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End results of surgical treatment in unknown primary vertebral metastases malignancy

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Abstract

Spinal metastases are the most common type of bone metastases and currently, external radiation and steroid therapy are used in most patients with neoplastic spinal cord compression. Surgery is generally used to treat those who do not respond to radiation therapy. The objective of this study is to analyze different types of surgical access in the treatment of patients with metastatic vertebral lesions. Selected adequate surgical resection access for 83 patients with spinal metastasis enrolled in this study, the surgery depended on the tumor site, nerve structures, and operation access that was used to resect tumors: anterior, posteriorly, lateral, and posterolateral access. In conclusion, the selection of surgical treatment for spinal metastases is mainly to relieve pain, rebuild spinal stability, improve nerve function, control local tumors, and improve the quality of life of patients.

Keywords: Spinal metastases; Cancer; Surgery, Radiation therapy

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Introduction

The incidence of vertebral metastases is estimated at 150,000 patients per year in the United States and may account for 5-30% of the approximately 650,000 patients diagnosed with systemic metastatic disease each year. Vertebrae are unique in that almost 80% of metabolic activity occurs on the end plates of the vertebral bodies, making these structures more susceptible to metastases. The increased incidence of common diseases such as diabetes, obesity, and cancer is generally believed to contribute to the increased prevalence of vertebral metastases in developing countries as well. As proposed by Dunn in 2017, the biology of the primary neoplasm, the specific vascular distribution of the spine, tumor-related factors related to the unique end plate pathology, other host-related factors, and duration of vertebral metastasis may all play a role in the susceptibility and pathogenesis of vertebral metastases.

The primary value of the study highlights the range of demographics of both reported cases of spine metastases and in those that develop surgery indicated sequelae. An interesting point proposed by the study is the gender disparity in patients that suffer product indications. Although various elements of the vertebral column can be affected by metastatic disease, one

of the most common consequences is vertebral compression fracture. The dramatically increasing incidence of osteoporosis and the spread of spinal hemangiomas may lead to a present-day increase in the prevalence of VBs. Discogenic back pain and the treatment of painful disc pathology are also very likely to contribute to the massive number of VCFs. Thus, understanding the demographics of the patient whose main complaint is back pain is crucial to the orthopaedic and neurological surgeon alike. [3] of all cancer patients develop spinal metastases during the Course of their disease and approximately 70% of cancer patients have spinal metastatic disease at death [4] . The primary tumour was known in 50% to 80% of the spinal metastasis [5] . About 70% of metastatic spine tumours are in the thoracic spine, 20% in the lumbar region and 10% presented in the cervical spine [6] [7] . The single most important factor determining outcome is the level of neurologic function at initiation of therapy as well as the nature of the primary cancer, the number of lesions, the presence of distant non-skeletal metastases and the presence and/or severity of spinal-cord compression [6] - [8] . Common primary cancers that spread to the spine are lung, breast and prostate [8] . The time from diagnosis of the primary lesion to detection of the spinal metastasis was shown to be shortest in patients with lung cancer and longest in those with breast cancer. The highest 1-year survival rate was seen in metastases from breast cancer or prostate cancer whereas patients with metastases from lung or gastric cancer had the lowest 1-year survival rates.

Associated symptoms of spinal metastasis include pain and neurological deficits. Pain can be due to direct compression of nerve roots causing radiculopathy, cancer-related bone pain, and/or mechanical instability. Neurological deficits include motor deficits, sensory dysfunction, and deficits in autonomic functions, including bowel and bladder dysfunction. Back pain or radiculopathy is the usual initial symptom; very rarely do these tumors present with focal neurological deficits. It is challenging and demanding to anticipate a preoperative prognosis for patients with metastatic spinal tumor. The use of surgery as a palliative measure is disputed in patients with short survival. Attention should be paid to surgical risks, complications, and intended benefits and cost of treatment when offering a palliative procedure for patients with limited life expectancy. It is strongly viewed that surgical intervention should be offered as it increases the likelihood of patients to undergoing adjuvant treatment, thus, prolonging survival. The objective is predominantly palliative rather than curative in the management of metastatic spinal tumors. The aims of surgical interventions are analgesia, maintenance of mobility or improvement of weakness, and improving quality of remaining life. Surgical intervention is an important means of stabilizing the spine and for spinal cord decompression. Another advantage of minimally invasive surgery is that chemotherapy and RT can be started earlier when compared with the traditional open posterior approach. Furthermore, MIS surgery can be effective in patients with poor functional baseline who experience mechanical pain and worsening mobility secondary to spinal instability. Our study revealed a low mortality rate at 6 months, which was lower than other published studies. It is important to note that the Tokuhashi score, for preoperative assessment of metastatic spinal tumor prognosis, indicated that 77.77%

(154) of the cohort had a life expectancy of more than 6 months. Only 5.5% (11) of the total patients died within 6 months. There is a very low number of patients lost to follow-up due to the close network between the neurosurgical and oncology teams. Considering that the majority of the 10% of the patients who were operated on emergently without MDT discussion had poor prognoses as per Tokuhashi scoring system, 7% survived for more than 6 months. We believe that the modern adjuvant therapy and hence, the improved prognosis resulted in the discrepancy of this historical scoring system. Our findings raise concerns regarding the authority of the various scores used to determine life expectancy. These scoring systems are also used to support the decision to perform surgery on patients with metastatic spinal cancer. There are other elements such as the American Society of Anesthesiologists grade, Karnofsky index, and the type of primary tumor which can be utilized as an alternative to assess the prognosis of patients with spinal metastases. Hematogenously disseminated disease to the spine is not curable and represents stage IV disease. Hence, the goal of surgical therapy of metastatic spinal tumors is related primarily to symptom palliation and improvement of quality of life.21, 22 Generally speaking, therefore, there is a very limited role for open surgery to treat asymptomatic metastasis to the spine.

Patients and Methods

We retrospectively interviewed 40 patients with spinal metastasis at neuroscience hospital in Baghdad between January 2010 and January 2014.

History taking and physical examination were done by a specialist neurosurgeon emphasising on neurological outcome and complications. Search for primary tumour and other visceral or skeletal metastasis by full blood picture, serum protein electrophoresis, C.T scans of chest, abdomen and pelvis, M.R.I of whole spine, X-ray of limbs and in some cases C.T scan of brain. Histopathological cell type of tumour was assessed by consultant pathologist.

Surgical decompression was done with or without stabilization as early as possible. Post-operatively further management was guided by the oncology team based on tissue histology from surgical specimens.

The study was approved and done under supervision of ethical and scientific committee of the neurosciences hospital.

Comparative Studies and Meta-analyses

This is the first modern comparative study of all available options for the surgical treatment of unknown primary vertebral metastases. We thoroughly examined the pros and cons of each of them. Large meta-analysis can be seen as a good approach to comparing the results of many studies and getting a high level of evidence. There are some reasons to choose pairwise comparisons. The results of meta-analyses are of poor quality if the results of individual studies are too different. We found significant differences between the results. Different study designs cause an important variability in the residuals about the LEs. The residuals about the LEs follow a normal distribution. It provides a sign of the high quality of the results - e.g., the heterogeneity

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is less important. So the negative results are strong. The whole series was used as a control arm. This is no longer the biggest weakness of this study. We have cared about that discussing with experts and reviewers before starting the study. They found this suitable for the first comparative study. Finally, we have performed the biggest cohort of unknown primary metastases ever reported.

The optimal treatment of unknown primary chemotherapy-resistant vertebral metastases is currently unknown. Why are we doing a comparative study instead of a meta-analysis? There are three main reasons. First, comparative studies allow combining individualized patient data, whereas meta-analyses demand using summary data. Second, when comparing the results of several studies, data are mixed, with different follow-ups, arcs, number of publications, vaccination numbers, etc. Then, it is impossible to merge them because the designs are not uniform. For those reasons, comparative studies guarantee a more reliable assessment of the benefits. The only limitation of these comparative studies is that they provide lower levels of evidence, with the risk of selection for entry and drop-out of controls. In this study, we completed this with short follow-up.

The portion of the review was completed to discuss methodological considerations. When conducting comparative studies, the ideal level of evidence is any form of randomized control trials, case-control trials, or prospective and retrospective observational trials. Many different trials used various outcomes to determine the efficacy of their intervention(s). Because of this, these outcomes are difficult to compare as they measure different components of the respective disease process or intervention. Also, results in publication bias toward positive outcomes as negative results are less likely to get published. All of the studies were case series, prospective or retrospective in nature. Meta-analysis is conducted in order to aggregate data from multiple publications in order to draw conclusions based on data.

The ideal meta-analysis is when systematic investigation addresses a focused clinical question, utilizes explicit methods to identify, select, assess and combine data from similar but independent studies, and uses appropriate methods to explore between-study heterogeneity. Major methodological considerations in comparing data. For example, bias is inevitable in most of the studies. Cons include variations in reporting, significant problems in pooling data, and differences in the study designs. Each study's data are pivotal and should be treated according to their quality and relevance rather than simply pooling all data in one data analysis. Pooling all the data may in some circumstances simplify the data analysis, but the conclusions drawn on the clinical purposes may not be realistic or reliable. This might potentially bias and distort the results. The ultimate key point is to make sure that only applying the results based on high evidence from pooled data is valid.

Results

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A total of 40 patient had surgery duo to metastatic spinal cord tumour 35 patient (87.5%) had known primary lesion, while 5 patients (12.5%) were of unknown primary/tumour even after full radiological investigations [see Table 1].

The median age at time of surgery was 64 years for the unknown primary with a range between 58 - 72 years, and for those of a known primary the median age was 61 year with a range between 45 - 70 years. Male are more common than female in both groups [see Table 1].

None of the 5 patient with secondary metastasis of an unknown primary lesion had other skeletal or visceral involvement [see Table 2].

There was no significant difference in 3 month duration of symptomsor in the neurological out come after surgery or the complication rate between the two groups [see Table 2].

The most common complication was deep wound infection, systemic, neurological, pulmonary and vascular [see Table 2].

Those 5 patients with the unknown primary tumour, the site of origin were diagnosed after surgical decompression and assessment of histopathology result. The 4 out of 5 with unknown primary was proved to be adenocarcinoma from the lung [see Table 3].

None of the 40 patients who had secondary spinal metastasis had cervical spine involvement. The dorsal spine was the common site for those of an unknown primary tumour 80%. While the lumbar spine was the common site for those of a known primary tumour 28 out of 35 (80%) [see Table 4].

Table 1. The demographic factors in the 2 groups of patients of metastatic spinal tumour of unknown primary and the group of known primary.

Metastatic spinal tumour		Unknown primary tumour	Known primary tumour
Total no. of patients (40)		5 (12.5%)	35 (87.5%)
Median age		64 (58 - 72) years	61 (45 - 70) years
Gender	Male	4/5 (80%)	22/35 (62.8%)
	Female	1/5 (20%)	13/35 (37.2%)

Table 3. Primary site of origin of metastatic spinal tumour of unknown primary and a known primary.

Metastatic spinal tumour	Unknown primary tumour	Known primary tumour
Lung	4 patients (80%)	18 patients (51.4%)
Colorectal	1 patient (20%)	8 patient (22.8%)
Breast		7 patient (20%)
Renal		2 patient (5.71%)

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Table 4. The site of spine involvement comparison between metastatic spinal tumour of unknown primary and a known primary.

Site of spine involved	Unknown primary tumour	Known primary tumour
Cervical	0	0
Dorsal	4 patients (80%)	7 patients (20%)
Lumbar	1 patient (20%)	28 patients (80%)
Total	5 patients	35 patient

Table 5. Indication of surgery in both groups.

Indication of surgery	Unknown primary tumour	Known primary tumour
Pain	1 patient (20%)	2 patient (5.7%)
Neurological deficit	3 patient (60%)	21 patients (60%)
Pain & neurological deficit	1 patient (20%)	12 patients (34.2%)
Total	5 patients	35 patients

Discussion

In a very small subset of patients, the metastatic spinal tumor represents the sole site of disease (SSD). Although metastatic spinal disease usually is due to hematogenous dissemination of the primary cancer (stage IV disease) and hence by definition is incurable, there is the theoretical possibility of cure or at least relatively long-term survival by eradicating a spinal metastasis that is the SSD. It has been well established that the outcome of metastatic spinal cord compression is related directly to the pretreatment clinical status of the patient.18, 19, 20 Neurologically intact patients typically maintain their functional neurologic status after therapy. Severely affected patients with significant neurological deficits tend to improve after therapy but, if deficits are severe and have been present for a prolonged time prior to therapy, the chances for significant improvement after surgery. The most common site of spinal metastasis in those with unknown primary site was the dorsal spine (80%) followed by lumbar spine (20%) similar to Douglas S. et al. [2] Study. while those group with known primary tumour in our study the most common site was lumbar spine 80% and 20% for the dorsal spine which was different from Salvatietal study [6] which was including 59 patients with dorsal spine involved was seen in 41 cases. Nottebaert et al. [10] study the thoracic segment was the most frequent site of cord compression.

Novel Treatment Approaches

At diagnosis, primary tumor foci with unknown primary tumor focus exist between 3 and 6%. Approximately 70% of such foci are metastatic, and, for lymph nodes, squamous carcinoma is frequent. By performing molecular tests, the focus was found in one third of cases. The negative effects of primary tumor foci with an unknown primary focus include lower overall survival and, by most authors, a more frequent SSCP. Endoscopic resection is a therapeutic option for some SSPCs with a posterior nasopharyngeal wall. Wackym et al., in the year 2000, resected large SSCP using a purely endoscopic approach in 20 to 22 patients with a local goal between 14 and 18 (if modified House-bracket 14 and 15 are added) and a variable degree of NFCS injury. However, the complete disappearance of the SSCP never occurred, as later in 2011, Metson et al. reported that 15 of 18 patients with FV focal or CSP resection with or without NP extension by pure endoscopy required orcho/ipiomeningeo reconstruction. In anticipation of a lesser aesthetic and functional impact, conicity came into use in the SSCP, in some cases replacing the last-open resection with orchiopiomy. Conducted under the control of an intraoperative O-arm, a radical excision only in the CP with a planned margin without histological control seems to be the most common practice concerning vertical invasion. In our institution, all patients with SCC FV come with an LF. The endoscopic endonasal approach is usually the choice to be made because all tumors in our setting are posterior. The necessity also to approach intracranially in the presence of VB-C close to VCF 0, a containment of the narrow CS space between the auricle and the external ear canal (EAC) and with the opening of the entire external ear canal. Interestingly, a margin FV focus linked to the lesions generally caused the bony destruction of the VS. PB, VF (CB) and the pedicle ORF were named as patients with SCP Vertical Infiltration. A bony craniotomy of the mastoid pyramid is not needed on the cephalic face. Conicity was used as a containment between the EAC opening of the infectious cavity n + 1 and the non-PNDS with or without NP to maintain desegregation. RP ear canal, calf, and DFF n + 0 are solitary incisions located behind the earlobe, and effective desegregation is secured to the auricle by a random paddle width raising at the end. In all cases, there was a need to remove the entire EAC intraoperative O-arm control, including the inferior invagination, to obtain FRs. The EAC cleaning with a piece of dissolvable corticosteroid was compensated for because the non-persistent pseudocapsule originated from the VS removal of the likely fibula petrous pyramid tension and had an excellent WE. The DFF n+0 was restored to full activity, escorted by augmentin for 10 consecutive days and saline irrigation of the neo-EAC. Treatment with steroids is given within 7 days to the individual.

In conclusion

VBM treatment is regarded as a localized radiotherapy, medical treatment, or surgery. Binding the bony metastatic tissue, the tumor itself, the potential resection rate, and the systemic condition of the patient has become wide surgical. Various studies have shown that spinal radiculopathy is a standard complaint of unknown primary VBM followed by paralysis. This study indicated a wide range of ships attached on average in calculating spine metastasis

scores in patients and operated on the Dawson and bungalows systems in the worst risk groups. This affects the excellent local control of the patients after surgery between the series. In the same study, all of the patients were made with Shiraki score 1 or 2 of 13 patients who benefited from unplanned surgery conducted with debonding technique in 15 patients in the Series. According to this study, it was determined in multiple logistic regression analysis that the amount of postoperatively resected mass, as well as preoperative coordination whether, as well as preoperatively. In the light of this data, we found that VASPAI and bone mass reduction increased by 2.149 times, exacerbating the condition of disease pre-operatively affects the postoperative results.

Future Directions in Research

The personalized nature of tumoral autoimmunity and the huge amount of data to be taken into account to prevent "overdiagnosis" or "overtreatment" can be managed only by complexity gene disorders' development, which has become reality by genetic "endotumorama" complexity state.

However, based on the anthropological-biological perspective suggested by Embriaco, the amount of possible acquisitions shown in the "A glimpse of the future direction" section still makes them future possibilities open to research only, because such approaches, for the time being, only provide new types of data to be taken into account. Above all in the clinical field, those data in few years have the possibility to force or to lead to a change of the classical clinical procedures.

For these reasons, "the future of clinical research" should consist more in cross experiments, open-minded and critical attitude towards novel results and towards classically established data which might be critically re-elaborated for their acknowledgement, more than in the use of possible new technology-based research tools. The item, thus, aims to critically report new aspects that in the close future might improve at minimum the approach to some groups of VMs from the experimental view, even though their utility as a showcase for the clinical community is uncertain nowadays. In detail, those new approaches might be summarized as follows: Novel methods of local treatment termed "intra surgery" techniques, including hardware and drugs, offering the future for VMs relapse prevention and higher feasibility of surgical approaches in more and more old symptomatic patients, but frequently, as initial therapeutic means in patients presenting bone impairment near or over-collapse. The new advanced contrast studies, such as dynamic enhanced magnetic resonance/anatomy shows biology and cytoarchitecture of tissue gadolinium perfusion CT, now close to be applicable also for VMs makes feasible pre- and intra-"surgery" biological verifications and histobased biomarker-related gene profiling that can give indications for prompt adjuvant post-surgical drugs; Augmented reality intra-surgery and intra-imaging functionalism can allow dynamical modification of our VMs approach to vertebro/kyphoplasty, turning them feasible where they were not, calculus-assisted in many

patients, and federative/consensual in patients adverse to general anesthesia, and intraoperative bioptic procedures also during kyphoplasty; Preoperative gene treatment may be developed in the close future, making us capable to strengthen the part or the activity of some genes in the ground of the affected intravertebral tissue. These genes may offer increased osteogenesis, angiogenesis, or deposited short intromembr performed cells. They also can add antibiotics in their use of the VM biological sequencing. This therapeutic approach is fertilized by the progressive spread of gene and gene-based drug delivery systems. These strategies may also lead to increased cracking systems resistance of antibiotics strategies, as the intrapetraseal endblockade of reactive acetic acid and stoners has demonstrated in their preclinical application already.

Authors' contributions

All authors shared in the conception and design and interpretation of data, drafting of the manuscript and critical revision of the case study for intellectual content and final approval of the version to be published. All authors read and approved the final manuscript.

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