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Phase I/II clinical study of percutaneous vertebroplasty (PVP) as palliation for painful malignant vertebral compression fractures (PMVCF): JIVROSG-0202

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Background: The safety and efficacy of percutaneous vertebroplasty (PVP), a new treatment modality for painful malignant vertebral compression fractures (PMVCF) using interventional radiology techniques, were evaluated prospectively.
Materials and methods: After confirming the absence of safety issues in phase 1, a total of 33 cases were registered up to and including phase 2. Safety and efficacy were evaluated by National Cancer Institute—Common Toxicity Criteria version 2 and Visual Analogue Scale (VAS) at 1 week after PVP. Based on VAS score decreases, efficacy was classified into significantly effective (SE; ≥5 or reached 0–2), moderately effective (ME; 2–4), or ineffective (NE; <2 or increase).
Results: Procedures were completed in all 33 patients (42 vertebrae). Thirty days after PVP, two patients died of primary disease progression, but no major adverse reactions (>grade 2) were observed. Response rate was 70% (95% confidence interval 54% to 83%) [61% (n = 20) with SE, 9% (n = 3) with ME, and 30% (n = 10) with NE] and increased to 83% at week 4. Median time to response was 1 day (mean 2.4). Median pain-mitigated survival period was 73 days.
Conclusion: For PMVCF, PVP is a safe and effective treatment modality with immediate onset of action.
Key words: percutaneous vertebroplasty, interventional radiology, pain relief, vertebral metastasis, percutaneous cement plasty

introduction

The pain relief of painful malignant vertebral compression fractures (PMVCF) is one of the key elements for achieving better quality of life in patients under palliative care. The mainstay for pain relief is pharmacological therapy such as with nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids, and if patients are not responsive to these agents or have pain upon body movement, radiotherapy is administered. However, despite being a noninvasive therapeutic modality, radiotherapy is less than ideal because it requires 2–4 weeks to obtain a therapeutic effect and does not achieve complete pain relief in most cases [1, 2].

Since the report of percutaneous vertebroplasty (PVP) by Galibert et al. [3], in 1987, the technique has been widely reported [4–10]. These reports indicate that it is highly effective for prompt pain relief for metastatic vertebral tumors from any primary sites. On the other hand, severe, albeit rare, complications such as pulmonary embolism, cerebral infarction, cardiogenic shock, and spinal cord injury due to leakage of cement into the spinal canal have also been documented [11–13]. All these reports, however, have been retrospective in nature, and to our knowledge, no study has yet prospectively investigated the safety and therapeutic effect of this modality. Although it cannot be excluded that severe complications may very rarely occur, to minimize the frequency of reported complications, it is important to evaluate in a prospective study whether this procedure can be carried out safely when conducted by trained interventional radiologists for clearly defined indications.

Therefore, we undertook a phase I/II multi-institutional prospective study of PVP as Japan Interventional Radiology in Oncology Study Group (JIVROSG)-0202. In this study, we evaluated the safety and efficacy of PVP as a palliative intervention for patients with PMVCF.

materials and methods

patient selection

Patients were required to have an imaging [including radiography and computed tomography (CT)] diagnosis of changes in the thoracic or

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lumbar vertebrae caused by malignant tumor metastases or multiple myeloma, limitation of daily activities due to pain from the lesions and/or the risk of compression fracture, and no exposure of the vertebral tumors to the vertebral canal (defined as vertebral canal surface showing no tumor invasion on CT or magnetic resonance imaging). In addition, the patients had to have an Eastern Cooperative Oncology Group performance status (PS) of zero to three, preserved major organ function (bone marrow, heart, liver, lung, and kidney), and an anticipated survival of at least 4 weeks. Patients were excluded if their pain grade of Visual Analogue Scale (VAS) [14] was ≤2, they could not maintain the position needed for treatment, they had a bleeding tendency with bleeding time ≥5 min, fever ≥38°C, cardiac failure requiring continuous drug therapy, history of major drug allergy such as anaphylactic shock to any drugs, so as to minimize the possibility of cardiac toxicity due to the bone cement preparation, and/or confirmed or possible pregnancy. In addition, patients were judged ineligible for this trial if the vertebral lesions harbored possible active inflammation (tuberculous or other infectious), if marked vertebral flattening was present (defined as the height of the affected vertebral body showing a mean value of one-third of that of the superior and inferior vertebral bodies), if five or more continuous vertebrae were affected precluding evaluation of the therapeutic effect or if in a single session four or more vertebrae required therapy.

Both the ethics committee of the Japanese Society of Interventional Radiology and each institutional review board approved the protocol of this study before patient entry. All patients provided written informed consent.

collaborative institutions

This study was conducted in 10 institutions comprising JIVROSG. Each of these institutions has at least one full-time interventional radiologist certified by the Japanese Society of Interventional Radiology (Table 1).

study end points

The primary end point of this study was to evaluate the safety of PVP, and the secondary end point was to evaluate the efficacy of PVP for pain relief as well as the incidence and grade of adverse events.

study design

This study was a multi-institutional, single-arm, open-label, noncomparative trial. The phase I part of this trial was conducted using the 3 × 3 method proposed by the JIVROSG. This method was applied as follows. To be able to quickly terminate the study if the incidence of adverse events associated with this modality exceeded one-third of the patients, three separate groups with three cases each were enrolled at 4-week intervals. If severe adverse events of the first group with three cases, according to the National Cancer Institute—Common Toxicity Criteria (NCI-CTC) version 2.0 [15] or equivalent adverse events, were limited to one or less of the first three cases, then the second group with three cases was added. When the number of adverse events in the combined first and second groups with six cases was two or less, then the third group with three cases was added. If the number of adverse events of the total nine cases of all three groups was three or less, then subsequently all cases up to the target number were enrolled without distinguishing them into three different groups. If the incidence of adverse events in each of the first, second and third groups exceeded the above-noted permissible limits, the advisability of trial continuation or possible termination was rediscussed.

Table 1. Collaborative institutions

National Cancer Center Hospital
Kyoto First Red Cross Hospital
St Marianna University
Ibaraki Prefectural Central Hospital
Kansai Medical University
Iwate Medical University
Kanazawa University
Shinshu University
Aichi Cancer Center
Tochigi Cancer Center Hospital

In the phase II part of this study, 24 cases were enrolled. Since the treatment administered in phases 1 and 2 was exactly the same, the primary and secondary end points of the cases registered in phase 1 were evaluated together with those of the cases of phase 2. So, the primary and secondary end points were evaluated in all 33 cases.

The observation period for adverse events was defined as the 1-month period following the completion of the procedure. Subsequently, the presence/absence of pain recurrence at the treated site, the period of pain relief (absence of recurrent pain at the treated site from before therapy to obtaining a decrease of VAS score to ≤2), and patient survival period were investigated. In the follow-up investigation, recurrence was defined as occurring on the day on which pain worse than that before therapy was noted, with the period up to this day defined as the pain-mitigated survival period.

statistical analysis

In the phase I part of this study, a cohort size of nine patients was considered to make it possible to quickly terminate the study if the incidence of adverse events associated with this modality exceeded one-third. During phase I through phase II, the study was designed to detect adverse events having an incidence of at least 10%, setting 80% power, 10% predicted rate, and 30% unacceptable rate. We anticipated a protocol dropout rate of 10%. Thus, the target accrual number of patients was calculated to be 33. All enrolled patients were included for the intention-to-treat analyses.

registration of cases

The registration period extended from February 2003 until May 2006. To enter a patient into the study, the investigator had to log on to a restricted Web site using the JIVROSG data center, enter patient indication/contraindication data, and register the case. After the executive office verified the suitability of the entered data and the presence/absence of any missing items, a registration number specific to that patient was issued and the case registration procedure completed. Subsequently, all communications were limited to these issued patient registration numbers. PVP was commenced within 1 week of this patient registration.

interventional procedures of PVP

The interventional procedures of PVP in this study were conducted as follows. After injection of 0.5 mg atropine sulfate and securing a venous access, the patient was placed prone on the table used for fluoroscopy or CT fluoroscopy, and an electrocardiogram apparatus and blood pressure monitor were attached. Following disinfection of the puncture site and injection of local anesthesia, an 11–14 ga metallic needle was inserted up to the site where the bone cement was to be injected under fluoroscopic or CT-fluoroscopic guidance (Figure 1A). Acrylic bone cement was prepared, and the use of bone cement mixed with up to 30% bactericidal barium was recommended if bone cement was injected under fluoroscopic guidance (Figure 1B). The injection was stopped when sufficient bone cement was judged to have been distributed, after which the needle was withdrawn (Figure 1C). When multiple (up to three) vertebrae were to be treated, these steps were repeated for each vertebra. The patient was kept at bed rest for 2 h after the procedure.

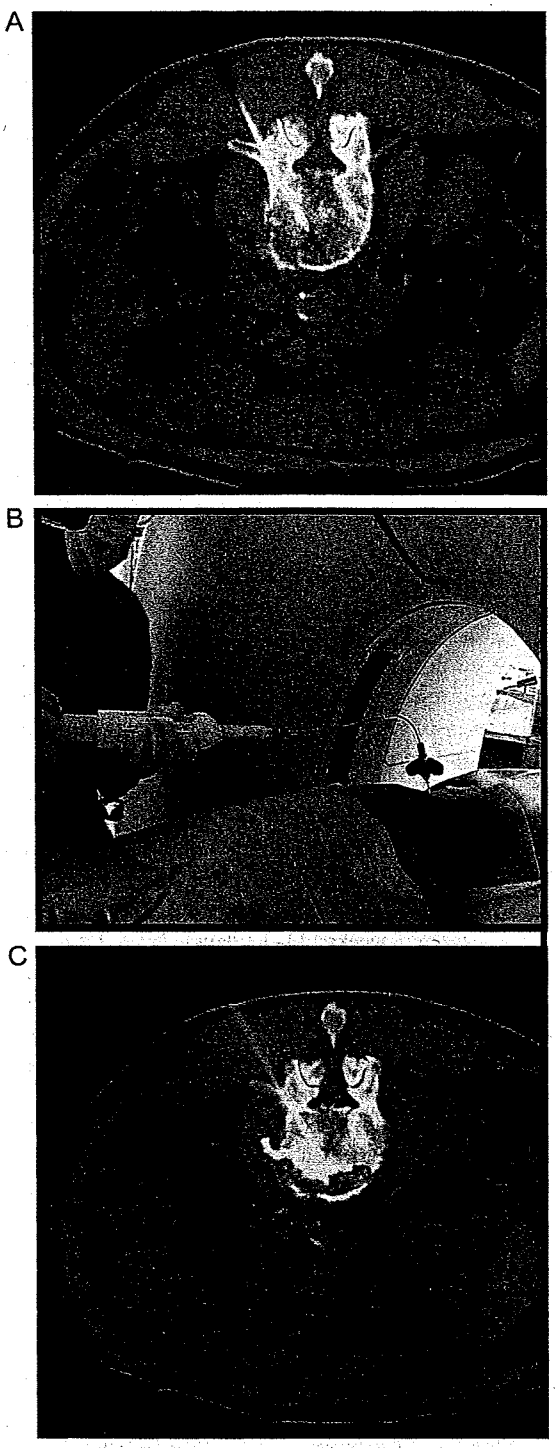

Figure 1. Interventional procedure of percutaneous vertebroplasty. (**A**) Insertion of 11–14 ga bone biopsy needle into the target vertebral bone through pedicle under fluoroscopic or computed tomography (CT)-fluoroscopic guidance. (**B**) Injection of acrylic bone cement under fluoroscopy or CT fluoroscopy monitoring. (**C**) Stop of the injection when adequate distribution is obtained.

combined and supportive therapies

To prevent possible infection, it is recommended that antibiotics be administered for 3 days following the procedure and that an anesthesiologist or other physician able to undertake emergency measures be present. Continued administration of any radiotherapy or analgesics, chemotherapy, and nerve block therapy used before therapy was permitted, including the wearing of corsets. With the exception of management of adverse events, surgical intervention for post-therapy pain, admixture of anticancer agents and/or antibiotics with the acrylic bone cement, and PVP using general anesthesia were not permitted.

observation items

The imaging findings including those of radiography and CT of the primary site and target vertebrae and compression grade were evaluated before therapy and at around 7 days after therapy. VAS score was determined at days 1, 3, and 7 and weeks 2 and 4. Also, before and after therapy, the patient items were evaluated at the specified times.

evaluation methods

The adverse events were evaluated by NCI-CTC version 2. The grade of pain was evaluated by the VAS. VAS scoring was done by having the patient himself note his degree of pain on a 10-cm long horizontal straight line. The efficacy of therapy was evaluated by changes in the VAS score noted 1 week after therapy. When the VAS score was ≤2 or when compared with before therapy a decrease of ≥5 was obtained, the therapy was judged to be significantly effective (SE). When the VAS score did not reach ≤2 but when compared with before therapy showed a decrease to <5 to ≥2, the therapy was judged to be moderately effective (ME). When despite therapy the VAS score decreased by <2 or showed an increase, the therapy was judged to be ineffective (NE). The efficacy of the therapeutic results was assessed by the proportion of the total cases achieving SE or ME. Regardless of any changes in the VAS score, the therapy was also judged to be NE if the need for analgesics increased as compared with before therapy. However, to investigate the timing of the pain-mitigating effect, VAS score was determined within 1 week before the start of therapy, the day after, 3 days after, and at 1, 2, 3, and 4 weeks.

In cases with painful bone metastases at multiple sites, treatment was permitted for all sites with indications for PVP at multiple sessions. However, one treatment session was limited to a maximum of three vertebrae. When all treatment sessions were finished, the degree of back pain was comprehensively evaluated by VAS.

results

There were no reports of severe adverse event in any of the nine cases enrolled in phase I. Thus, without any interruption the transition was made to phase II. There were a total of 33 cases from 10 institutions, comprising 16 males and 17 females with a mean age of 62 years (37–87 years) (Table 2). PS was zero in one case, one in seven cases, two in 12 cases, and three in 13 cases. Thirty cases had metastatic vertebral tumors, originating from lung, breast, and colon cancer in seven cases each, liver cancer in four cases, pancreas cancer in two cases, and tongue, esophagus, and skin cancer in one case each. The only primary vertebral tumor was multiple myeloma, which was present in three cases. Analgesics administered before therapy were NSAIDs alone in nine cases, opioids alone in 10, and both in 11. Radiotherapy was administered to the treated site in 11 cases. The mean interval between the two therapies was 46 days, and no pain-mitigating effect was obtained.

Forty-two vertebrae were targeted: 18 thoracic vertebrae (I, one; VII, three; VIII, three; IX, four; X, two; XI, two; and XII, three) and 24 lumbar vertebrae (I, one; II, seven; III, seven; IV, seven; and V, two). Changes in imaging findings at the treated sites comprised osteolytic changes in 35 vertebrae, mixed

changes in five vertebrae, and osteoblastic changes in two vertebrae, with the mean compression rate amounting to 75.8% (41%–106%). Three vertebral bodies, two vertebral bodies, and one vertebral body were treated in two, five, and 26 cases, respectively. In only a single case was the treatment divided into two sessions, being completed in a single session in all the other cases.

Table 2. Background of enrolled cases

Patient characteristics	
No. of patients	33[a]
Male	16
Female	17
Mean age, years	62 (37–87)
Primary disease	
Lung cancer	7
Breast cancer	7
Colorectal cancer	7
Liver cancer	4
Myeloma	3
Pancreatic cancer	2
Tongue cancer	1
Esophageal cancer	1
Skin cancer	1
Preradiotherapy to the target lesion	11 (mean interval 46 days)
Combined chemotherapy	16
Administered analgesics before therapy	
NSAIDs alone	9
Opioids alone	10
NSAIDs and opioids	11
Performance status (ECOG)	
0	1
1	7
2	12
3	13
Target VB ($N = 42$)	
1 VB	26
2 VBs	5
3 VBs	2
Thoracic VB ($N = 18$)	
I	1
VII	3
VIII	3
IX	4
X	2
XI	2
XII	3
Lumbar VB ($N = 24$)	
I	1
II	7
III	7
IV	7
V	2
Appearance of lesion	
Osteolytic	28 (35 VBs)
Mixed	3 (5 VBs)
Osteoblastic	2 (2 VBs)
Compression rate (height of target VB/height of next VB)	
Mean	75.8% (41%–106%)

[a]Nine for phase I and 24 for phase II.
NSAIDs, nonsteroidal anti-inflammatory drugs; ECOG, Eastern Cooperative Oncology Group; VB, vertebral bone.

CT fluoroscopy was used in 15 cases, fluoroscopy in 15, and a combination of the two in three. The mean time required per case and per vertebra was 49 min (20–120 min) and 39 min, respectively. The volume of bone cement administered was 1–8 ml [mean 3.5 ml, standard deviation (SD) 1.8 ml]. The bone cement preparations used were Osteobond (Zimmer, IN) in 22 cases, Simplex (Stryker, MI) in 10, and Bone Cement (Zimmer) in one. The recommended antibiotics were used in 19 of 33 cases (58%). The technical success rate was 100%, and in no cases were the interventional procedures provided by the protocol terminated prematurely.

In the evaluation of safety, adverse events during the therapy were limited to bleeding from the puncture site in a single case (3%), in which the bleeding was stopped with 5-min manual pressure. Adverse events of grade 3 or 4 of NCI-CTC version 2 or other correspondingly severe adverse events related to PVP were not observed, while two patient deaths caused by the progression of primary disease were observed within 30 days of PVP. An adverse event of PVP could not be excluded in only a single case (3%) with grade 2 serum hypoalbuminemia.

In the evaluation of clinical efficacy, the response rate was 70% (95% confidence interval 54% to 83%), being SE in 20 cases (61%) and ME in three (9%). The mean time to response was 2.4 days (median 1 day, SD 3.2 days). VAS score was 6.2 + 2.1 within 1 week before the start of therapy, 3.6 + 2.6 the day after, 2.5 + 2.6 after 3 days, and 2.4 + 2.3 at 1 week (5–8 days), 2.3 + 2.7 at 2 weeks (11–15 days), 2.0 + 2.2 at 3 weeks (15–26 days), and 1.8 + 2.3 at 4 weeks (26–29 days) (Figure 2).

Pain recurrence at the treated site was noted in 5 of 23 (22%) of the SE or ME cases. On the other hand, in 4 of the 10 cases (40%) in which the therapy was evaluated as ineffective in the first week, the result was subsequently judged to be ME. At 4 months after completion of enrollment, 14 patients were alive, 18 had died, and the survival status of one was unknown. The median survival period was 194 days (mean 270 days, SD 240

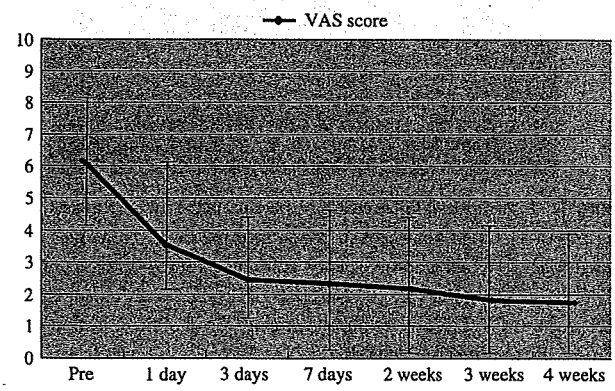

Figure 2. Changes in Visual Analogue Scale (VAS) score. The changes in the VAS values at the various observation time points are listed here. The curve shows the changes in mean values and the vertical line the standard deviation. Pain relief from the therapy is obtained by the third day, with a slow decrease in the VAS values also subsequently observed.

days). The median pain-mitigated survival period was 73 days (mean 230 days, SD 258 days).

discussion

The treatment of painful vertebral metastases and other conditions affecting vertebral bone remains a major challenge in patients under palliative care. Numerous studies have already validated the efficacy and safety of PVP in this context [4–7, 11]. However, all these were retrospective in nature, and no such prospective studies have yet been described. This prompted JIVROSG to undertake the present study to objectively evaluate this procedure by prospectively assessing its safety and clinical efficacy in a multi-institutional setting.

Regarding safety, we attributed the absence of severe complications in the present study to the strict patient selection criteria adopted by us, namely, the exclusion of cases with cardiac failure, a history of drug allergy, and tumors exposed within the vertebral canal, as well as the use of a highly precise fluoroscopy or CT fluoroscopy apparatus at the time of therapy, and the use during fluoroscopy of bone cement mixed with up to 30% bactericidal barium so as to facilitate the immediate recognition of extravertebral leakage. These results indicate that PVP is an extremely safe therapeutic intervention, provided that appropriate patient selection and apparatus use are adhered to, when carried out by an interventional radiology specialist.

In this study, pain was evaluated at 1 week after therapy, with an efficacy rate of 70% obtained, comparable to previously reported results of 70%–90% in the literature [4, 7, 10, 11]. However, most importantly, the therapeutic effect was apparent at a median 1 day (mean 2.4 days, SD 3.2 days), demonstrating a rapid pain-relieving effect. In contrast, the therapeutic response to the hitherto standard pain relief therapeutic modality used, namely, 10 sessions of radiotherapy at 3 Gy, has been reported to require 2–4 weeks to take effect [1, 2]. In this respect, thus, the rapidity of onset of the desired effect of PVP is clearly superior to that of radiotherapy. The median survival period of the enrolled cases was 194 days because ≥90 of them had bone metastases from malignant tumors and had a poor prognosis. In view of this fact, the selection of a therapeutic modality providing a prompt onset of pain relief becomes especially important. In contrast, in cases with vertebral body metastases highly sensitive to radiotherapy and/or with an anticipated long survival period, radiotherapy is the preferred option.

Recurrence of pain at the treated site was noted in 21% of cases. Since this therapy is not designed to exert an antitumor effect but rather to provide pain relief by strengthening weakened vertebrae, pain recurrence is unavoidable if the metastatic foci expand. The lack of a response in six patients was attributed to their poor general state. The present results based on a prospective study demonstrate that PVP can be carried out safely and shows marked efficacy, in particular fast-acting pain relief, provided that patient and equipment selection is appropriate and that an experienced physician is available. Since PVP is a therapeutic technique, its safety cannot be evaluated like that of a phase I trial for drugs in which drug doses are increased incrementally to determine the optimal doses to be administered. Therefore, in the present study, we adopted a modified design of phase I study for drugs. However, the number of cases in our study is not enough to confirm the safety of PVP. Additionally, the results of this study are insufficient to establish PVP as a standard therapy for patients with painful malignant vertebral body tumors. Thus, we are planning to conduct a phase III study comparing PVP and conventional treatments in this context.

conclusion

PVP was proved safe, clinically efficacious, and fast acting in this prospective study. Future studies enrolling larger groups of patients will be needed to further establish its role in the management of painful bone lesions as palliative care.

acknowledgements

This study is the first prospective one to evaluate the safety and efficacy of PVP as palliative care for end-stage cancer patients. The authors have received no funds related to this study and are aware of no conflict of interest. A part of this study was shown as a poster presentation at the meeting of the American Society of Clinical Oncology, Chicago 2007.

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Discordance between core needle biopsy (CNB) and excisional biopsy (EB) for estrogen receptor (ER), progesterone receptor (PgR) and HER2 status in early breast cancer (EBC)

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Background: Analysis of estrogen receptor (ER), progesterone receptor (PgR) and HER2 status in early breast cancer (EBC) is increasingly being conducted in core needle biopsies (CNBs) taken at diagnosis but the concordance with the excisional biopsy (EB) is poorly documented.

Patients and methods: Patients with EBC presenting to The Royal Marsden Hospital from June 2005 to September 2007 who had CNB and subsequent EB were included. ER and PgR were determined by immunohistochemistry (IHC) and graded from 0 to 8 (Allred score). HER2 was determined by IHC and scored from 0 to 3+. FISH analysis was carried out in HER2 2+ cases and in discordant cases.

Results: In all, 336 pairs of samples were compared. ER was positive in 253 CNBs (75%) for 255 EBs (76%) and was discordant in six patients (1.8%). PgR was positive in 221 CNBs (66%) and 227 (67.6%) EBs being discordant in 52 cases (15%). HER2 was positive in 41 (12.4%) of the 331 CNBs in which it was determined compared with 44 (13.3%) EBs and discordant in four cases (1.2%).

Conclusions: CNB can be used with confidence for ER and HER2 determination. For PgR, due to a substantial discordance between CNB and EB, results from CNB should be used with caution.

Key words: core needle biopsy, early breast cancer, estrogen receptor, HER2, progesterone receptor

introduction

Breast cancer is the most frequently diagnosed neoplasm among women in the United States and Western countries and is the second leading cause of cancer death among women [1]. Although it continues to be an important cause of cancer morbidity and mortality, the death rates have drastically decreased due to earlier detection and more effective treatment. Over recent years, the role of core needle biopsy (CNB) has become well established as an important diagnostic tool for both palpable and nonpalpable breast lesions and it is considered the method of choice for tissue sampling as part of the triple assessment of breast disease [2, 3]. The accuracy of the CNB for the diagnosis of breast carcinoma has been extensively studied and good concordance rate has been reported between CNB and excisional biopsy (EB) for diagnosis of breast carcinoma (91%–100%) with a specificity rate ranging from 96% to 100% [4, 5].

In addition to the histopathological diagnosis, there is a growing demand for prognostic information and in particular the determination of estrogen receptor (ER), progesterone receptor (PgR) and HER2 for treatment planning. In situations where neoadjuvant therapy is used, such information is often needed for selection of therapy and maybe the only tissue available for consideration of postsurgical care, e.g. in cases achieving a pathological complete response with treatment. Even in the presence of residual disease, there is also the concern of changes in the tumour profile due to treatment effect [6]

The status of ER, PgR and HER2 is critical in the management of patients with invasive breast carcinoma [7]. ER is a powerful predictive factor for response to endocrine treatment and long-term outcome. Similarly, HER2 overexpression has been associated with worse prognosis in patients with newly diagnosed breast carcinoma, is a determinant of response to trastuzumab and a possible marker of resistance to certain endocrine and chemotherapy treatments [8–10].

Due to the possible heterogeneous distribution of the antigens within the tumour, CNB may not accurately reflect the

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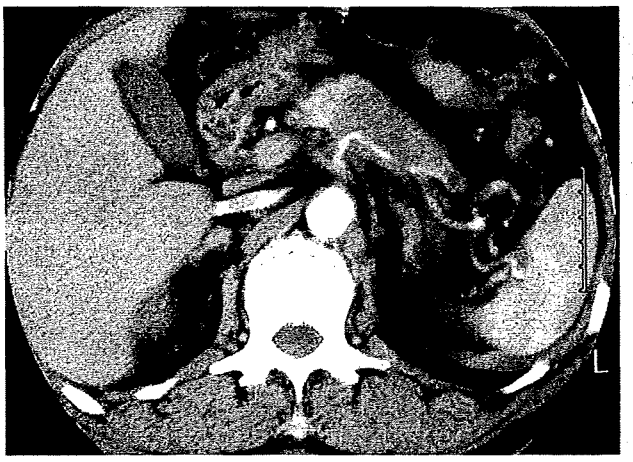
Ruptured pseudoaneurysm of the splenic artery complicating endoscopic ultrasound-guided fine-needle aspiration biopsy for pancreatic cancer

Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is a safe procedure, although major complications do rarely occur. Pseudoaneurysm rupture is an emergency that can cause life-threatening hemorrhage. An exceedingly rare case of ruptured pseudoaneurysm of the splenic artery following EUS-FNA is described.

A 62-year-old man was referred for investigation of a pancreatic tumor. On abdominal computed tomography (CT), a low-density area was seen running from the pancreatic body, involving the celiac and splenic arteries (**Fig. 1**). Angiography showed encasement of the splenic artery (**Fig. 2**). Therefore, EUS-FNA was performed with two separate passes into the lesion using a 22-gauge needle. Cytological analysis showed a pancreatic adenocarcinoma. Nineteen days later abdominal CT showed a pseudocyst in the pancreatic body and tail (**Fig. 3**), and 30 days later (i.e., 30 days after EUS-FNA) the patient developed hematemesis and hemorrhagic shock. Upper gastrointestinal endoscopy showed a hemorrhagic gastric ulcer in the posterior wall of the middle body (**Fig. 4**). Since endoscopic treatment was unsuccessful, angiography was performed and showed a pseudoaneurysm of the splenic artery. Coil embolization was performed in and around the pseudoaneurysm. After 7 days the pancreatic pseudocyst had narrowed (**Fig. 5**); there was no further recurrence.

The overall complication rate of EUS-FNA is 1%–2% [1]. The major complications are postaspiration infection in cystic lesions, bleeding, pancreatitis, and cervical and duodenal perforation [2]. Three different mechanisms are recognized as causing pseudoaneurysm formation [3], but all are called pseudoaneurysm because the end result is a cystic vascular structure surrounded by a fibrous wall. Pseudoaneurysms can rupture into the peritoneal cavity, retroperitoneum, gastrointestinal tract, biliary tract, and pancreatic duct. The most common vessel involved is the splenic artery as it runs along the pancreatic bed before reaching the spleen [4]. To our knowledge, this is the



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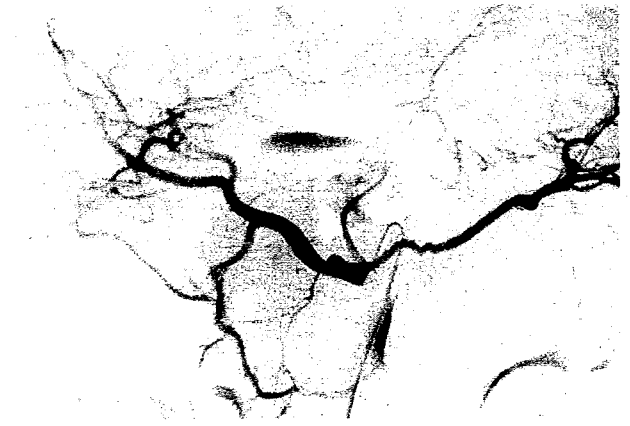

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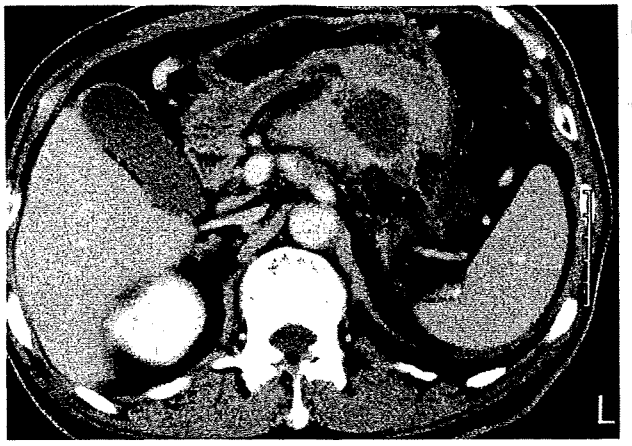

Fig. 3 Abdominal CT 19 days later showed a pseudocyst in the pancreatic body and tail.

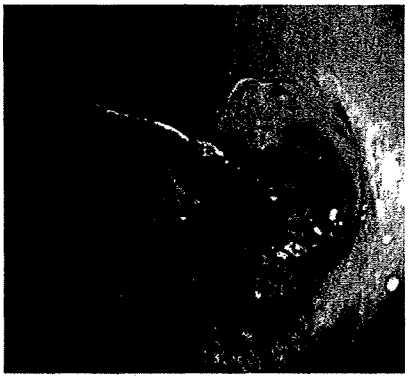

Fig. 4 Upper gastrointestinal endoscopy showed a hemorrhagic gastric ulcer in the posterior wall of the middle body.

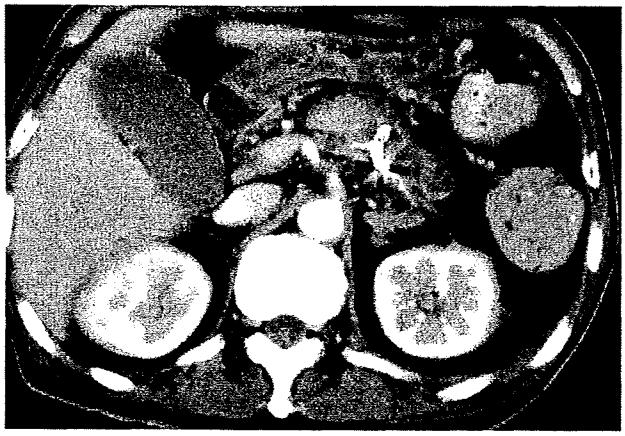

Fig. 5 Coil embolization in and around the pseudoaneurysm was performed, and 7 days later the pancreatic pseudocyst had narrowed.

first case report of a ruptured pseudoaneurysm of the splenic artery complicating EUS-FNA.

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Ruptured pseudoaneurysm of the splenic artery complicating endoscopic ultrasound-guided fine-needle aspiration biopsy for pancreatic cancer

Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is a safe procedure, although major complications do rarely occur. Pseudoaneurysm rupture is an emergency that can cause life-threatening hemorrhage. An exceedingly rare case of ruptured pseudoaneurysm of the splenic artery following EUS-FNA is described.

A 62-year-old man was referred for investigation of a pancreatic tumor. On abdominal computed tomography (CT), a low-density area was seen running from the pancreatic body, involving the celiac and splenic arteries (**Fig. 1**). Angiography showed encasement of the splenic artery (**Fig. 2**). Therefore, EUS-FNA was performed with two separate passes into the lesion using a 22-gauge needle. Cytological analysis showed a pancreatic adenocarcinoma. Nineteen days later abdominal CT showed a pseudocyst in the pancreatic body and tail (**Fig. 3**), and 30 days later (i.e., 30 days after EUS-FNA) the patient developed hematemesis and hemorrhagic shock. Upper gastrointestinal endoscopy showed a hemorrhagic gastric ulcer in the posterior wall of the middle body (**Fig. 4**). Since endoscopic treatment was unsuccessful, angiography was performed and showed a pseudoaneurysm of the splenic artery. Coil embolization was performed in and around the pseudoaneurysm. After 7 days the pancreatic pseudocyst had narrowed (**Fig. 5**); there was no further recurrence.

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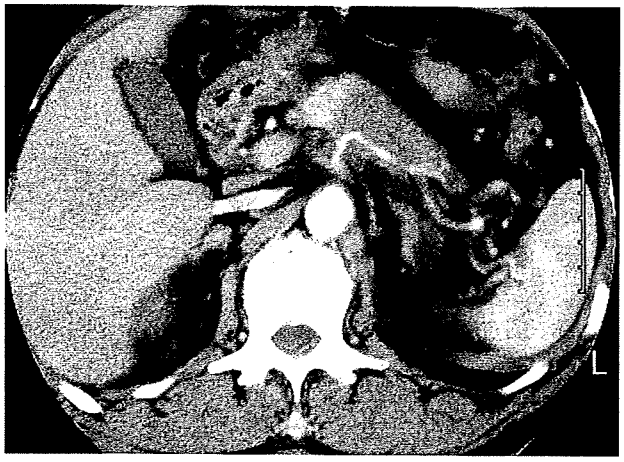

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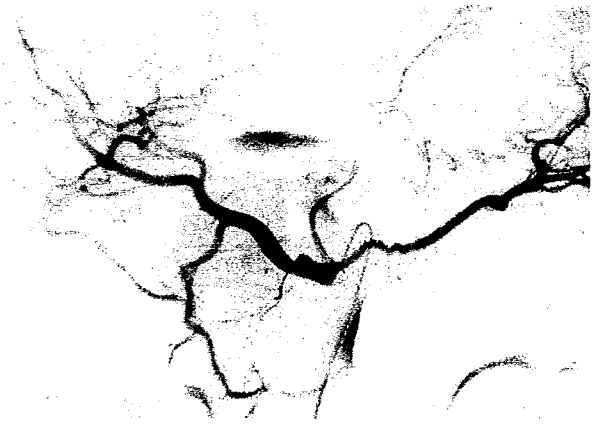

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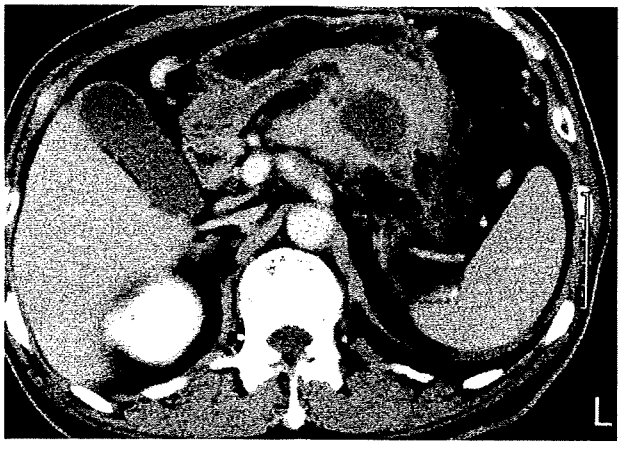

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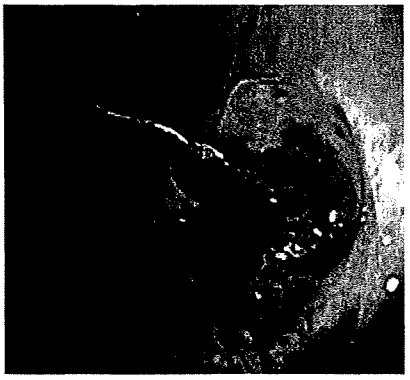

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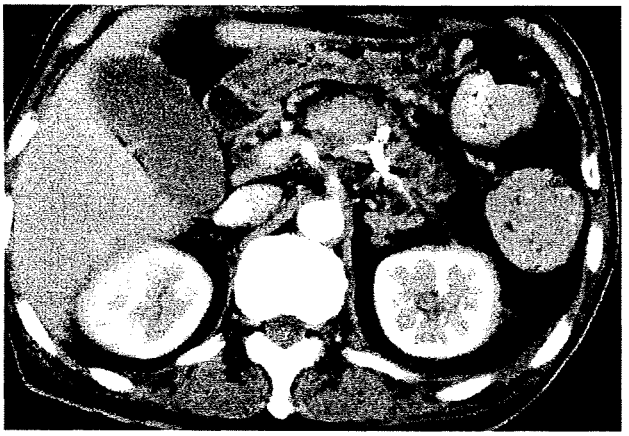

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