

Routine needle biopsy during vertebral augmentation procedures. Is it necessary?

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Abstract Vertebral augmentation procedures are currently widely performed to treat vertebral compression fractures. The purpose of this study was to determine the frequency of underlying previously unrecognized etiology in a consecutive series of patients undergoing kyphoplasty to treat vertebral compression fractures. A prospective histological evaluation of vertebral body biopsy specimens from presumed osteoporotic vertebral compression fractures were performed in order to identify aforementioned causes. Over a 2-year period, vertebral body biopsies from 154 vertebral levels were performed in 75 patients undergoing kyphoplasty for vertebral compression fractures. All patients received a preoperative workup that included plain

radiographs, MRI, whole body bone scan, and laboratory examinations. Bone specimens were obtained from affected vertebral bodies and submitted for histologic evaluation to identify the prevalence of an underlying cause. All specimens demonstrated fragmented bone with variable amounts of unmineralised bone, signs of bone-remodeling and/or fracture-healing. In 11 patients underlying pathology other than osteoporosis was identified (prostate cancer, 1; pancreatic cancer, 1; colon cancer, 1; breast cancer, 2; multiple myeloma, 3; leukemia, 1; and lung cancer, 2). In all but one patient the results of the biopsy confirmed the diagnosis suspected from the preoperative workup. For the last patient, namely the one with pancreatic cancer, the workup did not identify the origin of the primary tumor, although the patient was considered to have a compression fracture secondary to metastatic disease of unknown origin, the vertebral biopsy suggested the presence of adenocarcinoma which eventually was proven to be pancreatic cancer. In augmentation procedures for vertebral compression fractures, bone biopsy should be reserved for the patients where the preoperative evaluation raises the suspicion of a non-osteoporotic etiology.

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Introduction

Osteoporosis is considered an epidemic of the modern world. It affects approximately 28 million Americans and 5 million Europeans today, and this number is expected to increase in the near future. The most common complication of this problem is vertebral compression fractures (VCFs). Approximately 700,000 VCFs occur in the US each year

and approximately one-third of them are causing chronic pain [1]. In addition to the debilitating symptoms of pain that VCFs can cause, progressive loss of sagittal posture can have a tremendous impact on quality of life [2–10]. New minimal invasive techniques like percutaneous vertebroplasty and percutaneous kyphoplasty proved to be an effective treatment for treating the pain and preventing further collapse at the fracture level [11–16].

Some times VCFs are noted in several illnesses that cause secondary osteoporosis, like systematic lupus erythematosus, Cooley's disease, Paget's disease, metastatic lesions or after corticosteroid use for several times. During most of kyphoplasty procedures biopsy is not performed based on the hypothesis that most of the VF are caused by osteoporosis. The objective of this study was to determine the ability with needle biopsy during kyphoplasty procedure to identify unrecognized causes of vertebral compression fractures other than osteoporosis.

Materials and methods

Seventy-five consecutive patients who underwent kyphoplasty procedures for 154 acute to subacute symptomatic vertebral compression fractures were prospectively enrolled between 2002 and 2005 in our study. Of the 75 patients, 59 were females (78.6%) and 16 were males (21.4%). Mean age was 69 years with a range from 32 to 87 years old. In the 75 patients, 154 biopsy levels included T6 (2), T7 (4), T8 (5), T9 (6), T10 (5), T11 (17), T12 (24), L1 (28), L2 (27), L3 (17), L4 (13), and L5 (6). Thirty patients had a one-level vertebral body biopsy; 20 patients a two-level biopsy; 17 patients a three-level biopsy; seven patients a four-level biopsy; and one patient a five-level biopsy. Of the patients with single-level fractures, 15 had a lumbar fracture and 15 had a thoracic fracture. The fracture ages ranged from 1 to 10 weeks and were either severely disabling or persistently symptomatic, despite conservative treatment. Conservative treatment consisted of activity modification, bracing with different types of corset and medications like nonsteroidal anti-inflammatory drugs and analgesics for at least 1 week. A prospective histological evaluation of biopsy specimens from vertebral compression fractures was performed.

Inclusion criteria were the presence of a vertebral compression fracture, with persistent pain with a grade of >40% in Oswestry disability index (major disability) and ≥40% collapse of the vertebral body. The ODI is a validated disease-specific instrument for assessment of spinal disorders consisting of a 10-item ordinal scale instrument with six response alternatives for each item. The total score ranges from 0 to 100, where 100 is the worst disability. The items are pain intensity, personal care, ability to lift, walk,

sit, stand, sleep, sex life, social behavior, and traveling. For each item, normal function is 0 and worst is 5. The sum of the 10 "items" multiplied by 2 constitutes the ODI (0–100) [17].

Patients who had a hemoglobin level of <10 g/dL, or an erythrocyte sedimentation rate of >30 mm/h had a workup for multiple myeloma, including serum protein electrophoresis and urine protein electrophoresis.

All patients preoperatively were evaluated with anteroposterior and sagittal radiographs, bone scintigraphy and magnetic resonance imaging (MRI).

Two surgeons using identical techniques treated all patients. Most of the patients were elderly with mean age 69 years, most of them being over 75 years, with women over exceeding men (59 women, 16 men), with initial presumptive diagnoses of osteoporotic VCFs. Intraoperative bone biopsy was performed during kyphoplasty as a routine part of the procedure. After the procedure patients were given a soft corset for comfort.

Surgical technique

A radiolucent table and one c-arm fluoroscopy machine were used for every kyphoplasty procedure. For anteroposterior (AP) and lateral projections the c-arm was simultaneously turned above and orthogonally across the radiolucent table. The patients received general anesthesia, turned prone carefully on the table and all bony prominences were padded well. The fractures level was centered in both the anteroposterior and lateral projections before the skin was prepared and the patient draped.

With fluoroscopic guidance bilateral transpedicular in lumbar spine or parapedicular in thoracic spine access to the fractured vertebral body was obtained. A 1-cm incision was made just lateral to both pedicles. A Jamshidi needle (11-gauge Bone Access needle, Kyphon, Sunnyvale, CA) was passed through the incision and docked on the superior lateral border of the pedicle under AP imaging (2 o'clock position for the right side and 10 o'clock position for the left side). The needle is tapped down the pedicle with a mallet to a point just beyond the posterior cortex of the vertebral body. This is confirmed with frequent imaging to verify that the needle does not penetrate the medial wall of the pedicle. The direction of the Jamshidi needle is controlled so that the balloon will be positioned in the fracture. A 2-mm guide pin is passed through the Jamshidi needle. The needle is exchanged for an obturator followed by a working cannula (Osteointroducer, Kyphon), which is advanced to the posterior wall of the vertebral body. A bone biopsy is obtained by inserting and twisting an obturator while applying suction with a syringe. The osseous contents inside the cement administrator is extracted with a cement pusher and tagged accordingly. A

drill is manually twisted in the vertebral body to create a tract for the balloon catheter. The same procedure is repeated on the contralateral side.

Kyphoplasty was performed according to standard practices.

Histologic evaluation

The bone specimens were fixed in B5 solution (sodium acetate and mercury chloride, HgCl_2) for one and a half hours, then were embedded in 70% ethanol for half an hour and finally were decalcified in EDTA solution (disodium salt ethylene diamine tetraacetic acid disodium-TRIS-9 hydroxymethyl aminomethane) for one and a half hours. Then the bone specimens were embedded in 70, 80, 90 and 100% ethanol for 16 h at each concentration and finally rinsed with 100% ethanol.

The cell block preparation was processed in paraffin-embedded blocks and stained by the hematoxylin–eosin technique. Immunohistochemical studies included testing for plasma cell myeloma and lymphoma with the following cell markers CD45, CD3, CD5, CD10, CD20, CD23, Bcl-2 protein, lysozyme, Bcl-6 protein, kappa and lambda chain determinants.

In cases where solid malignancy was suspected ancillary studies, such as studies for AE1/AE3 cytokeratin and tumor markers (Ca 19-9, CEA, PSA, AFP, shown in Table 1) were performed for better tumor origin evaluation.

Slides were rinsed in phosphate-buffered saline (PBS) and primary antibodies were applied. After 1 h incubation at room temperature, the EnVison_® horseradish peroxidase system (Dako, Glostrup, Denmark) was applied. Bound antibodies

were visualized by incubation with diaminobenzidine/ H_2O_2 . Slides were counterstained with haematoxylin.

Results

All vertebral body specimens showed signs of bone-remodeling and/or fracture-healing. Additionally woven bone and cartilaginous tissue representing callus formation were often found. Histological studies identified pathology other than osteoporosis in 11 patients: 3 patients were diagnosed with myeloma (11 fractures), 1 patient with leukemia, and 7 patients with metastatic lesions and specifically 1 from prostate cancer, 1 from colon cancer, 2 from breast cancer (Fig. 1), 2 from lung cancer and 1 from pancreatic cancer. The remaining patients had osteoporotic fractures based on negative biopsies.

All specimens showed partially necrotic fragments of bone as well as area of fibrosis. Isolated areas of necrotic bone associated with viable bone and granulation tissue suggest that the necrosis was related to prior fracture. Some haematopoietic spaces were also seen along with woven bone and cartilaginous tissue showing features of fracture callus formation. In many of the same specimens, different stages of fracture-healing were present. Hemorrhage and fibrin deposition were present in three cases, suggesting the acute phase of fractures. In the same cases foci of either acute or chronic inflammation were present, presumably related to a recent fracture. A few specimens also contained fibrocartilage, presumably of intervertebral disc origin.

In the three patients with multiple myeloma the biopsies provided definite diagnoses of plasma cell dyscrasia. In two of these patients preoperative blood tests and serum electrophoresis had provided evidence of monoclonal cell population. In addition, in all three of them radiographic

Table 1 Antibodies used for immunohistochemical stains

Antibody	Source	Dilution
CD20 L26	Dako/Carpenteria	1:1,000
CD10	Novocastra	1:20
Bcl-6	Novocastra	1:20
Bcl-2	Dako/Carpenteria	1:160
CD45	Dako/Carpenteria	1:400
CD3	Dako/Carpenteria	1:200
CD5	Novocastra	1:60
CD23	Novocastra	1:20
Kappa, lambda	Dako/Carpenteria	1:16,000
Lysozyme	Dako/Carpenteria	1:1,500
AE1/AE3 keratin	Dako/Carpenteria	1:100
Ca19-9	Zymed	1:150
CEA(p)	Dako/Carpenteria	1:4,000
PSA	Dako/Carpenteria	1:200
AFP	Dako/Carpenteria	1:200

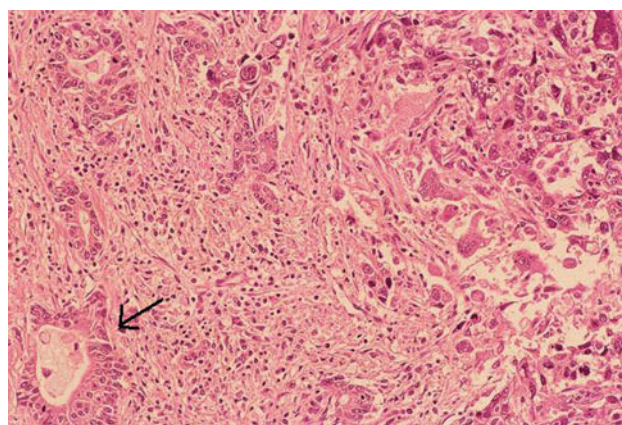


Fig. 1 Bone biopsy from a patient with metastatic ductal breast carcinoma with duct-like structures of tumor cells (arrow) (haematoxyline & eosin $\times 10$)

studies and MRI findings of the vertebral lesions were indicative of multiple myeloma.

In the patients with metastatic lesions with the exception of one, the preoperative workup had indicated a primary malignancy, which turned out to be the cause of the vertebral metastasis and resulting compression fracture. Only in one patient with ascites, lower limb radiculopathy and a lumbar fracture, who was being evaluated for identification for possible malignancy, histologic evaluation during kyphoplasty demonstrated tumor cells in cavities in between new bone trabeculae, consistent with a well differentiated adenocarcinoma with features resembling pancreatic cancer. The diagnosis of pancreatic cancer was then confirmed and the patient was referred for further oncologic tests. The extra cost added by the performance of bone biopsy was calculated to be 44 ± 24 Euros per patient in our public hospital.

Discussion

Minimally invasive methods of treating the symptoms of spinal compression fractures have attracted the attention and interest of both surgeons and patients over the past two decades.

Vertebroplasty and kyphoplasty are nowadays widely performed to treat low-energy vertebral compression fractures [2, 10, 11, 26–28]. However, it is important to distinguish the pain caused by a fracture from other causes of back pain. Patients requiring a percutaneous cement augmentation procedure are usually very fragile with multiple medical co-morbid factors [3, 4, 7, 9, 18–21]. Thus, the differential diagnosis should include not only osteoporosis, but also malignant tumor, benign tumor endocrinopathy, autoimmune disease, blood dyscrasias, and infection [1, 22, 23].

Osteolytic destruction of the vertebral bodies secondary to metastatic disease or multiple myeloma affects up to 70% of patients with these diseases [22, 23]. It is sometimes very difficult to determine whether the vertebral collapse is caused by osteoporosis or tumor metastasis when other blood tests and tumor markers are negative. Moreover, new spinal lesions in patients with known systemic malignancies may not always represent metastases or late recurrences of the established primary neoplasm. In addition, occult malignancy may be first detected in the spine. In up to 20% of symptomatic patients, lesions in the spine represent the first manifestation of cancer [23].

The nature of underlying pathology related to vertebral collapse is important regarding prognosis, assessing response to therapy, and long-term patient care. History, physical examination, and diagnostic imaging are standard for the evaluation of osteoporosis [3–5].

Bone scintigraphy provides useful information about bone turnover and thereby identifies any vertebral fracture

that has an ongoing healing process. Bone scans are sensitive for the detection of fractures but have low specificity for the diagnosis of underlying disease [25]. Magnetic resonance imaging of the spine is probably the single most useful test for determining fracture age, ruling out a malignant tumor and selecting the appropriate treatment [9, 10]. A limited number of simple blood tests are sufficient to discriminate most secondary forms of osteoporosis, but bone biopsies are necessary in cases when other findings are unclear or inconsistent [1, 24, 25].

Togawa et al. [24] recently performed a histological evaluation of 178 biopsy specimens obtained from 142 patients during 246 kyphoplasty procedures for presumed osteoporotic vertebral compression fractures. The biopsy specimens obtained from 30 patients (21%) were suggestive of osteomalacia, and one patient was diagnosed as having an unsuspected plasma cell dyscrasia. In addition, plasma cell dyscrasia was confirmed histologically in three patients. On the basis of these findings, the authors recommended that a vertebral body biopsy should be performed during each first-time vertebral augmentation procedure.

Shindle et al. [25] in a series of 238 patients after kyphoplasty and bone biopsy of the vertebral body biopsy specimen and iliac crest aspirate obtained from three patients showed hypercellularity with collections of lymphocytes and all three patients were diagnosed as having low-grade B cell lymphomas and were referred to specialists in hematology-oncology.

In our study, although there was relatively high number of vertebral fractures caused by an etiology other than osteoporosis, in all but one the final diagnosis was suspected by the preoperative laboratory and radiological workup and the bone biopsy only confirmed that suspicion. The one patient where the final diagnosis was not suspected (pancreatic adenocarcinoma), there was already high clinical suspicion of malignancy and the patient was being evaluated in that direction. Although the extra cost of performing the biopsy is relatively small in a public hospital in Greece, yet it is an extra cost which could be avoided in patients without suspicion of malignancy. The treating physician performing the augmentation procedures needs to identify the patients with prior suspicion of malignancy in order to avoid a missed diagnosis. Bone biopsy should be reserved only for the patients where the preoperative evaluation raises the suspicion of an etiology other than osteoporosis and should not be performed routinely.

Conclusion

In augmentation procedures for vertebral compression fractures, bone biopsy should be reserved for the patients

where the preoperative evaluation raises the suspicion of a non-osteoporotic etiology.

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