Vertebroplasty for vertebral compression fractures secondary to Cushing's syndrome induced by an ACTH-producing bronchial carcinoid tumour

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ABSTRACT

Adrenocorticotropic hormone (ACTH)-producing bronchial carcinoid tumours are a rare cause of Cushing's syndrome. Cushing's syndrome is frequently complicated by osteoporosis, which results in an increased tendency for the development of vertebral compression fractures. Percutaneous vertebroplasty has been shown to be an effective treatment option in the setting of painful osteoporotic compression fractures refractory to conservative therapies. We report a case where vertebroplasty was performed on a 36-year-old woman with osteoporosis and compression fractures secondary to hypercorticolism. A bronchial carcinoid tumour was found to be the source of excess ACTH production. Three-level percutaneous vertebroplasty resulted in a marked improvement in pain.

Keywords: adrenocorticotropic hormone, bronchial carcinoid tumour, carcinoid tumour, Cushing's syndrome, osteoporotic vertebral fracture, vertebral compression fracture, vertebroplasty

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INTRODUCTION

Bronchial carcinoid tumours represent 1%–5% of all primary lung tumours.[1] These neuroendocrine tumours are known to secrete a number of different peptides, including adrenocorticotropic hormone (ACTH). Approximately 2% of patients with bronchial carcinoid tumours will develop Cushing's syndrome.[2] Hypercorticolism is well known to cause bone loss. We report the use of vertebroplasty in a patient with osteoporosis and compression fractures secondary to Cushing's syndrome caused by an ACTH-producing bronchial carcinoid tumour.

CASE REPORT

A 36-year-old previously-healthy, non-smoking Caucasian woman initially presented three years earlier with lower leg oedema, stiff joints, fatigue, shortness of breath and a rash. A chest radiograph at that time revealed hilar and mediastinal lymphadenopathy, as well as a 1.4 cm nodule in the left upper lobe of the lung, leading to a clinical diagnosis of sarcoidosis. Her symptoms improved without steroid treatment for more than one year, but she later began to gain weight, experience hot flushes, develop acne and hirsutism, as well as easy bruising, thin hair and amenorrhoea. Her morning cortisol and ACTH were found to be 1,124 (normal range 140–690) nmol/L and 15 (normal range 0–15) pmol/L, respectively. Cortisol was partially suppressed to 322 nmol/L with high dose dexamethasone, suggestive of Cushing's disease. The Cushing's syndrome was thought to be secondary to a pituitary adenoma, as a 2-mm pituitary lesion was detected on magnetic resonance imaging. The patient underwent transsphenoidal resection of the lesion but pathology was negative for adenoma. Following this procedure, her morning cortisol level remained very high at 1,358 nmol/L with 24-hour urine cortisol of 12,894 (normal range 30–220) nmol/L.

Subsequent to the transsphenoidal resection, petrosal venous sampling with corticotropin-releasing hormone challenge was performed, which confirmed an ectopic source of ACTH. The lung nodule that had been detected two years previously, came into suspicion, but an octreotide scan was found to be negative. The lesion was then biopsied under CT guidance, revealing an ACTH-producing bronchial carcinoid tumour. Approximately six months after having undergone transsphenoidal resection of the pituitary lesion, the patient underwent a left upper lobectomy of the lung to remove the tumour. Resection margins and lobar lymph nodes were negative for malignancy. Prior to lobectomy, the patient's morning cortisol measured 435 nmol/L and ACTH 16.1 pmol/L, with no suppression of cortisol by either low or high

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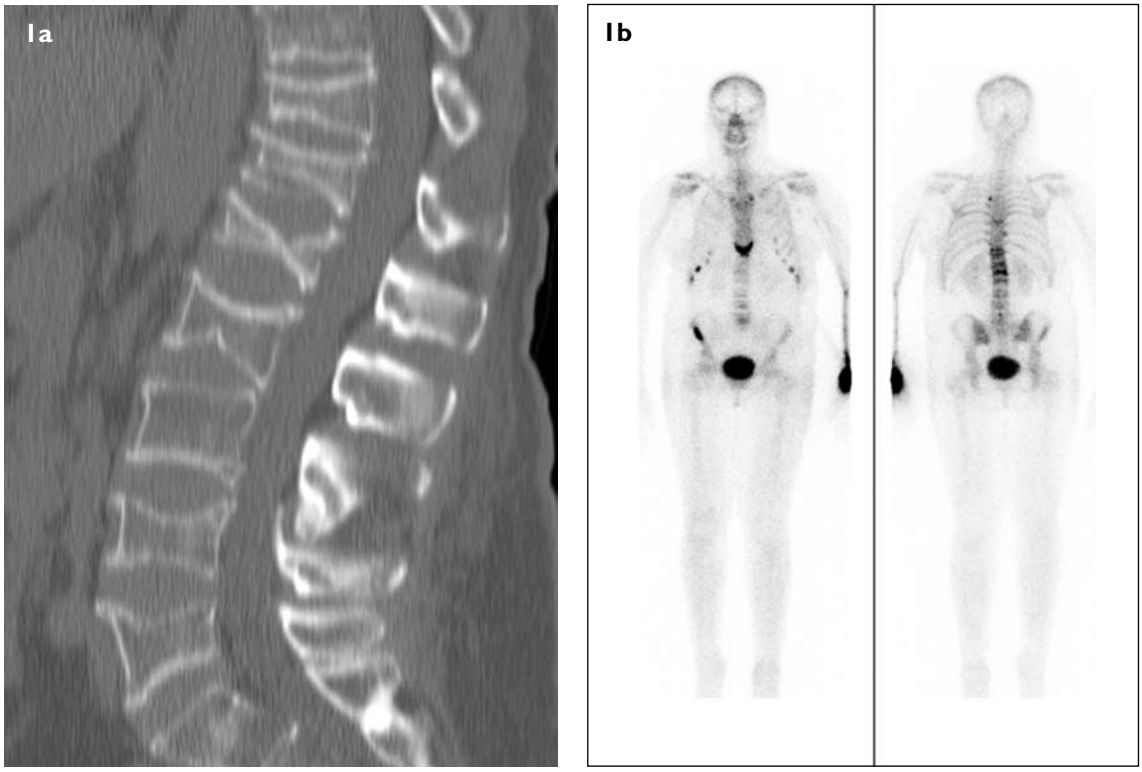


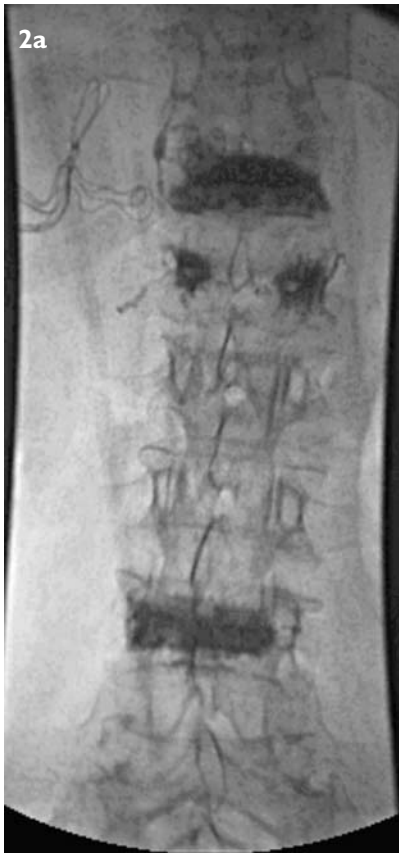
Fig. 1 (a) Reconstructed sagittal CT image shows numerous wedge compression fractures involving the thoracic and lumbar spine on a background of osteopenia. (b) Anterior (left) and posterior (right) delayed phase whole body bone scan images show increased radiotracer uptake clustered in several compression fractures about the thoracolumbar junction.

dose dexamethasone. Her Cushingoid features had been progressing in severity. On examination, she exhibited moon facies, facial plethora, supraclavicular and cervical fat pads, central adiposity, hirsutism, violaceous striae, thin skin, oedema and proximal muscle weakness. She had also developed hypertension and osteopenia, which was initially detected with plain radiography. Postoperatively, a significant reduction in cortisol and ACTH occurred (17 nmol/L and < 0.3 pmol/L, respectively).

Previous to resection of the lung tumour, the patient experienced significant back pain precipitated by an accidental fall. The pain worsened over a four-month period, requiring narcotics for partial relief. She was awakening from her sleep, required assistance with walking and could not bend forward due to the pain. Spinal compression fractures were detected at T7 and from T11–L2, L4 and L5 vertebra (Fig. 1). On clinical evaluation, the pain localised to the thoracolumbar junction and L4 vertebra. Percutaneous vertebroplasty was performed at the T12, L1, and L4 levels. The procedure was done in one session under conscious sedation administered by an anaesthesiologist with the patient prone, following 1% lidocaine/0.5% marcaine administered from the skin to the periosteum. Biplane fluoroscopy (GE Advantax, Milwaulkee, WI, USA) was used to guide the transpedicular punctures using an 11G vertebroplasty needle at L4, and 15G needles at T12 and L1 levels. At L1 level, bilateral punctures were made (Fig. 2). At each level, Cook Osteofirm bone cement was injected (Fig. 3); 1.2, 1.4, 1.1 ml of cement were injected in the T12, L1 and L4 vertebral bodies, respectively. No complication was encountered. The preprocedural pain measured using the visual analogue scale was 8.0, and the postprocedural value was 4.5. Bone mineral density measurement made after the procedure revealed a T-score of –1.6 at spinal levels L2/3, and a T-score of –3 in the left femoral neck, confirming the clinical and radiological suspicion of osteoporosis. No follow-up bone mineral density was available.

DISCUSSION

Approximately 25% of all carcinoid tumours are found in the respiratory tract,[2] with bronchial carcinoids representing 1%–5% of all primary lung tumours.[1] Bronchial carcinoids are a type of malignant neuroendocrine tumour; a category that also contains well-differentiated neuroendocrine carcinoma (atypical carcinoid), large-cell neuroendocrine carcinoma and small-cell lung carcinoma.[2] They are thought to originate from Kulchitsky cells in the bronchial mucosa.[3] Onset tends to occur before 40 years of age, with men and women affected equally. These tumours are not thought to be related to smoking. Carcinoid tumours are most often located in the main stem bronchi and penetrate



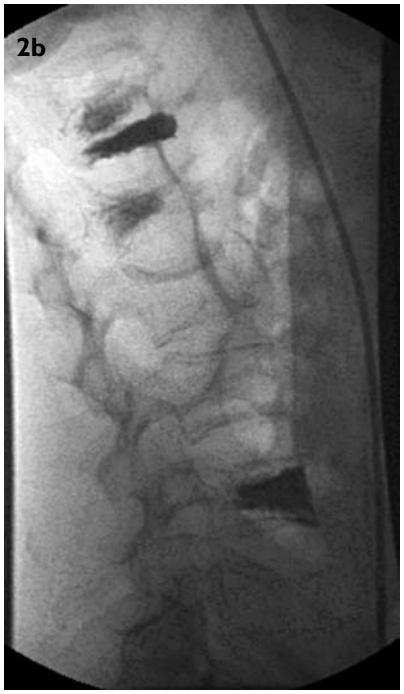


Fig. 2 (a) Anteroposterior and (b) lateral fluoroscopic images taken during vertebroplasty show intravertebral cement distribution. Cement focally fills the lateral portions of the L1 vertebral body reflecting bilateral punctures performed at this level.

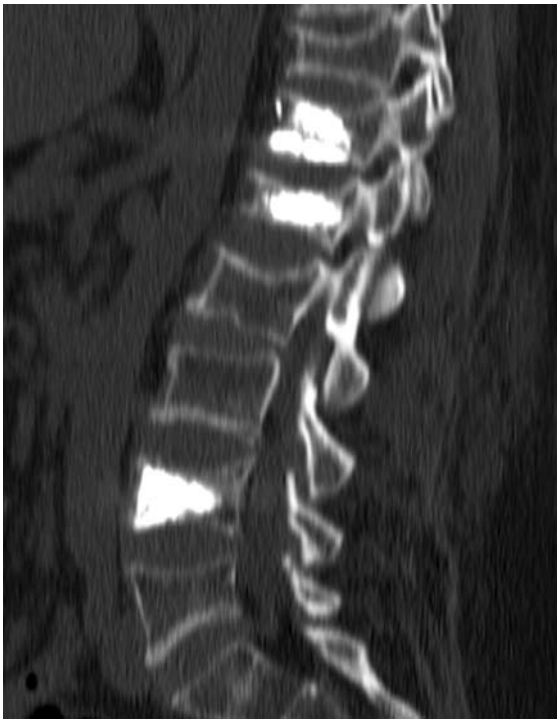


Fig. 3 Reconstructed sagittal CT image post-vertebroplasty shows cement distributed within the T12, L1 and L4 vertebral bodies.

into the lumen, rarely growing larger than 3–4 cm. On histological examination, they are composed of nests, cords and masses of cells separated by a delicate fibrous stroma. The cells are quite regular, with uniform round nuclei and few mitoses. With electron microscopy, many dense-core neurosecretory granules are seen and may contain various peptides.[1]

Paraneoplastic syndrome is defined as symptomatology in a person with cancer that cannot be explained by local or distant spread of the neoplasm, or by hormones produced by the tissue in which the cancer arose.[1] The most common peptide secreted by bronchial carcinoids is serotonin, occurring in as many as 12% of patients with such tumours.[4] Carcinoid syndrome, however, is quite rare, occurring in only 2% of patients. Approximately 2% of patients with bronchial carcinoids develop Cushing's syndrome as a result of ACTH secretion.[2] Bronchial carcinoids cause approximately 1% of all cases of Cushing's syndrome,[4] yet are the most common source of ectopic ACTH secretion, at 25%.[5] Patients with bronchial carcinoids most typically present with respiratory symptoms, such as haemoptysis, cough, lung infections, chest pain and shortness of breath. It is unusual for a paraneoplastic syndrome to be the first presentation. Surgical resection is the treatment of choice, and prognosis is very good. Five-year survival rates for typical carcinoids range from 87% to 100%, and ten-year survival rates, from 82% to 87%.[2] Metastasis are uncommon, occurring in fewer than 15% of patients.[3]

Osteoporosis is a common feature of Cushing's syndrome, with a prevalence of 48%– 90%.[6] In one

study of 90 patients with ectopic ACTH secretion, 50% were found to have osteoporosis or fracture.[7] Patients who develop osteoporotic vertebral compression fractures have a 12.6-fold increased risk of developing subsequent fractures of the axial skeleton.[8,9] Since the first reported use of vertebroplasty in the treatment of a cervical haemangioma, numerous reports have suggested that it is effective in the treatment of refractory osteoporotic compression fractures, with 70%–95% of patients experiencing an improvement in pain within 72 hours of the procedure, with stable pain reduction at 24 months.[10,11] The technique is minimally invasive, with inherently lower morbidity than the existing internal fixation techniques used in spinal surgery. Ideally, steps towards primary prevention of osteoporosis in susceptible populations should be made by optimising modifiable risk factors, including diet and activity. In cases of known osteoporosis, conservative and medical therapies should be used in concert, to salvage bone density. In rare cases, as presented, specific reversible causes of osteoporosis should be addressed. To the best of the authors' knowledge, there has not been a case reported, in which percutaneous vertebroplasty was used in the treatment of painful vertebral compression fractures secondary to osteoporosis associated with Cushing's syndrome, induced by ectopic ACTH secretion by a bronchial carcinoid tumour.

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