Case Series

Vertebroplasty for Treatment of Osteolytic Metastases at C2 Using an Anterolateral Approach

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Background: The clinical management of osteolytic metastases involving C2 is unique, because it is challenging to approach these lesions. Symptoms may vary from local pain to progressive neurological deficit. Surgery or radiotherapy have been the treatments of choice for several years; however, surgery may not be an option for patients with multiple metastases and poor general medical status, and radiotherapy carries the risk of vertebral collapse and consequent neural compression due to delayed bone reconstruction. Through different approaches, vertebroplasty has been introduced into clinical practice as an alternative to traditional surgical and radiotherapy treatments of osteolytic metastases at C2.

Objective: This study aimed to evaluate the safety and efficacy of vertebroplasty with an anterolateral approach for osteolytic metastases at C2 under fluoroscopic guidance.

Study Design: Vertebroplasty in 13 patients with osteolytic metastases at C2 and its clinical effects were evaluated.

Setting: This study was conducted in an interventional therapy group at a medical center in a major Chinese city.

Methods: Thirteen consecutive patients were treated with vertebroplasty via an anterolateral approach. The researchers followed up with the patients for 3 to 12 months, with an average of 9.2 months. The clinical effects were evaluated with the visual analog scale (VAS) pre-operatively and at 3 days, one month, 3 months, 6 months, and 12 months post-operatively.

Results: Thirteen consecutive patients were successfully treated with a satisfying resolution of painful symptoms. Extraosseous cement leakages were found in 5 cases without any clinical complications. VAS scores decreased from 7.6 ± 0.9 pre-operatively to 2.1 ± 1.9 by the 3-day post-operative time point, and were 1.8 ± 1.7 at one month, 1.7 ± 1.8 at 3 months, 0.9 ± 0.8 at 6 months, and 0.6 ± 0.5 at 12 months after the procedure. There was a significant difference between the mean pre-operative baseline score and the mean score at all of the post-operative follow-up points ($P < 0.001$).

Limitations: This was an observational study with a relatively small sample size.

Conclusions: Vertebroplasty via an anterolateral approach is an effective technique to treat osteolytic metastases involving C2. It is a valuable, minimally invasive, and efficient method that allows quick and lasting resolution of painful symptoms.

Key words: Vertebroplasty, C2, anterolateral approach, osteolytic metastasis, pain

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Vertebroplasty is a minimally invasive method for pain control and prevention of the further vertebral collapse and the spinal cord compression in the spinal metastases (1,2). However, vertebroplasty at C2 presents technical difficulties and requires caution to avoid potential injury of the vital structures that surround the C2 vertebra. To the best of our knowledge, there exist only limited data in published literature from case reports and a small number of series describing vertebroplasty as a treatment for osteolytic metastases involving C2. For this report, we reviewed data on 13 patients with C2 osteolytic metastasis treated with vertebroplasty via an anterolateral approach under fluoroscopic guidance, and we evaluate the procedure's efficacy and safety.

Methods

Patients

We performed a retrospective review of all patients with C2 osteolytic metastasis who underwent vertebroplasty in our hospital between March 2003 and May 2012. Before the procedure, all patients gave informed consent, and information from patients' medical records and radiographic studies were acquired with approval from our institutional review board. For this study, 13 patients were included (8 men and 5 women; age range 41 – 73 years; mean age 59.8 years). All of the patients presented with severe pain without neurological deficit that was related to the spinal lesions; various analgesics and chemotherapeutic regimens were given before the procedures. The primary tumors were classified in 5 categories (Fig. 1). Vertebroplasty was performed in patients who were not candidates for surgery due to debilitation or multifocal spinal disease. Radiation therapy was not indicated in 9 patients because the patients had already received the maximum radiation dose for local lesions. In 4 patients, the procedures were performed pre- or post-radiotherapy for rapid stabilization of the vertebrae due to the delayed and incomplete pain control provided by radiation therapy. Eight patients had multiple spine metastases, and 4 of them had more than 2 levels involved in the cervical spine. Rigid cervical collars were prescribed to all patients to prevent the development of neurological deficit due to the high risk of subluxation and angulation of the fracture.

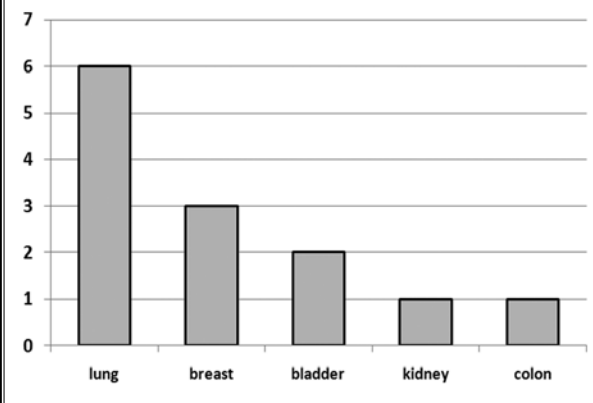

Fig. 1. *Etiologic outcome of C2 lesions.*

Imaging Assessment

All patients were given enhanced computed tomography (CT) and magnetic resonance imaging (MRI) examinations before the procedure to evaluate the lesion type (osteolytic, osteoblastic, or mixed), to determine the lesion invasive range with or without cortical breakthrough, and to identify the positional relationship of the carotid sheath and the vertebral artery to define the anterolateral access path with multiplanar reconstructions. After the procedure, a plain CT examination to assess cement leakage was conducted in all patients.

Procedure

All procedures were performed in an angiography suite with a C-arm digitalized x-ray system (Angiostar, Siemens, Erlangen, Germany; Innova 4100, GE, USA). Before the procedure, all patients were given intravenous antibiotic prophylaxis (2 g of cefazolin; Qilu Pharma, China), which continued post-procedure for 3 to 5 days. The patients were in the supine position with a soft cushion underneath the neck and shoulder that slightly hyperextended the cervical spine. Conscious sedation and analgesia were obtained with IV flunitrazepam (Versed, Roche Pharmaceuticals, Shanghai, China) and buprenorphine hydrochloride (Institute of Pharmaceutical Research, Tianjin, China). The patients were kept alert enough to state whether any pain developed during the procedure. Local anesthesia was given at the selected needle-puncture site, which was at approximately one cm below the edge of the mandibular angle and at the ventral edge of the sternocleidomastoid muscle. Turning the patient's head away from the side of entry and thrusting the jaw superiorly lessened some of the angulation. The carotid pulse was palpated

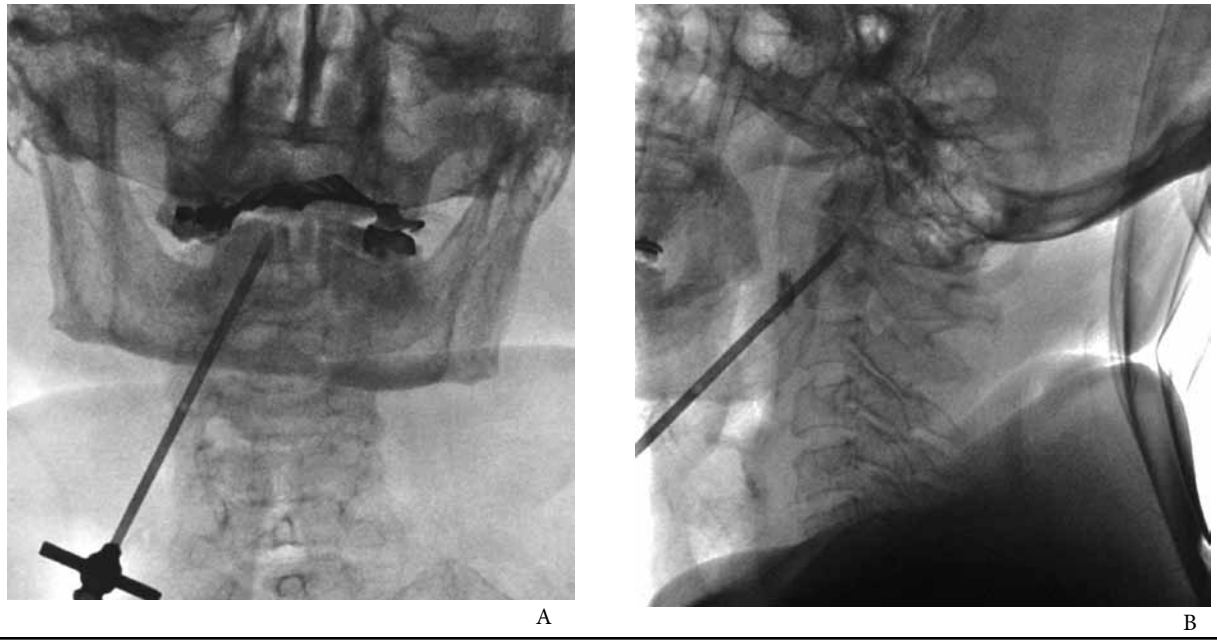

Fig. 2. *Anteroposterior (a) and lateral (b) radiographs obtained after placement of the needle show its oblique trajectory and the approach to C2.*

by the operator's index and middle fingers, and the carotid sheath structures were displaced posterolaterally by manual palpation. Atropine (0.6 to 1.0 mg) was administered intravenously to prevent a vasovagal response related to compression of the carotid body receptors before this maneuver. Initially under continuous anteroposterior fluoroscopy, the needle puncture was made between the carotid sheath and the airway. A 14-gauge, 10-cm-long beveled needle (LADI (T) 2002 No. 2040120, Guanlong, Jinan, China) was introduced in front of the fingertips used to displace the carotid sheath in an oblique (posterior, cranial, and medial) direction. The needle was then positioned with its tip in the anteroinferior vertebral wall of C2. After confirming the correct position of the needle tip with anteroposterior and lateral fluoroscopy, the needle was rotated and advanced to be placed in the middle of the vertebral body (Fig. 2).

Once the needle was in place, bone cement (polymethyl methacrylate, [PMMA]) was prepared by mixing powder cement polymer with barium sulfate powder and liquid monomer until it formed a high-viscosity paste (MAIT 2000 No. 302176, Tianjin, China). The cement was loaded into a screw-type 10 mL syringe for further usage, while care was taken to expel air from the syringe. The cement was incrementally injected into the lesion with 0.5 mL aliquots under continuous lateral fluoroscopic guidance (Fig. 3). The injection was stopped when the bone cement filled up the lesion, or when any epidural leakage occurred. If any paraspinal leakage of cement occurred, the injection was

Fig. 3. *Lateral radiograph obtained after vertebroplasty shows cement deposition in C2.*

temporarily halted to allow the cement to harden, after which the injection was resumed, with a changing of direction of the bevel and the position of the needle tip. The volume of injected cement was determined and recorded using a graduated syringe. A routine biopsy was performed before cement injection.

Pain Evaluation

Patients' pain levels were assessed according to the visual analog scale (VAS) score; a score of 0 indicated no pain, and a score of 10 indicated the most pain imaginable. The appraisal standards of pain relief included

1. complete relief (CR): no pain remained after treatment;
2. partial relief (PR): pain improved compared with before treatment and was now moderate, and general sleep was not disturbed;
3. moderate relief (MR): pain improved but was still apparent, and sleep was disturbed;
4. no relief (NR): pain did not significantly change compared with that before treatment.

The patients maintained the previous doses of narcotic drugs for 48 hours after the procedure. Thereafter, the patients were permitted to discontinue their medical treatment gradually according to the decrease in pain. Pain was considered improved when pain relief was complete or partial and the narcotic drugs were completely stopped. VAS scores were established at pre-operation as a baseline. All patients had clinical re-evaluation, which was repeated at 3 days, one month, 3 months, 6 months, and 12 months post-operatively, or until the patient died.

Statistical Analysis

Data were analyzed using a commercially available statistical software package (SPSS for Windows, version 12.0, 2003; SPSS, Inc., Chicago, IL, USA). Data was expressed as mean ± SD. The results at all of the study's time points were compared using a paired t-test, with a *P* value of less than 0.05 considered statistically significant.

Results

Vertebroplasty was successfully performed with an anterolateral approach in 13 patients. The amount of cement injected per level varied between 2.0 and 4.0 mL (mean 3 ± 0.8 mL). Cement deposition in all lesions was satisfactory. Cement leakages were detected in 5 treated vertebrae and localized to the anterior epidural space (n = 1) (Fig. 4), the pre- or paravertebral space (n = 3) (Fig. 5), and the epidural venous plexus (n = 1). No clinical complications were observed in any of these patients. At 3 days after the procedure, complete relief of pain was achieved in 7 patients, partial relief in 4 patients, and moderate relief in 2 patients. Mean VAS score decreased from 7.6 ± 0.9 pre-operatively to 2.1 ± 1.9 by 3 days after the operation. During the clinical follow-up for all 13 patients, 2 died within 3-4 months, 6 died within 8-11 months, and 5 were still alive after 12 months. Mean VAS score remained low throughout the follow-up period, with 1.8 ± 1.7 at one month, 1.7 ± 1.8 at 3 months, 0.9 ± 0.8 at 6 months, and 0.6 ± 0.5 at 12 months, respectively. There was a significant difference between the pre-operative baseline and each time point of the post-operative follow-up ($P < 0.001$) (Table 1). It is worth noting that 4 patients exhibited mild odynophagia after the procedure. The symptom gradually disappeared over approximately 3 days. All 4 cases suffering from multiple metastases of the cervical spine underwent multi-level punctures in the one-stage operation.

Discussion

The C2 is a part of a complex biomechanical system in the upper cervical spine. It is surrounded by a number of delicate neurological and vascular structures, and it participates in the cranial movement in different planes: extension, flexion, rotation, lateral bending, axial loading, and distraction (3). Thus, having osteolytic metastases involving C2 is a threatening condition. Clinical management of the lesions includes open surgery, radiotherapy, and vertebroplasty. However, open surgery may not be an option in patients with multiple metastases and poor general medical status (4). Radiotherapy is the standard palliative treatment for metastatic bone tumors, reducing pain in 60 – 90% of patients within 10 – 14 days after the start of therapy, and maximum benefit is obtained after 12 – 20 weeks (5). The late onset of pain alleviation after the therapy is not acceptable for patients with unbearable pain. More importantly, radiotherapy can result in minimal and delayed (2-4 months after the start of irradiation) bone reconstruction, and this delay in bone reconstruction increases the risk of vertebral collapse and consequently of neural compression (1). Moreover, additional radiotherapy cannot be performed again in patients with recurrent pain in whom radiotherapy has already been performed, due to the dangers of radiation-induced myelopathy. Therefore, radiotherapy might not be the best choice for patients with a poor overall prognosis and a short expected life span.

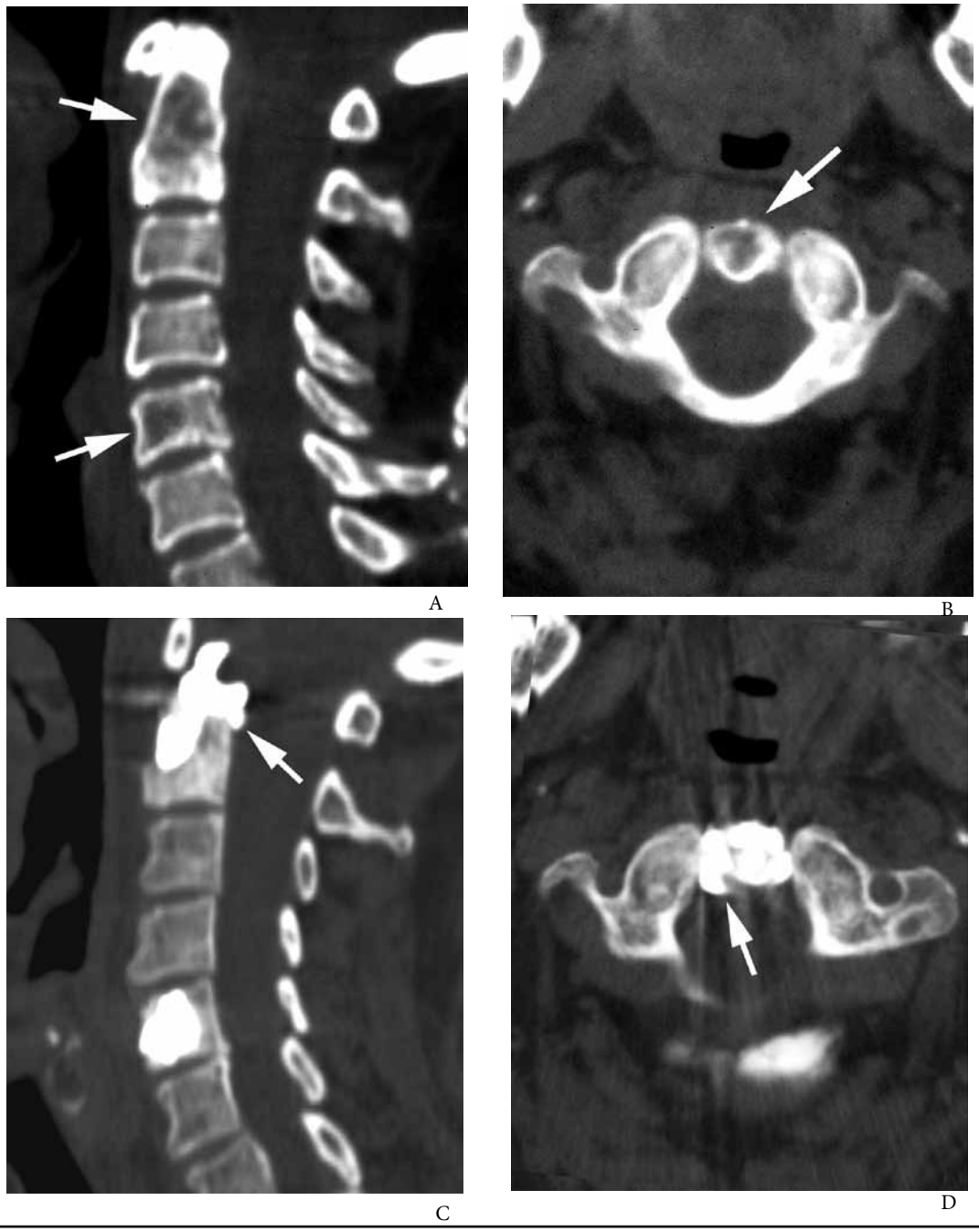

Fig. 4. *Pre- and post-operative sagittal and axial CT images of the upper cervical spine. Pre-operative sagittal (a) and axial (b) CT images show osteolytic lesions in C2 and C5 (arrows). Post-operative sagittal (c) and axial (d) CT images show satisfactory cement distribution over the osteolytic lesion in the body of C2 and cement leakage in the anterior epidural space (arrows). Satisfactory cement filling in C5 osteolytic metastases is also seen.*

Vertebroplasty is a minimally invasive technique that can provide pain relief and produce immediate bone strengthening and vertebral stabilization when the lesion threatens the stability of the spine (6,7). The procedure can be proposed as part of the local treatment in association with radiation therapy or a systemic

therapy (hormonotherapy, chemotherapy, and biphosphonates) (8). Vertebroplasty of C2 can be performed using anterolateral, posterolateral, translateral, and direct transoral approaches under fluoroscopic and/or CT guidance (9-12); from a technical point of view, the procedure is more challenging than those in the thoracic and lumbar spine because of potential dangerous complications related to the local unique anatomical features. In normal anatomy, many neural and vascular structures pass through the C2 vertebral body on their way to supporting functions throughout the body; C2 is surrounded by the larynx and pharynx anteriorly, the carotid space laterally, the vertebral artery and cervical nerve posterolaterally, and the thecal sac posteriorly. It is crucial to avoid these structures during interventional procedures. The local anatomic structures related to the different vertebroplasty approaches are shown in schematic illustrations (Fig. 6), which focuses on the important osseous, muscular, vascular, and neural structures.

The transoral approach is the most straightforward

Fig. 5. *This post-operative CT image shows cement leakages in the prevertebral space (arrow).*

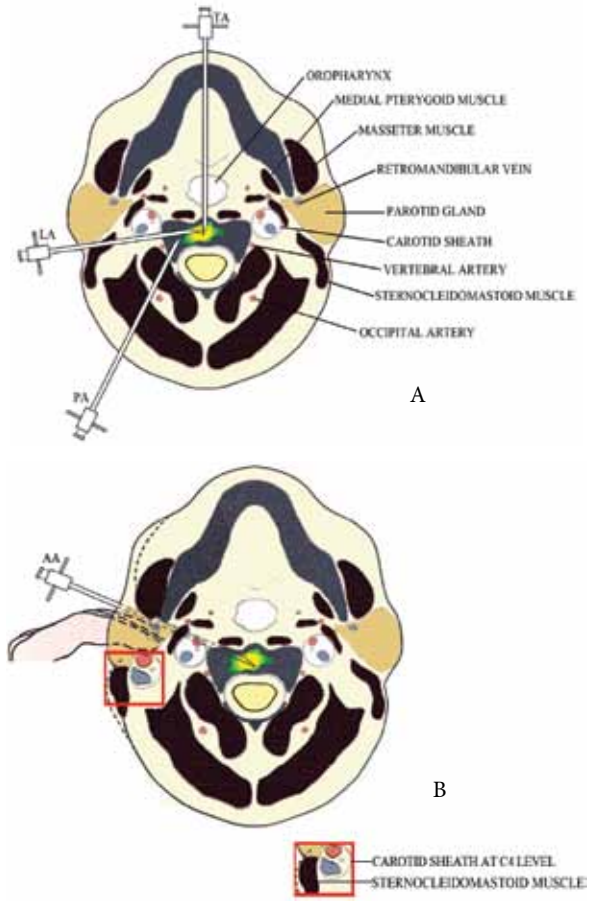

Fig. 6. *Anatomic schematic illustrations of the needle trajectories to C2 body/dens lesions. Anatomic structures are shown on the right side of the diagram; the needle trajectories are shown on the left side. TA: transoral approach; LA: lateral approach; PA: posterolateral approach (a); AA: anterolateral approach (b).*

Table 1. VAS scores of patients at pre-operative and each post-operative time point of follow-up.

Parameters	Pre-op	Post-op 3 days	Post-op 1 month	Post-op 3 months	Post-op 6 months	Post-op 12 months
	(N = 13)	(N = 13)	(N = 13)	(N = 13)	(N = 11)	(N = 5)
Mean ± SD	7.6 ± 0.9	2.1 ± 1.9	1.8 ± 1.7	1.7 ± 1.8	0.9 ± 0.8	0.6 ± 0.5
Versus Pre-op	-	$P < 0.001$	$P < 0.001$	$P < 0.001$	$P < 0.001$	$P < 0.001$

approach under CT and/or fluoroscopic guidance. The needle is inserted through the posterior pharyngeal wall via the open mouth and advanced through the retropharyngeal space. The approach is less demanding technically; however, there is a potential risk of infection (including retropharyngeal abscess, meningitis, and encephalitis) because maintaining a sterile field is often difficult with the transoral approach (13). Furthermore, mandatory nasopharyngeal intubation in patients with a potentially unstable cervical spine would be very difficult (10,11,13). The posterolateral approach is performed with the patient in a prone position. The needle is inserted through the posterior cervical space and advanced into the C2 lesion in the anterior, cranial, and medial direction. The advantage of this approach is that it does not require general anesthesia, which can be hazardous to a generally debilitated patient. However, this approach carries a risk of injury to the vertebral artery, and it is not suitable for lesions in the anterior arch of the cervical spine (14-16). The lateral approach to the upper cervical spine is described so far in only 3 studies (12,17,18). There is a potential space between the carotid sheath and the vertebral artery lateral to the C1-3 level. The needle is inserted directly through this space into the upper cervical lesion under CT and/or fluoroscopic guidance. However, this approach carries a risk of injury to the great vessels and may not be possible in some patients due to anatomical variations in its location. In addition, the procedure takes longer due to being performed under CT guidance.

The anterolateral procedure is performed with the patient in a supine position and requires slight hyperextension of the head to elevate the mandible, allowing an easier approach to the C2 vertebral body. The needle is introduced through the parapharyngeal, retropharyngeal, and prevertebral spaces. Before the procedure, CT and MRIs should be reviewed carefully with multiplanar reconstructions, focusing on the location and extent of the lesions and their relationship to adjacent structures that may influence the needle's trajectory. Familiarity with neck anatomy and careful planning of the procedure are necessary for a procedure that is both precise and safe. During the procedure, the needle should be advanced carefully with carotid sheath structures displaced posterolaterally by manual palpation, aiming for the anteroinferior vertebral wall of C2, just to the proximal side of the midline. It is vital to avoid injury to the submandibular gland; jugular vein; carotid artery; vertebral artery; cranial nerves IX, X, XI; and oropharynx. Prophylactic antibiotics must also be given intravenously to prevent secondary infection before and after the procedure. The routine use of intravenously administered prophylactic antibiotics has been reported by Mathis et al (19), while Kallmes et al (20) reserve use of these for patients who are substantially immunocompromised. However, complications have been reported in the anterolateral approach, including C2 neuralgia due to cement leakage and cerebellar infarction (10). Furthermore, the anterolateral approach may be not practical in patients with severe pain who cannot maintain overextension (21).

Although different approaches exist, we prefer the anterolateral approach for performing vertebroplasty in C2 because the procedure carries a low risk of infection and can be performed under fluoroscopy, which provides greater real-time guidance than CT does. In addition, the procedure can be performed under local anesthesia, avoiding intubation in patients whose clinical condition is compromised and whose cervical spines are potentially unstable.

On the basis of our results, vertebroplasty using an anterolateral approach was successfully performed in all 13 cases without clinical complications. Significant pain improvement (CR + PR) was found in most cases (85%). VAS scores decreased significantly at 3 days after the operation and remained low throughout the follow-up period. Mean VAS differed significantly from the pre-operative baseline to each post-operative time point ($P < 0.001$). Regarding post-operative mild odynophagia in 4 cases with multiple metastases of the cervical spine, we believe that this transient and mild complication was related to soft-tissue injury resulting from the multi-level anterolateral approach punctures in the one-stage operation.

One limitation of this study was the small size of the patient sample. In addition, most patients were in the late stage of the disease, a fact that limited the generalization of our data and long-term follow-up. However, to the best of our knowledge, this study represents the largest series of patients with metastasis yet published, demonstrating the benefit of vertebroplasty for the treatment of osteolytic metastases at C2 using an anterolateral approach. A much larger group of patients might reveal a higher complication rate, especially treatment failure. However, although our initial study design was more susceptible to the effects of bias, we believed it was a practical way to evaluate the efficacy of this technique because the current opportunity to perform the procedure was so limited.

Conclusion

Vertebroplasty using an anterolateral approach is safe, feasible, and effective in the treatment of patients with osteolytic metastasis in C2. Considering the higher risk of complications of the procedure in this region, it is strongly recommended that the treatment be carefully performed by an experienced specialist who is familiar with local anatomy.

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