The role of magnetic resonance imaging and positron emission tomography-computed tomography combined in differentiating benign from malignant lesions contributing to vertebral compression fractures

Ashish Aggarwal, Pravin Salunke, Bala Raja Shekhar¹, Rajesh Chhabra, Paramjeet Singh², Anish Bhattacharya³, Ravi Garg

Department of Neurosurgery, ¹Radiodiagnosis and ³Nuclear Medicine, PGIMER, Chandigarh, ¹Neurosurgery, Kamineni Hospital, Hyderabad, India

E-mail: Ashish Aggarwal - aagarwal_7@yahoo.com; Pravin Salunke - drpravin_salunke@yahoo.co.uk; Bala Raja Shekhar - drbalup@ yahoo.com; Rajesh Chhabra - drrajeshchhabra@gmail.com; Paramjeet Singh - param.pgdr@yahoo.com; Anish Bhattacharya - anishpgi@yahoo.com; Ravi Garg - ravi_piseces@yahoo.co.in

*Corresponding author

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Abstract

Background: Obtaining tissue confirmation of the underlying pathology is the gold standard for establishing the etiology of nontraumatic vertebral compression fractures. However, newer investigative modalities such as the magnetic resonance imaging (MRI) and positron emission tomography-computed tomography (PET-CT) combined potentially offer the ability to distinguish between benign and malignant lesions, thereby circumventing the need for invasive tissue diagnostic/biopsy procedures.

Methods: Twenty-four patients with nontraumatic, spontaneous vertebral compression fractures were prospectively studied. After clinical evaluation, all patients underwent MRI (with/without contrast) focusing on the spinal lesion, followed by whole-body PET-CT. This was followed by fine needle aspiration cytology (FNAC) of the lesion to confirm the diagnosis. The sensitivity and specificity of MRI and PET-CT studies were calculated for benign vs. malignant lesions.

Results: The sensitivity/specificity of MRI for benign lesions were 78.57%/90%, while the sensitivity/specificity values of PET-CT for benign disease were 92.8%/90% respectively. Alternatively, the sensitivity/specificity of MRI for malignant lesions were 90%/78.57%, while the sensitivity/specificity of PET-CT for malignant disease were 90%/92.8%, respectively. Furthermore, the sensitivity for diagnosing malignant lesions utilizing both studies together was 100%, but the algorithm was not specific. Additionally, the specificity for MRI and PET-CT combined was 100% for benign lesions. PET-CT also helped in monitoring responses to empirical antitubercular treatment (ATT) therapy. Of interest, FNAC was inconclusive in four cases in which PET-CT findings helped further in either obtaining a tissue diagnosis from another location or institution of empirical therapy in suspected cases of tuberculosis.

Conclusions: The specificity for MRI and PET-CT combined was 100% for benign lesions. Unfortunately, the specificity for MRI and PET-CT combined was not 100% for malignant vertebral lesions, though it was sensitive. The PET-CT scan was an...
INTRODUCTION

Differentiating benign from malignant disease responsible for vertebral compression fractures is challenging. Although magnetic resonance images (MRI) has well-established criteria for distinguishing between benign vs. malignant spinal disease, these criteria are fallible. However, when MRI scans are combined with positron emission tomography and computed tomography (PET-CT) studies, together they better specify the pathology of vertebral lesions, while the latter (PET-CT) screens the body for lesions at other sites. Standardized uptake values (SUVs) of various tissues may further help differentiate benign from malignant disease. Although tissue diagnosis is still considered the gold standard (e.g., utilizing fine needle aspiration cytology [FNAC]), the combined diagnostic accuracy of MRI and PET-CT in differentiating benign from malignant disease requires further investigation.

MATERIALS AND METHODS

A prospective study was performed involving 24 patients (18 males and 6 females) who presented with nontraumatic spontaneous vertebral compression fractures. Patients with osteoporosis, degenerative disease, and disc herniations were excluded. All patients underwent MRI (with/without contrast) of the spine involving the affected region, followed by whole-body PET-CT. Additionally, all patients had FNAC of the lesion at the primary spinal site or other sites picked-up by PET-CT (e.g., subjected to FNAC in case where cytology from primary site was inconclusive).

Specifics of diagnostic studies

MRI studies (1.5 Tesla Siemens Magnetom) with/without gadolinium (0.1 mmol/kg) were labeled as benign (preservation of bone marrow/paravertebral abscess/collection) vs. malignant (convex bulge of posterior vertebral cortex, pedicural disease, and paraspinal soft tissue mass).

PET-CT included acquisition of both the PET and CT images. CT was done at 140 kV + 18 mA. CT was done for anatomical localization and also as an attenuation map. PET was done after injection of 10-20 mci of 18 F fluoro deoxy glucose (FDG) intravenously and images were taken 50-60 minutes after injection on a GE-discovery machine. The results were interpreted both visually and semi-quantitatively. Liver SUV values were taken as baseline. Malignant lesions were those with SUV values >2 SD of liver SUV and were categorized as benign if the values were <2 SD of liver SUV.

CT-guided FNAC of the lesion was done in all patients, and the results were compared with MRI and PET-CT results. When FNAC was inconclusive, tissue diagnosis from other sites of involvement seen on PET-CT was obtained. In cases where there were no other sites involved, the provisional diagnosis was based upon radiological finding. Empirical therapy was started for suspected benign pathology such as tuberculosis, and in these cases, the final diagnosis was guided by the response to empirical antitubercular treatment (ATT) therapy.

RESULTS

Sensitivity and specificity of MR vs. PET-CT in distinguishing benign disease

Of the 24 patients in this series, 14 had tuberculosis (benign disease). MRI, PET-CT, and FNAC were consistent with benign pathology in 10 of 14 patients [Table 1]. The sensitivity/specificity of MRI in diagnosing benign lesions was 78.57%/90%, while the sensitivity/specificity of PET-CT for diagnosing benign lesions was 92.8%/90%, respectively. Furthermore, the specificity for diagnosing benign lesions utilizing both studies together was 100%, but the algorithm was not sensitive [Table 2].

Sensitivity and specificity of MR vs. PET-CT in malignant disease

For 6 of 10 patients with malignant disease, all 3 studies (MRI, PET-CT, and FNAC) were positive for malignancy. Six of these patients had the following malignant lesions with metastases; thyroid malignancy (follicular carcinoma; two patients), prostate adenocarcinoma (three patients), and adenocarcinoma of the lung (one patient). For the remaining four patients, however, the three investigations did not unanimously suggest malignancy; these included three patients with multiple myeloma, and one patient with lymphoma. Two of these four patients were accurately diagnosed by FNAC [Table 1]. The remaining two patients have been described in the FNAC section.

The sensitivity/specificity of MRI in picking up malignant lesions was 90%/78.57% and for PET-CT was 90%/92.8%, respectively. The sensitivity was 100% for diagnosing a malignant lesion with both investigations combined, though it was not specific.

Key Words: Benign, malignant, magnetic resonance imaging, positron emission tomography-computed tomography, vertebral compression collapse
Sensitivity and specificity for FNAC

There were four patients in whom the FNAC was inconclusive. For the two with suspected malignancy on MRI and PET-CT (e.g., PET-CT showed multiple lytic lesions in one, and iliac bone involvement in the other), FNAC biopsies from the clavicle and iliac bone proved malignant. The remaining two patients were suspected of harboring benign lesions; the PET-CT suggested benign disease and showed mediastinal lymph nodes in one patient, while no other site of uptake was demonstrated in the second patient. Of interest, both with suspected benign disease responded to empirical ATT that was successfully monitored utilizing PET-CT (e.g., response to therapy) over 8 months of treatment (e.g., showed resolution of lesion) [Figure 1].

DISCUSSION

The clinical evaluation alone often fails to delineate the etiology of nontraumatic vertebral compression fractures. Unfortunately, even multiple radiological studies combined are not 100% sensitive or specific for distinguishing between benign or malignant disease. This, therefore, still requires subjecting patients to FNAC for establishing a diagnosis, target therapy, and assess the prognosis.

Sensitivity and specificity of MRI in distinguishing benign vs. malignant disease

The sensitivity and specificity of MRI in differentiating benign from malignant lesions have been studied previously. The criteria used by Cho and Chang to diagnose malignant lesions included; the presence of an epidural mass, pedicle enhancement, bulging of the posterior vertebral cortex. The criteria used by William et al. to diagnose benign lesions was preservation of the bone marrow [Table 2]. We combined these criteria (vide supra) to differentiate benign from malignant lesion on MRI.

In our study, MRI alone missed one case of malignancy (out of 10) and misdiagnosed 3 cases of benign disease (out of 14). This was possibly because

Table 1: Summary of results of investigative modalities and comparison with final diagnosis

| Final diagnosis (on FNAC and/or response to therapy) | No. of patients | No. of patients accurately diagnosed on MRI | No. of patients accurately diagnosed on PET-CT | No. of patients accurately diagnosed on FNAC |
|-----------------------------------------------------|----------------|-------------------------------------------|---------------------------------------------|---------------------------------------------|
| Benign                                              | 14             | 11                                        | 13                                          | 12*                                         |
| Malignant                                           | 10             | 9                                         | 9                                           | 8*                                          |

*FNAC from the involved spine in two patients was inconclusive. The diagnosis was finally established by FNAC from other sites as directed by PET-CT; **FNAC in two patients was inconclusive. Both MRI and PET-CT suggested benign lesions. They responded to empirical ATT

Table 2: Literature review and comparison with present study

| Author                | Sensitivity of MRI for malignancy (%) | Sensitivity of PET-CT (%) | Specificity of MRI (%) | Specificity of PET-CT (%) |
|-----------------------|---------------------------------------|--------------------------|------------------------|--------------------------|
| Cho and Chang[2]      | 63.33                                 | 100                      | 82.60                  | 29.41                    |
| Miniam et al.[1]      | Not a part of study                    | 86                       | Not a part of study    | 83                       |
| William et al.[5]     | 88                                    | Not a part of study      | 63.63                  | Not a part of study      |
| Present study         | 90                                    | 90                       | 78.57                  | 92.8                     |

Figure 1: (a) and (b) pretreatment PET-CT images showing increased uptake in the region of upper cervical vertebrae. FNAC was inconclusive. Empirical ATT was started. (c) and (d) posttreatment (8 months after starting ATT) PET-CT images showing normal uptake in the previously diseased region
tuberculosis of the vertebral body may destroy the pedicle and the posterior cortex in absence of a paravertebral collection at times, mimicking malignancy on MRI.

Sensitivity and specificity of fluoro deoxy glucose PET-CT in distinguishing benign vs. malignant disease

FDG PET-CT can be considered as adjunctive method for diagnosing and differentiating malignant from benign vertebral compression fractures. In comparison with MRI, FDG-PET-CT showed slightly higher sensitivity and lower specificity [Table 2]. In our study PET-CT missed one patient in each of the groups. When both the modalities were combined, the specificity for diagnosing a benign lesion was 100%.

A major problem in selecting mean SUV max as the sole criteria for differentiating benign and malignant lesions is that no single cut off can be suggested. According to Laufer et al., the mean SUV values of lesions with active cancer were 7.1 and 2.1 in benign lesions (P <0.02). However, Harkirat et al. reported SUV max values of 21 in tuberculosis. Despite these limitations, PET-CT has multiple advantages. First, whole body screening picks up sites other than the involved spine thereby giving a broader picture of disease. Second, in cases of indeterminate FNAC results, the site of FNAC can be guided by involvement of other more accessible sites such as subcutaneous lymph nodes, other bones, thyroid gland, etc., Finally, in cases where empirical therapy (ATT) is started, the disease progress and response to therapy can be monitored by repeating PET-CT. This has not been mentioned in the literature previously.

CONCLUSION

In conclusion, MRI and PET-CT combined are 100% specific for diagnosing benign lesions. In case either or both of them suggest a malignant tumor, further work up, especially including a tissue diagnosis is warranted for pathological confirmation. PET-CT had the advantage of picking up more accessible lesions for tissue diagnosis vs. lesions found in the spine. Additionally, PET-CT could be utilized to follow response to treatment for benign lesions (e.g., tuberculosis) being empirically treated with ATT. Of note, major limitation of this study was the small sample size.

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