Vertebral multiple myeloma with pathological fracture: the most common etiology for emergency spine surgery in patients with no cancer diagnosis on admission

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OBJECTIVE Vertebral compression fractures are common in multiple myeloma (MM). Modern treatment paradigms place emphasis on treatment with radiation, with surgery reserved for cases involving frank instability or severe neural compression. However, experience at the authors’ institution has led them to suspect a more prominent role for surgical intervention in some settings. The authors undertook the present study to better understand the incidence of MM in undiagnosed patients who require urgent surgery for pathological vertebral fracture.

METHODS The authors reviewed a prospectively collected database of all patients who underwent surgery with the senior author at their main hospital between June 1, 1998, and June 30, 2020. Patients admitted from the emergency room or after transfer from another hospital who then underwent surgery for pathological fracture during the same admission were included in the final analysis. Patients scheduled for elective surgery and those with previous cancer diagnoses were excluded.

RESULTS Forty-three patients were identified as having undergone urgent surgical decompression and/or stabilization for pathological fracture. Histopathology confirmed diagnosis of MM in 22 (51%) patients, lung metastasis in 5 (12%) patients, and breast metastasis in 4 (9%) patients. Twelve (28%) patients were diagnosed with other types of metastatic carcinoma or undifferentiated disease. Sixteen of 29 (55%) men and 6 of 14 (42%) women were diagnosed with MM (p = 0.02). Seventeen of 34 (50%) patients who underwent surgery for neurological deficit, 5 of 6 (83%) patients who underwent surgery for spinal instability, and 0 (0%) patients who underwent surgery for pain with impending spinal cord injury were diagnosed with MM (p = 0.12).

CONCLUSIONS A majority of patients presenting to the authors’ hospital with no history of malignancy who required urgent surgery for pathological compression fracture were found to have MM or plasmacytoma. This disease process may affect a significant portion of patients requiring decompressive or stabilizing surgery for compression fracture in academic medical centers.

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KEYWORDS multiple myeloma; neurosurgery; pathological; fracture; incidence; operative

Multiple myeloma (MM) is a disease caused by the diffuse, uncontrolled proliferation of plasma cells. Recent estimates indicate that nearly 140,000 new cases are diagnosed each year worldwide. Bone disease occurs in 80% of patients, with bone pain as the first symptom in 70% of patients. Vertebral compression fractures occur in 55%–70%, sometimes resulting in significant deformity with or without neural compression. Solitary plasmacytoma is a precursor to MM, characterized by a tumor mass that results from the focal proliferation of plasma cells without systemic involvement of the bone marrow. Spinal involvement is thought to be prominent in both entities, given the fact that vertebral bodies contain a high amount of hematopoietic bone marrow compared to other parts of the body.

The role surgery plays in treating pathological fractures caused by MM and plasmacytoma has long been a topic of debate, because procedural intervention attains rapid relief of symptoms but with high rates of morbidity and mortality. Patients with MM are at higher risk for thromboembolic complications and have a suppressed immune system, resulting in higher rates of infection. Some authors have described favorable outcomes in selected patients with surgical stabilization. Particularly in patients with...
preoperative deficits, surgery has been effective in improving functioning and restoring structural stability.\textsuperscript{10-14} Other authors have suggested cement augmentation as a less invasive alternative to improve structural deformity and alleviate pain in several series.\textsuperscript{15-19} However, other studies have demonstrated favorable outcomes in patients treated with radiation alone, even in the presence of neural compression or evidence of radiographic instability.\textsuperscript{20,21}

Current international guidelines recommend primary treatment with radiation unless there is evidence of frank instability or rapid neurological deterioration necessitating surgery first.\textsuperscript{22} Indeed, neurosurgical trainees are taught that MM is a disease treated primarily with radiotherapy unless there are extenuating circumstances.\textsuperscript{23} Coupled with earlier disease detection following the advent of MRI,\textsuperscript{24} these factors have contributed to a consensus within the neurosurgical community that MM is generally not a surgically treated disease.

However, experience at our institution has led us to suspect a more prominent role for surgery in MM in some practice settings. In particular, patients with no history of malignancy frequently present to our tertiary referral center at a large public hospital with pathological fracture requiring urgent decompression and stabilization. Many are later diagnosed with MM or plasmacytoma after surgery, having been subjected to a rapid, preoperative metastatic workup that failed to yield a diagnosis. We undertook this study to quantify the incidence of MM in undiagnosed patients who required urgent surgery for pathological vertebral fracture.

\section*{Methods}

This study was conducted after approval by the institutional review board. We reviewed a prospectively collected database of all patients who underwent surgery with the senior author (A.D.L.) at a single hospital between June 1, 1998, and June 30, 2020. Lesion characteristics, demographic information, and surgical indications were recorded for patients with pathological fracture who were treated surgically. Surgical indications were delineated as neurological deficit, spinal instability, or refractory pain with impending spinal cord injury. Only patients admitted from the emergency room (ER) or after transfer from another hospital who then underwent surgery during the same admission were included in the final analysis. Additionally, patients were only included if there was no previous cancer diagnosis prior to arrival in the ER, or if the patient had been treated for cancer more than 10 years prior with no other evidence of recurrence. Patients who were scheduled for surgery on an elective basis also were not included.

We defined pathological fracture as a fracture occurring either spontaneously or after minor trauma, secondary to malignancy arising from the vertebral body and resulting in bony deformity. In all cases, lesions were imaged with CT and contrasted MRI and classified as pathological fracture preoperatively by the senior author and an attending neuroradiologist. All treated fractures had evidence of epidural spinal cord compression (ESCC) or nerve root compression (Bilsky grade 2–3).\textsuperscript{25} Patients with intradural disease, with disease exhibiting extensive infiltration of the paraspinal musculature and/or viscera consistent with connective tissue malignancy, or with characteristics strongly suggestive of primary bone tumors were excluded.

\section*{Statistical Analysis}

Continuous variables are reported as means with standard deviation for normally distributed data, and medians with interquartile range for nonnormally distributed data. Categorical variables are reported by frequency. Between-group comparisons were performed with Pearson chi-square and 1-way ANOVA tests. Fisher’s exact test was used when greater than 80% of values were less than 5. All statistical analysis was performed using IBM SPSS (version 24; IBM Corp.).

\section*{Results}

A total of 43 patients were identified as having undergone urgent surgical decompression and/or stabilization for pathological fracture with the senior author. Histopathology confirmed diagnosis of MM in 22 (51%) patients, lung metastasis in 5 (12%) patients, and breast metastasis in 4 (9%) patients. The remaining 12 (28%) patients were diagnosed with other types of metastatic carcinoma or undifferentiated disease. The thoracic spine was primarily involved in 25 (58%) cases, whereas the cervical and lumbar spine were involved in 9 (21%) cases each. Other characteristics of included patients are given in Table 1.

Sixteen of 29 (55%) men and 6 of 14 (42%) women were diagnosed with MM (p = 0.02). Seventeen of 34 (50%) patients who underwent surgery for neurological deficit, 5 of 6 (83%) patients who underwent surgery for spinal insta-
bility, and 0 (0%) patients who underwent surgery for pain with impending spinal cord injury were diagnosed with MM (p = 0.12). Patients diagnosed with MM had a mean age of 58 years, and patients diagnosed with breast, lung, and other/undifferentiated metastasis had a mean age of 54, 61, and 59 years, respectively (p = 0.83). Comparison of presenting features by histopathological diagnosis are given in Table 2. A sample case is shown in Fig. 1.

**Discussion**

Most cases of MM will have spinal involvement, and surgery is considered in instances in which patients present with neural compression or significant instability. However, MM is generally not regarded as a surgical disease because management strategies include a combination of autologous stem-cell transplant, radiation, and chemotherapy.26 Nevertheless, we have suspected that in some practice settings MM is more often treated first with surgery.

In this study we reviewed the incidence of MM in patients with no history of malignancy who presented with pathological fracture that required urgent surgery at our hospital. We found that a majority of patients were diagnosed with MM (51%). There was a tendency for these patients to be male (73%, p = 0.02), and most patients

### TABLE 2. Comparison of histological diagnosis in patients with pathological fracture undergoing surgery during the same admission

| Characteristic         | Breast Mets | Lung Mets | Other Mets | MM/Plasmacytoma | p Value |
|------------------------|-------------|-----------|------------|----------------|---------|
| **Sex**                |             |           |            |                |         |
| Female                 | 4 (29)      | 0 (0)     | 4 (29)     | 6 (42)         | 0.02*   |
| Male                   | 0 (0)       | 5 (17)    | 8 (28)     | 16 (55)        |         |
| **Race**               |             |           |            |                |         |
| Black                  | 1 (11)      | 2 (23)    | 3 (33)     | 3 (33)         | 0.39*   |
| Hispanic               | 0 (0)       | 2 (15)    | 2 (15)     | 9 (70)         |         |
| Non-Hispanic White     | 3 (16)      | 1 (5)     | 6 (32)     | 9 (47)         |         |
| **Surgical indications**|           |           |            |                |         |
| Neurological deficit   | 2 (6)       | 5 (15)    | 10 (29)    | 17 (50)        | 0.12    |
| Spinal instability     | 1 (17)      | 0 (0)     | 0 (0)      | 5 (83)         |         |
| Pain                   | 1 (33)      | 0 (0)     | 2 (67)     | 0 (0)          |         |
| **Spinal level**       |             |           |            |                |         |
| Cervical               | 0 (0)       | 1 (11)    | 2 (22)     | 6 (67)         | 0.89*   |
| Thoracic               | 4 (16)      | 3 (12)    | 7 (28)     | 11 (44)        |         |
| Lumbar                 | 0 (0)       | 1 (11)    | 3 (33)     | 5 (56)         |         |
| **Age in yrs, mean ± SD** | 54 ± 13   | 61 ± 5    | 59 ± 11    | 58 ± 12        | 0.83    |

* Statistically significant according to Fisher’s exact test.
who underwent surgery for MM had a neurological deficit (77%, p = 0.12). For all pathology types, fractures of the thoracic spine were most common, accounting for 58% of all fractures seen.

Widely accepted treatment algorithms suggest treatment of ESCC with radiation therapy in cases in which tumors are known to be radiosensitive. However, a significant number of patients with MM still ultimately undergo surgery. Earlier studies suggest that as many as 20%–40% of patients with MM or plasmacytoma undergo some form of spine operation. The prevalence of surgery despite the proven efficacy of radiation is likely to be attributable in part to the effectiveness of surgery in alleviating neurological symptoms, including paraparesis. Among patients with spinal cord injury secondary to metastatic disease, lung metastasis and MM/plasmacytoma are the most common pathologies.

Other surgical guidelines recognize a need for surgery in some instances of ESCC secondary to metastatic disease. A 2016 review by Laufer and colleagues supported surgery for progressive neurological deficits in the setting of ESCC secondary to metastatic disease. They recommend careful consideration of duration and severity of symptoms in evaluating patients for surgery, as well as oncological burden—noting, however, that decompression should not be delayed to establish a diagnosis. Other characteristics to consider include spinal level involved, mechanical pain, lytic appearance, subluxation, severity of vertebral body collapse, and involvement of posterior spinal elements. Based on our results, patients with undiagnosed MM may be more likely to possess features associated with ESCC that require surgery.

In contrast to patients presenting to the clinic for evaluation, often following referral by an oncologist with an established diagnosis, those presenting to the ER at a public hospital often face more barriers to care. Earlier studies have found that among patients seeking care at the ER in urban public hospitals, more than 60% reported no source of regular care and 48% reported waiting to seek care. ER use in public hospitals has also been shown to be the primary source of ambulatory care for patients treated there. Consequently, presentation and appropriate management may vary widely in comparison to a comprehensive cancer center where patients would be expected to have earlier diagnosis and closer follow-up. In this sense, the patient base is an important consideration when delineating the role for surgery in MM.

Understanding that MM is the most common pathology in cancer-naive patients presenting to the ER with vertebral instability and/or neurological deficit will help the spine surgeon in his or her acute management including diagnostic (e.g., serum electrophoresis) and treatment decisions.

Conclusions

A majority of patients presenting to our hospital with no history of malignancy who required urgent surgery for pathological compression fracture were found to have MM or plasmacytoma. This disease process may affect a significant portion of patients requiring decompressive or stabilizing surgery for compression fracture in academic medical centers.

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Author Contributions

Conception and design: Levi, Jamshidi. Acquisition of data: Burks, Elarjani, Govindarajan. Analysis and interpretation of data: Burks. Drafting the article: Burks. Critically revising the article: all authors. Reviewed submitted version of manuscript: Levi, Burks. Statistical analysis: Burks, Elarjani. Study supervision: Levi.

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