablation and Augmentation; Multilevel Vertebral Painful Metastases; O-Arm Intra-Operative Targeted Navigation

Abbreviations

RFA: Radiofrequency Ablation; VAS: Visual Analogue Scale; CT: Computed Tomography; MRI: Magnetic Resonance Imaging: MPNST: Malignant Tumor of the Peripheral Nerves

Introduction

Thanks to the help of different scoring systems [1,2] related to the prognosis of patients with spinal metastases, it has been proven that the survival of these patients depends fundamentally on the biology of the primary tumor. Considering advances in treatment standards and specific systemic therapies, a significant increase in the survival of these patients has been achieved today [2,3].

As a result, many patients who develop new or multiple spinal metastases that can no longer be treated with surgical techniques of total removal or additional irradiation; suffer with increasing frequency of severe pain, despite analgesic and bisphosphonates treatments instituted.

These are produced by tumor infiltration and in some cases by nerve compression.

In advanced periods of the disease, these pains cannot always be resolved by further increasing the doses of analgesics, or by traditional curative procedures, including complex surgeries lasting several hours.

The use of a percutaneous thermal ablation combined with a body augmentation, represents an additional possibility of solving this problem, effectively reducing the pain caused by tumor infiltration. [4-18].

However, many patients with metastases at more than one level also tend to have intra-spinal tumor growth, which additionally requires a minimally invasive decompressive surgical technique to improve their pains secondary to nerve compression.

Considering the importance of ensuring optimal palliative therapeutic results in all these cases, it seems obvious that the use of a navigation system and a high-resolution radiological system should also be included in the performance of the minimally invasive procedures.

In an attempt to improve the quality of survival of patients with multiple spinal metastases, this study evaluates the benefits of using percutaneous radiofrequency ablation and augmentation techniques, in some cases also combined with minimally invasive decompression techniques. These procedures were guided by virtual intraoperative navigation images and finally controlled by intraoperative computerized images obtained with an O-Arm.

Materials and Methods

Over a period of two years, the author of this study treated all referred patients with multiple spinal metastases refractory to conventional analgesic therapy, by using an O-Arm navigation system (Medtronic Louisville, USA), to perform radiofrequency ablations with additional augmentation (RFA) (STAR - StabiliT® Vertebral Augmentation system; DFINE Europe GmbH, Mannheim).

Most of the metastatic tumor mass in these patients were inside their vertebral bodies.

The lesion produced by radiofrequency was carried out through an electric heating of the tumor tissue with liquefaction of the proteins.

All patients treated in this way received general anesthesia and were placed in the prone position.

After carrying out the conventional preparations, the skin was incised to a length of less than 1.5 cm on the spinal apophysis of one of the affected vertebrae, and the reference instrument for navigation with the O-Arm was fixed to it (Figure 1).

In this way, the data were acquired for intraoperative navigation, and then guided by virtual images; the necessary number of cannulas (coaxial cannula caliber 10) were introduced to perform ablations in the affected segments in mono or bipedicular form. (Figure 2).

A bipedicular approach was employed if the bony metastasis was noted to cross the midline.

Ablation within each vertebral body was performed using an articulating bipolar radiofrequency probe, permitting percutaneous navigation within the vertebral body.

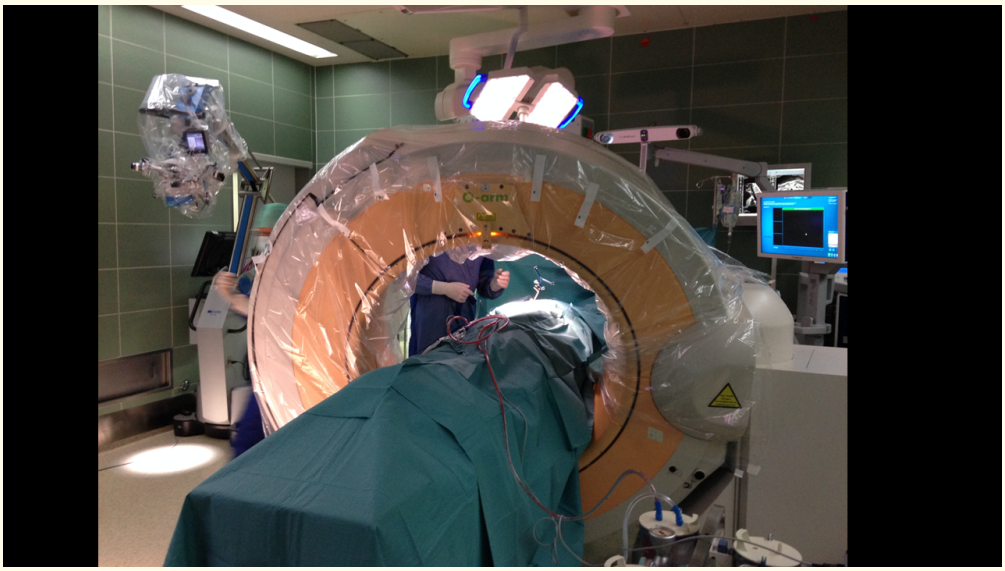

Figure 1: O-Arm and navigation system prepared for data acquisition.

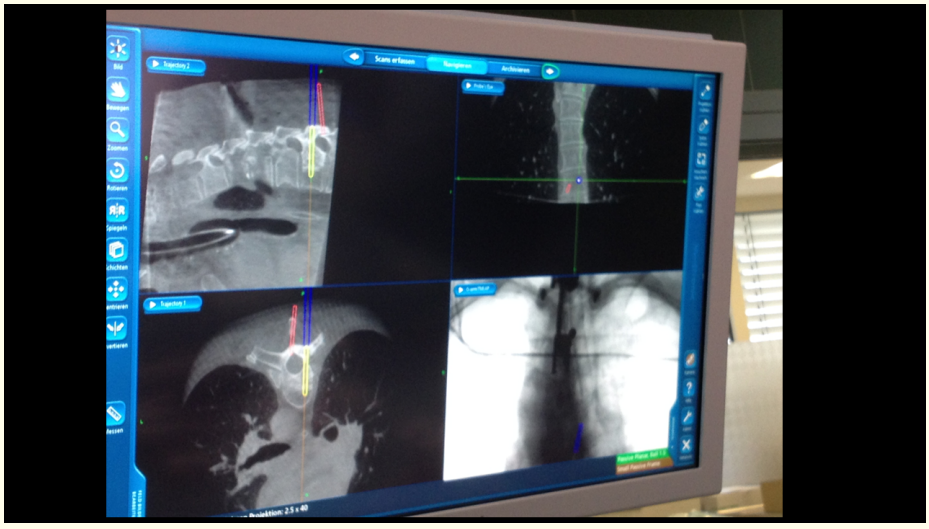

Figure 2: Intraoperative virtual navigation through a monopedicular approach.

The ablation electrode has a flexible tip that moves forward once the needle is inserted. This electrode can be bent at convenience to enlarge the ablation area.

The needle through which the electrode is inserted has an insulated tip, which prevents overheating, and a temperature sensor ten millimeters from the insulating tip, which controls the ablation temperature.

RFA thermal energy was applied to achieve the desired ablation zones using the thermocouples located on the electrode shaft to confirm and quantify the ablation zone. Repositioning of the tip was performed as necessary, to create overlapping zones and attempt complete tumor ablation.

Treatment was controlled by adjusting the power while monitoring the ablation temperature in situ.

The procedure was considered successful if adequate overlapping ablation areas covering the metastatic lesion within the vertebrae were achieved, according to the preoperative plan.

Then, a high viscosity cement heated by RF was used, to perform the filling of the cavities produced by the radiofrequency. This procedure was carried out via the same guiding cannula. The cement infusion was controlled fluoroscopically.

In selected cases, an intra-procedural computed tomography scan was performed to evaluate the ablative zone, the exact location of the cement and the presence of a possible residual metastatic lesion.

In cases without obvious instability but with intraspinal tumor growth with secondary compression of nerve structures, minimally invasive microscopic decompressions were also performed.

Pre-operative patient evaluations included a complete neurological assessment, physical examination, spine MR imaging, and hematological evaluations. MRI sequences consisted of axial and sagittal T1 and T2, sagittal short tau inversion recovery MRI (STIR-MRI), and axial and sagittal T1 fat suppressed post-contrast imaging.

Patients were evaluated at admission, dismission and one month later by using a standard 10-point visual analogue scale (VAS) to assess back pain with zero being no pain and 10 the worst pain. Pain medication use was monitored for changes before and after RF-treatment.

A follow up of the neurological condition was also performed and the procedure related morbidity (surgical bleeding, infections, and wound disorders) were additionally evaluated. Radiological evaluations included: 1) MRI calculated percentage of tumour infiltration area on involved vertebrae; 2) CT assessed morphological changes and percentage of cemented treated vertebrae.

Data were electronically stored and independently assessed. Commercially available statistical software (SPSS for Windows, version 11.5.1) was used to compare the examined data. VAS values and the follow up of the neurological condition were examined with the t test for equality of means and a Mann-Whitney U test. Values of $P < .05$ were considered significant.

Results

Repeated thermal ablation procedures were performed on 40 vertebrae of the 16 patients affected.

Twelve of them had previously been irradiated and submitted to chemotherapy.

All of them presented pain on more than one level. The mean age of the patients was 56 years (range 36 to 72); the mean time of onset of pain was 4 months; the surgeries lasted an average of 74 minutes.

No neurological deterioration was observed in any of the treated patients. The mean VAS score decreased from a preoperative score of 8.3 to 3.2 at patient discharge ($p < .001$), and 4.1 ($p < .001$) 1 month later.

The mean percentage of vertebral bodies infiltrated by the tumor on MRI was 52% and the mean percentage of cemented vertebral bodies observed on computed tomography images was 46%. A good individual anatomical-radiological overlap between both areas was confirmed.

In the postoperative period, a clear reduction in the use of narcotic drugs was observed. Pain relief was not related to the percentage of vertebral cementation, suggesting that thermal injury was the main mechanism involved in its resolution.

In only one case there was a leakage of cement into the spinal canal, which was detected during the operation and immediately removed. One month later, no delayed radiological changes (new tumor growth, cement-induced tumor displacements, or vertebral instability) were found.

A monopedicular approach was performed in 32 and bipedicular in 8 vertebrae.

The neurological deficit present preoperatively, improved to different degrees in the 9 patients who received microsurgical decompression.

Lesion`s aetiology included a wide variety of metastatic lesions including lung, renal cell, breast, lymphoma, malignant tumor of the peripheral nerves (MPNST), and multiple myeloma.

Pre-operatively, 14 (75%) patients reported use of prescribed narcotics for pain relief. One-months following RFA, patients reported using physician prescribed narcotics decreased from 14 to 6 patients.

Illustrative cases

Caso 1

This is a 78-year-old female patient who was admitted with a history of breast cancer and metastases to several organs. She's already been nephrectomized and irradiated. Currently and for two months she suffers pain in the thoracolumbar region, refractory to any type of treatment (VAS 8).

She has a Karnofsky score of 60%, and no focal neurological deficits are found.

MRI shows diffuse spinal metastases. Compared to the previous study, there is tumor progression Th8-10.

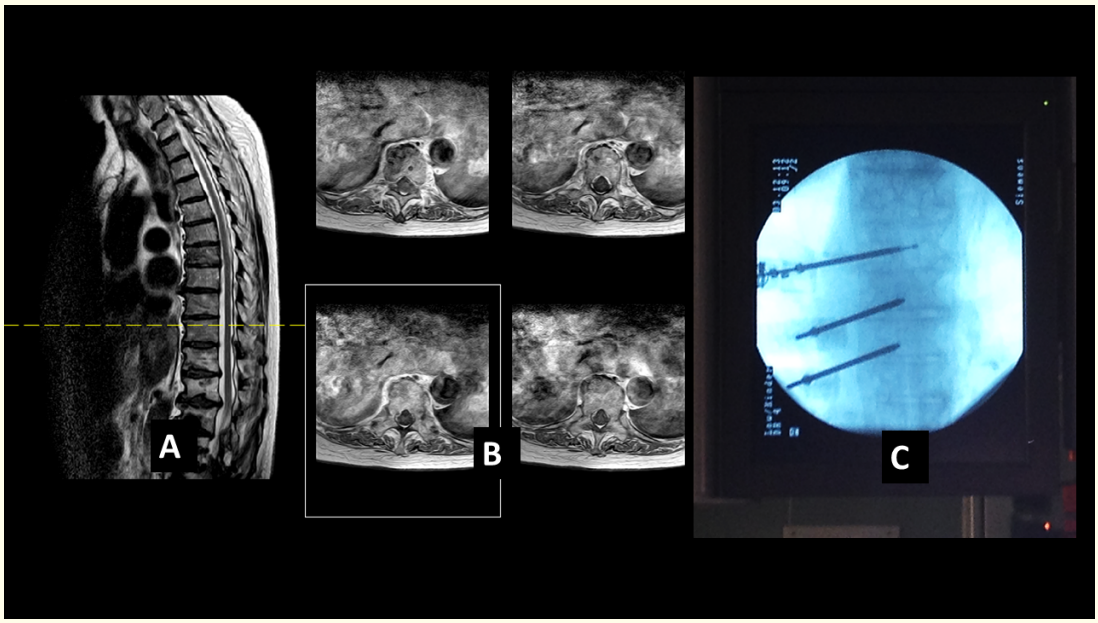

Figure 3: A and B: The current MRI compared with previous studies confirmed an active tumor growth in the vertebral bodies Th 8-9 and 10, coinciding with the painful symptomatology. C: Intraoperative radioscopic image with three cannulas positioned through a monopedicular approach (fluoroscopic control where the tip of the thermal ablation electrode is observed in the upper vertebra, before proceeding to the cementation).

The patient did not present any complications and was discharged with a VAS score 2.

Caso 2

This is a 49-year-old male patient who was admitted with back pain (VAS 8), with multiple metastases of an active-growing adenobronchial carcinoma in the vertebral bodies TH8, TH10, and L1.

The primary tumor encloses the main bronchus and the right pulmonary artery and is unresectable. He has metastases in the right suprarenal gland and received a short time ago palliative Th 7-9 radiation with a linear accelerator of photons with a limit energy of 18 und 6 MV up to 30 Gy, associated with chemotherapy (3 cycles of second-line Cis/Pemetrexed). His Karnofsky score was 80 and so far, he has only experienced a slight improvement in pain. MRI shows a radiological tumor progression: Th8, Th10 and L1 (Figure 4).

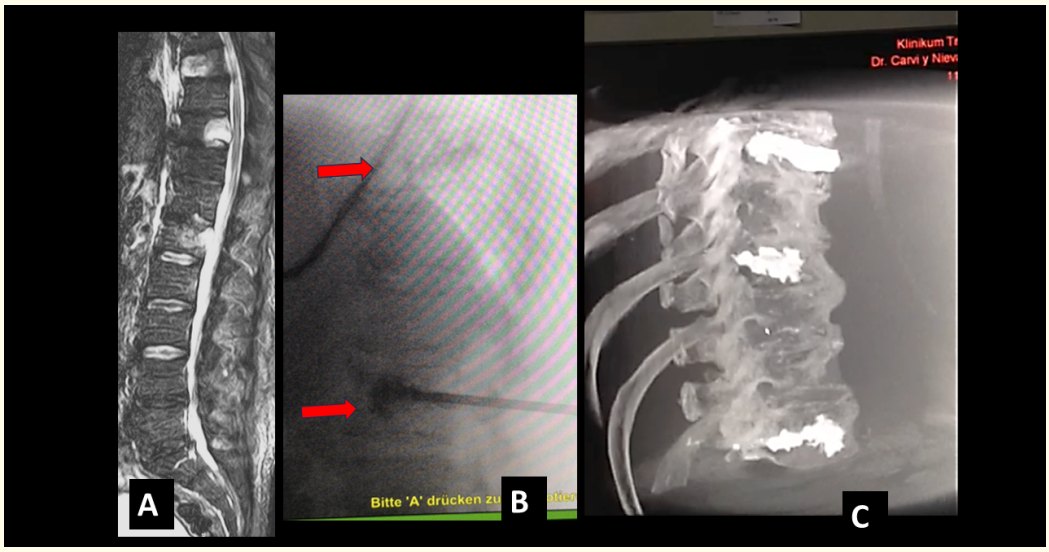

Figure 4: A(left): MRI showing an active-growing Adeno-Bronchial Carcinoma in the vertebral bodies TH8, TH10, and L1. B (middle): Intraoperative fluoroscopic control of post ablation cementation Th 10 and L 1 (arrows), C (right): Image of three-dimensional and rotational intraoperative control with the O-Arm.

The patient did not present any complications and improved his pain, being discharged with a VAS score of 3.

Caso 3

This is a 59-year-old man who was being treated for multiple metastases of a malignant tumor of the peripheral nerves (MPNST). Karnofsky-score 70%.

Metastases involved the bone system in several regions of the body, cervical lymph nodes, lung, and liver.

Upon admission there was an absence of neurological deficits. MRI shows metastases to thoracic and lumbar vertebral bodies (Figure 5).

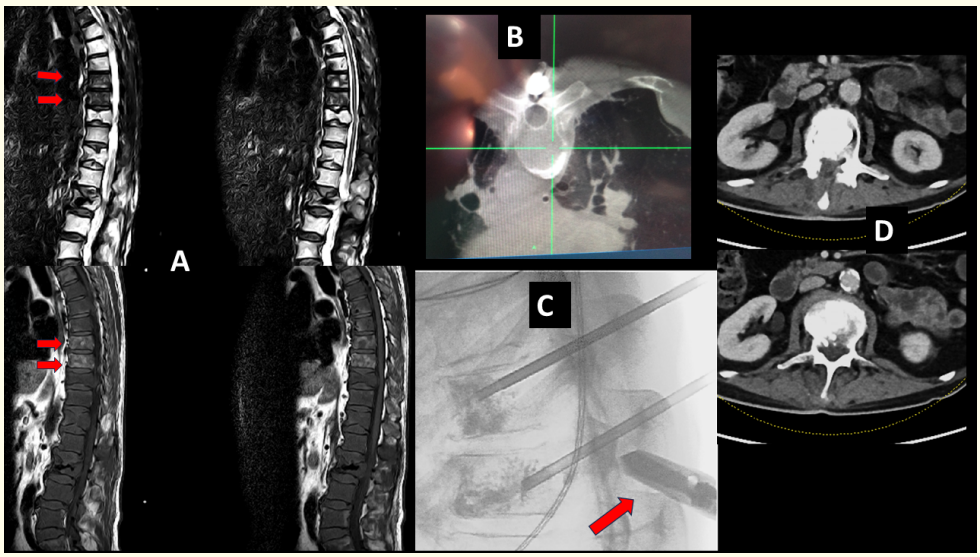

Figure 5: A (left): four sagittal MRI images showing active tumor growth Th 8 and Th 9. B: Intraoperative virtual image of the monopedicular approach with navigation. C: Image of intraoperative fluoroscopic cementation control (big arrow shows the reference instrument for navigation attached to one of the treated vertebrae. D (right): CT-scan controlling the distribution of cement on both treated levels.

His consultation was due to severe and refractory pains resistant to medical treatment in the thoracic region at the level of the vertebral bodies Th8-9 with functional restriction. His VAS was 8. Among other diseases he presents arterial hypertension, and renal insufficiency.

Post-operative images confirm a good percentage distribution of the cement, which overlaps the areas preoperatively infiltrated by the tumor. The patient did not present any complications and improved his pain, being discharged with a VAS score 2. Unfortunately, he died two months later due to diffuse metastases to other organs.

Caso 4

This is a 26-year-old male patient with Karnofsky score 60. Tumor disease: Disseminated follicular lymphoma under treatment for 8 years with current cervical and thoracal progression, At level Th 2 high-grade spinal cord compression and TH 10 with root involvement. (Figure 6). Currently severe cervical and lumbar pain (VAS 9). Requires recurrent platelet and red blood cell transfusions due to pancytopenia.

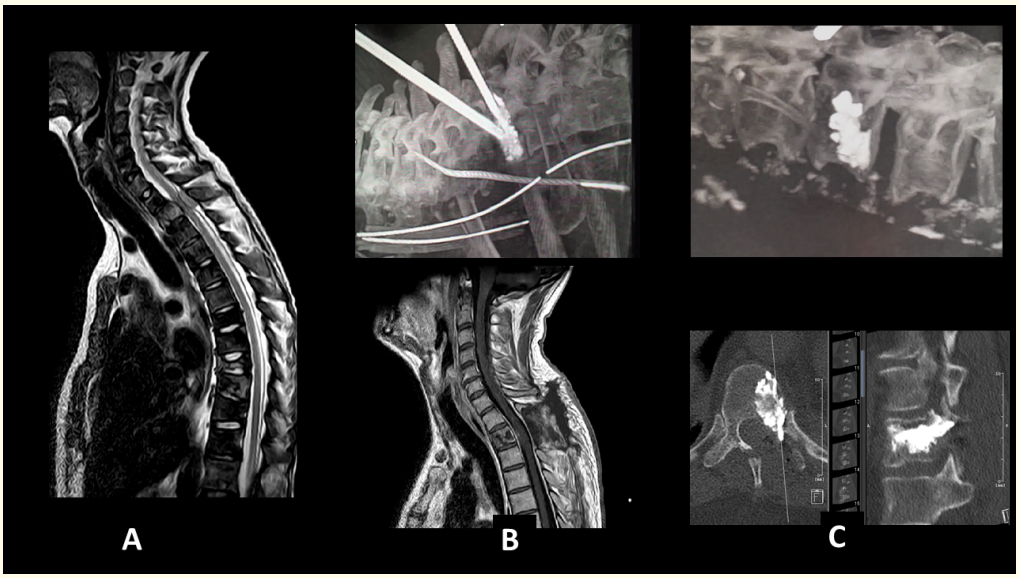

Figure 6: A (left): MRI showing active metastases Th 2 and Th10. The upper with medullary compression. B: (above) Image of three-dimensional and rotational intraoperative control at the level Th2 with the O-Arm. Intraoperative image of the bipedicular approach after microsurgical decompression, ablation, and cementation, (below) MRI control of the same level; C: (above) Image of three-dimensional and rotational intraoperative control at the level Th10 with the O-Arm. (below) CT-scan control images axial and sagittal of the cement distribution at the same level.

Due to his general condition, it was decided to palliatively treat vertebral metastases with radiofrequency; but additionally, two microsurgical nerve decompressions were performed at both levels during the same procedure. Post-operative images confirm a good percentage distribution of the cement, which overlaps the areas preoperatively infiltrated by the tumor. The patient was discharged with a VAS score 1.

Discussion

In patients with spinal metastases, curative surgical treatments that offer complete resection of the metastasis, accompanied by anterior and dorsoventral spinal reconstruction techniques, should now be clearly differentiated from palliative surgical treatments that tend to reduce pain in patients at an advanced stage of their disease [19-22].

Unlike curative surgical possibilities, in later stages of the disease, there is an understandable restriction on the complexity of the surgeries to be performed. In the case of a high-risk intervention, such as on bloc resection, the survival prognosis of the patient to be treated should be at least between 12 and 24 months [23,24].

However, in such cases, minimally invasive surgical techniques can still be used, which offer palliative solutions to some of the problems not yet resolved, such as pain refractory to conventional therapies.

The characteristics of vertebral pain due to metastatic infiltration can be described as local pain, of a progressive nature, which originates from increased pressure around tumor growth. Generally, the size of the osteolytic change is correlated with the intensity of the pain [25].

Tumor compression of neural structures may change the characteristics of pain, giving it a root distribution pattern or somewhat more diffuse in the case of leptomeningeal compression and infiltration.

Not only the side effects produced by increasing the dose of many anti-analgesics, but also the limited irradiation load allowed to adjacent nerve structures, lead to a reduction in the chances of achieving an adequate analgesic effect in advanced stages of metastatic disease.

On the other hand, as far as irradiation is concerned, significant pain relief occurs in 60 to 90%, and real pain absence occurs only in 40 to 60% of the treated cases [26-28]. This effect on pain sensation occurs in 70% of patients within 10 to 14 days and in 90% within three months following irradiation. If new tumor growth occurs, this effect tends to disappear.

In some of these cases, conventional irradiation may also be combined with stereotactic irradiation. In the series of Ryu., *et al*. such patients received initial treatment with conventional irradiation of 10 × 2.5 Gy, followed by stereotactic treatment [29]. These authors report a significant improvement in the pain symptoms of their patients. However, depending on the type of tumor being treated, there is not always a guarantee of early improvement.

Tumor entities that show a good response to irradiation within 1 to 6 months when evaluated for a recalcification rate are breast cancer. (62%), followed by prostate cancer (57%), bronchial carcinoma (28%) and renal cell carcinoma (11%) [25].

Beyond this, even in many of these cases a flattening of the affected vertebra cannot be avoided since sclerosis and recalcification only occur after a relatively long period of bone reconstruction.

Regarding the analgesic effect of irradiation, this is independent of the total irradiated dose, but has the disadvantage that only higher single doses provide a rapid analgesic effect in contrast to lower single doses.

Similarly, it can be stated that drug treatment of nociceptive pain of bone metastases, in most cases, normally responds to the administration of opiates [30]. However, in the case of vertebral metastases, bone infiltration pain may be accompanied by neuropathic pain with a root component of burning sensation or electrifying pain, which will also require the use of anticonvulsants (e.g., gabapentin) and in some cases also antidepressants (e.g., amitriptyline, doxepin) [31-33].

Unfortunately, concomitant administration of opiates, and other drugs such as bisphosphonates and some others with immunological anticancer effects, also leads to secondary complications such as urinary tract infections, upper respiratory tract infections, constipation, and joint pain.

Because of all the aforementioned limitations, it is always advantageous to have additional therapies that reduce the pain experienced by patients with several vertebral metastases.

The additional pain improvement achieved with the use of percutaneous radiofrequency has been previously confirmed by several authors [8,9-11-13,15,34].

In the absence of tumor neural compression, but with a predominant painful destruction of the vertebral body, this procedure allows a liquefaction of tumor proteins, and the application of cement to the vertebrae, achieving a relative but in many cases sufficient secondary segmental stabilization.

The cementation with or without augmentation, as has already been shown in traumatic processes, restores the resistance of the affected vertebra and prevents additional kyphosis [35-37]. Both techniques significantly reduce pain in compressive fractures of tumor-affected vertebral bodies and improve the overall functional status of patients with metastatic spinal disease and myeloma [38-41].

However, if nerve structures are being affected by the growth of metastasis, their use may show some limitations. Some of these limitations can be partially compensated if the surgeon simultaneously and during the same procedure releases the affected nerves using minimally invasive techniques.

These techniques, as well as those designed to safeguard stability, will be facilitated in achieving their objectives, if they are used in combination with intraoperative navigation [42,43]. Several authors have even confirmed the superiority of navigation-based instrumentation, particularly in cases of anatomical deviations [44,45].

If these advantages are added to the implementation of an intraoperative CT-scan device, images of superior quality will be obtained, and the accuracy of the surgical procedure will be further improved.

As recently confirmed, navigation coupled with the O-arm had significant advantages in accuracy over navigation with 3D C-arm fluoroscopy [46].

Considering the small margin of therapeutic error left by patients who are in a rather palliative stage of their metastatic spinal disease, it is always advisable to take all kinds of precautions to reduce the number of possible complications.

Finally, although the rate of complications with the use of ablation and augmentation is low, (3 %) [47], and that the additional use of this technology improves safety standards, cement leakage towards the spinal canal may still occur, as was observed in one of our cases.

The advantage of being able to perform an intraoperative tomography with the O-Arm, prevented this complication from being underestimated, and allowed us the consequent and immediate solution of the problem.

Conclusion

Radiofrequency ablation and augmentation procedures coupled with intraoperative navigation performed with an O-Arm reported several benefits in all patients treated with multiple-level vertebral metastases. These allowed to improve the accuracy of the procedures, achieve a prompt resolution of the pain suffered by the patients and reduce the time of surgical and X-ray exposure, with a very low complication rate.

Conflict of Interest

There is no conflict of interest with the above-mentioned firms.

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