Case report

Cement pulmonary embolism after percutaneous vertebroplasty in a patient with cushing's syndrome: A case report

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ABSTRACT

Background: Vertebroplasty is a procedure most commonly used for vertebral compression fractures. Although it is a relatively safe procedure, complications have been reported. Cement embolism is seen in 2.1\textendash{}26\% of patients after percutaneous vertebroplasty.

Case presentation: a 38-year-old male who was diagnosed with cushing's syndrome, underwent percutaneous vertebroplasty for his thoracic osteoporotic compression fractures. 24-hours following vertebroplasty, he presented to emergency department with acute-onset dyspnea and chest pain. Chest radiography showed an opaque linear lesion in left pulmonary artery which was suggestive of cement embolism. Pulmonary spiral CT-scan further confirmed the diagnosis. The patient's symptoms improved over time, and warfarin was started with close cardiopulmonary assessments for indicators of cement embolus removal.

Conclusion: in patients with pulmonary cement embolism, conservative treatment may be recommended rather than a surgical removal except when the obstruction is extensive enough to cause hemodynamic changes. Given that all the related studies have suggested that pulmonary thromboembolism can occur as a complication due to bone cement leakage, discovering new cement alternatives and/or injection devices, seems beneficial.

1. Background

Vertebroplasty is a minimally invasive procedure most commonly used for vertebral compression fractures which was first introduced by Galibert et al., in 1987 [1]. In this procedure, polymethylmethacrylate (PMMA) is injected directly into the vertebral body through its pedicle, to restore the height partially, stabilize bony trabeculae, and alleviate pain. Due to its minimal invasion and immediate pain relief, percutaneous vertebroplasty gained popularity for the treatment of painful tumor infiltration disease such as multiple myeloma [2], and metastatic carcinoma [3\textendash{}5], and for patients who have refractory pain due to osteoporotic thoracolumbar compression fractures [6\textendash{}8] Although it is a relatively safe procedure, complications have been reported [9,10]. Acrylic cement of polymethylmethacrylate injected into the vertebral body can leak into the paravertebral venous system and reach the pulmonary artery via the azygos vein leading to a cement pulmonary embolism [11\textendash{}15]. Pulmonary embolism of cement is seen in 4.6\% of patients after percutaneous vertebroplasty. It can be asymptomatic and is directly related to the frequency of paravertebral venous leak, but not to the number of vertebral bodies treated [16]. Here, we report a case of cement pulmonary embolism following vertebroplasty for thoracic compression fracture.

2. Case report

This is a 38-year-old smoker male who is a truck driver. He visited his family physician in July 2017, because of unintentional weight gain and a debilitating back pain. In physical examination he had a buffalo hump and central obesity, thus he was prescribed symptomatic treatment for his back pain and referred to an endocrinologist to evaluate for cushing's syndrome. His laboratory studies in following month showed a significantly high level of 24-h urinary free cortisol which was repeated 3 times and a plasma ACTH of 82pg/ml, which was suggestive of an ACTH-dependent cushing's syndrome. The urinary free cortisol after low and high-dose dexamethasone suppression test reported to be 546 and 764 mcg/24h respectively, which means resistance to dexamethasone and a negative test result. A magnetic resonance image (MRI) of pituitary following gadolinium administration was done which showed no abnormality. Because of the discordance between pituitary MRI, plasma ACTH level, and high-dose dexamethasone suppression...
test results, inferior petrosal sinus sampling (IPSS) was done by interventional radiologist, which showed a petrosal/peripheral ACTH ratio of less than 2. An ectopic ACTH syndrome was suggested which could not be localized with chest and abdominal CT scan. Ketoconazole was administered to control the cortisol excess, while planning for a bilateral adrenalectomy. The patient was also evaluated for his refractory back pain. MRI revealed diffuse osteopenic signal changes in lumbar vertebrae and multiple sites of compression fracture in all thoraco-lumbar vertebral bodies. Bone densitometry showed osteoporosis most severe at spine (mean Z-score and T-score < −2.9). As the patient was symptomatic, the decision has been made to proceed with vertebroplasty. High viscosity cement was injected into T7 to T12 vertebral bodies under fluoroscopic guidance in February 2018. The total volume of injected cement was 4 cc in each level. The patient tolerated the procedure and was discharged uneventfully. 24-hours following his vertebroplasty, he presented to our emergency department with a history of sudden-onset dyspnea and chest pain. Vital signs were within normal limits except tachycardia. He had no hypoxia, fever, chills, cough, and hemoptysis. The ECG was normal, except sinus tachycardia and cardiac troponins were negative. Echocardiography revealed no regional wall motion abnormalities with a 50% ejection fraction, a tricuspid valve regurgitation, and mildly increased systolic pulmonary artery pressure (35 mmHg). Chest radiography showed an opaque linear lesion in the left pulmonary artery (Fig. 1), which raised the suspicion of bone cement pulmonary embolism. Parenteral anticoagulation was started, and patient underwent pulmonary spiral CT-scan which revealed artifact-like hyperdense area in main pulmonary artery and left pulmonary artery suggestive of cement embolism (Figs. 2 and 3). During the hospitalization, patient’s symptoms resolved, and warfarin was started. Cardiovascular surgery consultants recommended medical rather than surgical treatment with close cardiopulmonary monitoring for any signs and symptoms suggestive of worsening embolism. The patient was asymptomatic when he was discharged. Serial cardiac and pulmonary assessments will be carried out looking for increased pulmonary artery pressure as an indicator for the removal of the cement embolus.

3. Discussion

We present a case of 38-year-old man who underwent a T7 to T12 vertebroplasty because of osteoporotic compression fractures, and subsequently had a pulmonary cement embolization to his pulmonary arterial circulation, which was treated non-operatively with anticoagulation.

Operative treatment of vertebral compression fractures has included percutaneous vertebroplasty for the past 30 years. Introduced by Galibert et al. [1] in 1987, this procedure gained popularity steadily and is used as an immediate pain relief method, in osteoporotic compression fractures [6–8] and for treatment of tumor infiltration disease such as metastatic carcinoma [3–5], and multiple myeloma [2]. Efficacy of vertebroplasty in alleviating pain, is not without controversy according to Buchbinder et al. [17] and Kallmes et al. [18] studies, which showed no improvement in pain and pain-related disability in osteoporotic spinal fractures.

Bone cement leakage is of particular concern. Cement leakage into the spinal canal can lead to canal stenosis and cord compression [19,20], and cement leakage into the intervertebral foramina can cause nerve root compression [21]. Additionally, cement leakage into the perivertebral system and inferior vena cava (IVC) can drift toward the right heart and pulmonary arterial system with catastrophic results such as cardiopulmonary arrest [33,34], acute kidney injury [22], paradoxical embolism through a patent foramen ovale [23], and death [10,24,36]. Arterial embolization to the aorta and anterior spinal artery has also been described [25,26]. The risk of cement pulmonary embolism first reported by Padovani et al. [27] exists with both vertebroplasty and kyphoplasty, but the exact rate is uncertain because the patients are not routinely screened for cement embolism [28]. The incidences of pulmonary cement embolism after vertebroplasty ranges from 2.1% to 26%, with much of this variation resulting from which imaging technique is used and whether the study is prospective or retrospective [16,29–32]. Clinical features of cardiopulmonary side effects of cement leak in percutaneous vertebroplasty and kyphoplasty include precordial chest pain and tightness [33–36], dyspnea [35–38], cyanosis, palpitation [34], acute respiratory distress syndrome (ARDS).
Table 1

| Outcome | Clinical manifestation | Indication | Gender | Age (years) | Author/Publication date |
|---------|----------------------|------------|--------|-------------|-------------------------|
| Uneventful recovery | Anticoagulant + Supportive oxygen | Chest pain, hemoptysis, dyspnea, hypoxia | F | 41 | Padovani et al. (1999) |
| Uneventful recovery | Supportive oxygen + Anticoagulant | Chronic osteoporotic pain and symptomatically patient | F | under | 1999 |
| Uneventful recovery | Supportive oxygen + Anticoagulant | Intermittent claudication, chronic dyspnea, and cardiac failure, dyspnea and chest discomfort | M | 60 | 2002 |
| Died | Open heart surgery for hemopericardium and cement removal | Compression fracture | M | 57 | 2003 |
| Discharged | Endovascular cement removal | Chronic osteoporotic pain | F | 60 | 2003 |
| Discharged | No treatment | Asymptomatic | F | 65 | 2006 |
| Discharged | No treatment | Asymptomatic due to multiple myeloma | F | 65 | 2006 |
| Died | Anticoagulant | Respiratory distress | F | 68 | 2006 |
| Discharged | Anticoagulant | Progressive dyspnea | F | 65 | Yoo et al. (2004) |
| Discharged | No treatment | Asymptomatic | F | 68 | Pleser et al. (2004) |
| Discharged | Open heart surgery for hemopericardium and cement removal | Compression fracture | F | 68 | 2005 |
| Died | Anticoagulant | Respiratory distress | F | 68 | Barragan-Campos et al. (2006) |
| Discharged | No treatment | Asymptomatic | F | 64 | 2006 |
| Discharged | No treatment | Asymptomatic | F | 64 | 2007 |
| Discharged | No treatment | Asymptomatic | F | 65 | 2008 |
| Discharged | Right cardiac catheterization | Failed cement removal | F | 68 | 2009 |
| Discharged | Endovascular cement removal | Chest pain palpitation | F | 51 | Braiteh et al. (2009) |
| Discharged | Anticoagulant | Surgical cement removal | F | 64 | 2009 |
| Discharged | Anticoagulant | Asymptomatic | F | 64 | 2010 |
| Discharged | No treatment | Asymptomatic | F | 76 | 2010 |

(continued on next page)
| Outcome | Treatment | Clinical manifestation | Indication | Gender | Age (years) | Author/Publication date |
|---------|-----------|------------------------|------------|--------|-------------|-------------------------|
| Discharged | Conservative management | Dyspnea | Osteoporotic fracture pain | F | 79 | Radcliffe et al. (2010) |
| Reported asymptomatic, and clinically silent patients with PCE in 26% of patients treated with PVP | | | | | |
| | Anticoagulant | Hypotension | Pneumonia | F | 57 | Calhoun et al. (2012) |
| Reported 25 cases of PCE after PVP in 244 patients whom 1 patient was symptomatic from PCE | | | | | |
| Discharged | Anticoagulant | Hypoventilation | Pneumonia | F | 78 | Abd El-Rahman et al. (2012) |
| Died | Percutaneous retrieval of large cement fragment | Mechanical ventilation | Multiple pulmonary emboli seen in fluoroscopy | ARDS | | |
| | | | | | |
| Discharged | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Cohen et al. (2012) |
| Reported 23 cases of PCE after PVP in 244 patients whom 1 patient was symptomatic from PCE | | | | | |
| Discharged | Anticoagulant | Hypoventilation | Pneumonia | F | 63 | Venmans et al. (2010) |
| Reported asymptomatic and clinically silent patients with PCE in 26% of patients treated with PVP | | | | | |
| | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Luetmer et al. (2011) |
| Discharged | Anticoagulant | Hypoventilation | Pneumonia | F | 79 | Radcliffe et al. (2010) |
| Discharged | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Kim et al. (2012) |
| Discharged | Anticoagulant | Hypoventilation | Pneumonia | F | 82 | Rappaport et al. (2013) |
| Discharged | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Calhoun et al. (2012) |
| Discharged | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Garcia-Hontan et al. (2013) |
| Discharged | Anticoagulant | Hypoventilation | Pneumonia | F | 68 | Llano et al. (2013) |
| Discharged | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Calhoun et al. (2012) |
| Discharged | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Garcia-Hontan et al. (2013) |
| Discharged | Anticoagulant | Hypoventilation | Pneumonia | F | 68 | Llano et al. (2013) |
| Discharged | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Calhoun et al. (2012) |
| | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Garcia-Hontan et al. (2013) |
| | Anticoagulant | Hypoventilation | Pneumonia | F | 68 | Llano et al. (2013) |
| | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Calhoun et al. (2012) |
| | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Garcia-Hontan et al. (2013) |
| | Anticoagulant | Hypoventilation | Pneumonia | F | 68 | Llano et al. (2013) |
| | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Calhoun et al. (2012) |
| | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Garcia-Hontan et al. (2013) |
| | Anticoagulant | Hypoventilation | Pneumonia | F | 68 | Llano et al. (2013) |
| | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Calhoun et al. (2012) |
| | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Garcia-Hontan et al. (2013) |
| | Anticoagulant | Hypoventilation | Pneumonia | F | 68 | Llano et al. (2013) |
| | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Calhoun et al. (2012) |
| | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Garcia-Hontan et al. (2013) |
| | Anticoagulant | Hypoventilation | Pneumonia | F | 68 | Llano et al. (2013) |
| | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Calhoun et al. (2012) |
| | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Garcia-Hontan et al. (2013) |
| | Anticoagulant | Hypoventilation | Pneumonia | F | 68 | Llano et al. (2013) |
| | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Calhoun et al. (2012) |
| | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Garcia-Hontan et al. (2013) |
| | Anticoagulant | Hypoventilation | Pneumonia | F | 68 | Llano et al. (2013) |
| | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Calhoun et al. (2012) |
| | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Garcia-Hontan et al. (2013) |
| | Anticoagulant | Hypoventilation | Pneumonia | F | 68 | Llano et al. (2013) |
| | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Calhoun et al. (2012) |
| | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Garcia-Hontan et al. (2013) |
| | Anticoagulant | Hypoventilation | Pneumonia | F | 68 | Llano et al. (2013) |
| | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Calhoun et al. (2012) |
| | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Garcia-Hontan et al. (2013) |
| | Anticoagulant | Hypoventilation | Pneumonia | F | 68 | Llano et al. (2013) |
| | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Calhoun et al. (2012) |
| | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Garcia-Hontan et al. (2013) |
| | Anticoagulant | Hypoventilation | Pneumonia | F | 68 | Llano et al. (2013) |
| | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Calhoun et al. (2012) |
| | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Garcia-Hontan et al. (2013) |
| | Anticoagulant | Hypoventilation | Pneumonia | F | 68 | Llano et al. (2013) |
| | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Calhoun et al. (2012) |
| | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Garcia-Hontan et al. (2013) |
| | Anticoagulant | Hypoventilation | Pneumonia | F | 68 | Llano et al. (2013) |
| | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Calhoun et al. (2012) |
| | Anticoagulant | Hypoventilation | Pneumonia | M | 69 | Garcia-Hontan et al. (2013) |
| | Anticoagulant | Hypoventilation | Pneumonia | F | 68 | Llano et al. (2013) |
| Outcome                  | Treatment                      | Clinical manifestation | Indication                      | Gender | Age (years) | Author/Publication date |
|--------------------------|-------------------------------|------------------------|---------------------------------|--------|------------|------------------------|
| Discharged               | No treatment                  | Asymptomatic           | Painful fracture                | M      | 72         | Guirguis et al. (2015)  |
| Discharged               | No treatment                  | Dyspnea responding to nitroglycerine | Compression fracture pain       | F      | 70         | Nooh et al. (2015)      |
| Discharged               | Anticoagulant                 | Dyspnea                | Not clear                       | F      | 69         | Polli et al. (2015)     |
| Discharged               | Open-heart surgery            | Sudden onset chest pain | Chronic back pain               | M      | 65         | Schuerer et al. (2015)  |
| Uneventful recovery      | Cardiopulmonary bypass        | Chest pain             | Not clear                       | F      | 63         | Shi et al. (2015)       |
| Discharged               | Anticoagulant                 | Dyspnea                | Traumatic fracture              | M      | 70         | Shroff et al. (2015)    |
| Discharged               | Not clear                     | Pulitation Chest pain  | Osteoporotic fracture           | F      | 54         | Awwad et al. (2016)     |
| Discharged               | Anticoagulant                 | Asymptomatic           | Fracture due to bone metastasis | F      | 51         | Chai et al. (2016)      |
| Uneventful recovery      | Open-heart surgery            | Dyspnea                | Osteoporotic fracture           | M      | 28         | Diab et al. (2016)      |
| Discharge                | Open-heart surgery            | Dyspnea                | Traumatic fracture              | M      | 64         | Focardi et al. (2016)   |
| Discharge                | No treatment                  | Asymptomatic           | Osteoporotic fracture           | F      | 58         | Gabe et al. (2016)      |
| Discharge                | No treatment                  | Asymptomatic           | Fracture due to multiple myeloma| F      | 58         | Gorospe et al. (2016)   |
| Discharge                | No treatment                  | Asymptomatic           | Not clear                       | M      | 32         | Memarpour et al. (2016) |
| Uneventful recovery      | Endoscopic Robot-assisted open heart surgery | Chest pain, Tachycardia, Hypotension, Pericarditis, Atrial fibrillation | Osteoporotic fracture pain | F      | 72         | Molby et al. (2016)     |
| Uneventful recovery      | Open-heart surgery            | Chest pain, Right ventricular penetration | Compression fracture | M      | 49         | Park et al. (2016)      |
| Not clear                | Not clear                     | Dyspnea                | Osteoporotic fracture           | F      | 77         | Botia Gonzalez et al. (2017) |
| Discharged               | Anticoagulant                 | Asymptomatic           | Traumatic compression fracture   | M      | 59         | Chang et al. (2017)     |
| Not clear                | Not clear                     | Palpitation            | Traumatic compression fracture   | M      | 65         | Gianculli et al. (2017) |
| Uneventful recovery      | Anticoagulant                 | Chest pain Pleural effusion | Osteoporotic fracture | F      | 57         | Hatzantonis et al. (2017) |
| Uneventful recovery      | Steroids Anticoagulant        | Fever, Respiratory distress, hemoptysis | Bone neuro-ectodermal tumor | F      | 15         | Ramanathan et al. (2017) |
| Uneventful recovery      | Anticoagulant                 | Hypoxemia              | Fracture of femur               | F      | 96         | Talec et al. (2017)     |
| Uneventful recovery      | Anticoagulant Surgical removal| Dyspnea, Chest pain   | Not clear                       | M      | 57         | Wu et al. (2017)        |

M = male, F = female, PCE = pulmonary cement embolism, ARDS = acute respiratory distress syndrome, PVP = percutaneous vertebroplasty.
and cardiac arrest [12], although some patients with pulmonal cement embolism are asymptomatic [41–44]. The symptoms of cement embolism occurs more commonly days to months after, rather than during the procedure [12,24,39,45]. The cement used in vertebroplasty is of such high density compared to lung field that the visualization of cement emboli on CXR is quite striking, but multiple dense opacities with a branching shape which are scattered randomly or diffusely throughout the lungs are more common [16,29,44]. In our patient, CXR showed an opaque linear lesion in the left pulmonary artery without significant scattered lesions in the lungs. Echocardiography is a safe and non-invasive modality to evaluate hemodynamic status and to reveal the probable echogenic material in the cardiac chambers [46,47]. Chest CT scan accurately shows the locations, the lengths, and the number of cement emboli [35].

Abdul-Jalil et al. proposed that PMMA has a prothrombotic property and can cause endothelial injury, which can result in additional thrombosis [48]. The formation of PMMA toxins can cause direct cellular injury by increasing membrane permeability through releasing inflammatory mediators, and superoxide production. Pulmonary cement embolism finally shares similar pathophysiological similarities with pulmonary embolisms [40].

The cornerstone of treatment of pulmonary cement embolism is close cardiopulmonary monitoring and anticoagulation [27,49–53] but there are some reports of cement embolism requiring surgical removal (including cardiopulmonary bypass and arteriography) [33,35–39,54–56]. Choe et al. proposed that asymptomatic pulmonary cement embolii should not alter medical treatment [16]. In Venman’s study, all 11 patients with venous PMMA migration remained asymptomatic during 1-year follow up [31]. Krueger et al. proposed a management algorithm that includes conservative approach for peripheral asymptomatic cases, anticoagulation for the symptomatic peripheral and asymptomatic central emboli, and surgical treatment for symptomatic central embolism only [57]. We selected anticoagulation and close monitoring for our patient regarding the published case reports of cement embolism which is summarized in Table 1. Because of non-degradable and toxic properties of PMMA, attempts have been made to explore alternative materials that are more suitable for vertebroplasty and kyphoplasty [58–60].

4. Conclusion
In patients with pulmonary cement embolism, conservative treatment may be recommended rather than a surgical removal except when the obstruction is extensive enough to cause hemodynamic changes. Given that all the related studies have suggested that pulmonary thromboembolism can occur as a complication due to bone cement leakage, discovering new cement alternatives and/or injection devices, seems beneficial.

Funding
None.

Availability of data and materials
All data and materials described in the manuscript will be freely available to any scientist wishing to use them for non-commercial purposes.

Authors’ contribution
Authors contributed equally to this paper.

Competing interests
The authors declare that they have no competing interests.

Consent for publication
Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor of this journal.

Ethics approval and consent to participate
Not applicable.

Acknowledgements
None.

Appendix A. Supplementary data
Supplementary data related to this article can be found at https://doi.org/10.1016/j.rmr.2018.06.009.

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