Disappearance of lung adenocarcinoma after total en bloc spondylectomy using frozen tumor-bearing vertebra for reconstruction

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Title: Disappearance of lung adenocarcinoma after total *en bloc* spondylectomy using frozen tumor-bearing vertebra for reconstruction

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Abstract

Purpose: Total en bloc spondylectomy (TES) is a surgical procedure performed to achieve complete resection of an aggressive benign spinal tumor or a malignant spinal tumor. When reconstructing the spine after resection, we have been using liquid nitrogen-frozen resected spine bearing tumor as a bone graft, expecting an immunological response to tumor-specific antigen(s). The purpose of this article is to report a successful treatment case of lung adenocarcinoma metastasis with TES and this cryotherapy.

Methods: A 59-year-old male presented with rapid progression of neurological deterioration of the lower limbs due to a spinal metastasis from T8 to T10. The primary lung adenocarcinoma had already been excised under thoracoscopy. The patient underwent TES with reconstruction using frozen tumor-bearing vertebra for the bone graft.

Results: One month after surgery, a new nodule appeared at the right middle lobe of the lung. However, we carried out no biopsy of the newly emerged nodule and the patient received no adjuvant chemotherapy or radiotherapy. Six months after surgery, the tumor vanished. No local recurrence or metastasis of the tumor has been observed until now.

Conclusions: TES with liquid a nitrogen-frozen tumor specimen could be a promising therapeutic option for cancer patients with spine metastasis.

Keywords: total en bloc spondylectomy; lung cancer; frozen autograft; immunotherapy

Introduction

Total en bloc spondylectomy (TES) is a surgical procedure performed to achieve complete resection of an aggressive benign spinal tumor or a malignant spinal tumor.[1] The outcome of this procedure has been reported to be favorable with regard to the local control. [2-4] To improve the patient survival rate, a new technique, which combines TES with cryosurgery, is now being used at in our faculty.[5, 6] This procedure consists of the resection of the vertebral body with the metastatic tumor, freezing of the tumor with liquid nitrogen then using it for bone grafting.[7] This has been performed to cause tumor-induced cryoimmunology.[8] This surgery was approved by the ethics committee of Kanazawa University. We previously reported a case with metastatic thyroid cancer at T4. After TES with cryosurgery, the serum level of thyroglobulin decreased without any other adjuvant therapies, indicating activated antitumor immunity.[5]

We herein present the case of a patient with a metastatic lung adenocarcinoma from T8 to T10, whose newly emerged lung metastasis vanished after TES with cryosurgery. Written consent was obtained from the patient for the publication of this case.

Case report

History and presentation. A 59-year-old male with rapidly worsening back pain was admitted to a nearby hospital. Magnetic resonance imaging (MRI) revealed a spinal tumor at T8, T9 and T10 (Fig. 1). Metastatic cancer was suspected, and he underwent a detailed survey. A lung tumor at the left upper lobe was found by whole body CT (Fig. 2). The patient underwent excisional biopsy with

thoracoscopy for this lesion. A diagnosis of lung adenocarcinoma was confirmed based on the pathological findings. The patient was then referred to our hospital to treat the metastatic spinal tumor. During our preoperative evaluations, rapid progression of the neurological deterioration of the lower limbs occurred. An emergency spinal operation was performed.

Operation. *En bloc* resection of the posterior elements of T8, T9 and T10 was performed by pediculotomy with a thread wire saw. Then, the anterolateral aspect of the vertebral bodies was dissected, and the affected vertebral bodies (T8-10) were removed after posterior fixation with instrumentation. The excised vertebral bodies were frozen with liquid nitrogen for 20 minutes. These bones were crushed into pieces and used as a bone graft for spinal reconstruction with local bone (Fig. 3). In addition, frozen tumor tissue was implanted under the skin of the axillary fossa, expecting that the ground up tumor would provide tumor-specific antigens.

Postoperative course. The patient's weakness of the lower limbs improved immediately after the operation. One month after the operation, a new nodule at the right middle lobe was detected by a whole body CT performed as part of the routine postoperative follow-up in patients with spine metastases. We retrospectively checked the lung CT, which had been taken preoperatively, and found that the nodule had already existed (Fig. 4), but that the nodule had gradually grown larger during observation (Fig. 4). We strongly suspected the possibility of metastasis, and planned to excise the nodule. We referred the patient to two specialist respiratory surgeons, and a specialist radiologist. They agreed with us about the diagnosis of the newly-emerged nodule. We continued to

perform meticulous observation of the case, and in a CT scan taken five months later, the tumor had vanished (Fig. 4). No recurrence of the tumor or instrument failure has been observed until one year after operation (Fig. 5).

We routinely check the blood levels of interferon-γ (IFN-γ) and interleukin-12 (IL-12) in patients with metastatic spinal tumors as markers of antitumor immunity[5]. The checks are performed right before the operation and one and three months after surgery. In the present patient, the preoperative IFN-γ level was 8.4 UI/ml, and at one month after surgery, the level was 5.8 IU/ml, so it was not elevated. However, three months after surgery, the level had increased to 22.2 IU/ml. Similar changes were also observed in the level of IL-12. The preoperative level of IL-12 was 3.6 pg/ml, which was similar to the level one month after surgery (3.4 pg/ml), but the level increased up to 18.1 pg/ml three months after surgery. This suggests that an antitumor immune response might be activated in this case.

Discussion

This is a report of a successful case whose metastatic spinal and lung metastasis were treated with TES with a liquid nitrogen-frozen tumor specimen. The most interesting finding of this case was that fact that a newly emerged (postoperative) lung metastasis vanished without any additional adjuvant therapies.

Lung cancer is the leading cause of cancer death, and the rate of lung adenocarcinoma is increasing. Although the prognosis of lung adenocarcinoma varies with its histological pattern, the most important factor is the tumor-nodal-metastasis stage.[9] Bone metastasis is known to be a factor that negatively impacts the patients' survival.[10] However, our previous study showed that there

was a favorable prognosis for patients with lung carcinoma metastasis to the spine after the TES procedure.[11]

At present, the immunotherapy for lung cancer mainly consists of two strategies, one is which increases the tumor immunogenicity by using cancer vaccines, and the other overcomes tumor-associated immunosuppression using immune checkpoint inhibitors.[12] The cryotherapy was used in the present study with the aim of inducing immunocompetence against the cancer cells by using the frozen tumor specimen as antigens. We previously reported the successful treatment of metastatic spinal thyroid cancer with multiple lung metastases using a similar approach.[5] In that case, the lung metastases gradually decreased in size and number after the operation. However, that case was also treated with ^{131}I therapy after the operation as an adjuvant therapy. In the present case, the metastatic nodule vanished without any adjuvant therapy.

Cryotherapy as systemic therapy for cancer has been gaining interest. Breast cancer cells treated with cryoablation induced a tumor-specific T-cell response in mice.[13] The injection of intratumoral dendritic cells following the cryoablation of prostate cancer prolonged survival and reduced lung metastasis in mice.[14] All of these reports were promising, but had been performed in rodents, not humans. There have been few reports of the successful treatment of humans with cryotherapy.[5, 15] The present report suggests that cryotherapy may represent a valid systemic cancer therapy.

The major limitation of this report is that we could not confirm the pathological diagnosis of the newly emerged nodule. It is possible that it could have been an inflammatory mass. However, we strongly suspected that it was a metastasis, because the nodule enlarged over time. In addition, specialist

respiratory surgeons and a radiologist agreed with our assessment. And another major limitation of this report is that follow-up period was relatively short. The follow-up period was only one and a half years, and it was not confirmed whether there was a complete disappearance of the newly emerged nodule.

Conclusions

We herein reported the successful treatment of a metastatic spinal tumor with newly emerged lung metastasis using TES and cryotherapy. TES with a liquid nitrogen-frozen tumor specimen could be a promising therapeutic option for cancer patients with spine metastasis as both a local and systemic treatment.

Conflict of interest

The authors declare no conflicts of interest concerning the materials or methods used in this study or the findings specified in this paper.

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Figure Legend:

Figure 1.

T2-weighed MRI of the thoracic spine. (a) Sagittal view, (b) axial view. The metastatic tumor was at T8 and T9, and partially invaded the upper corner of T10. It also protruded into the spinal canal.

Figure 2.

Lung CT showing the primary lung adenocarcinoma (arrow).

Figure 3.

A postoperative X-ray of the thoracic spine. (a) AP view (b) lateral view

Figure 4.

Pre- and postoperative CT scans showing the growth and disappearance of the lung nodule. (a) Pre-operation, (b) right after the operation, (c) one month after the operation, (d) six months after the operation.

Figure 5.

Postoperative CT scans showing the bone graft packed in the cage. (a) coronal plane (b) sagittal plane.

Figure 5
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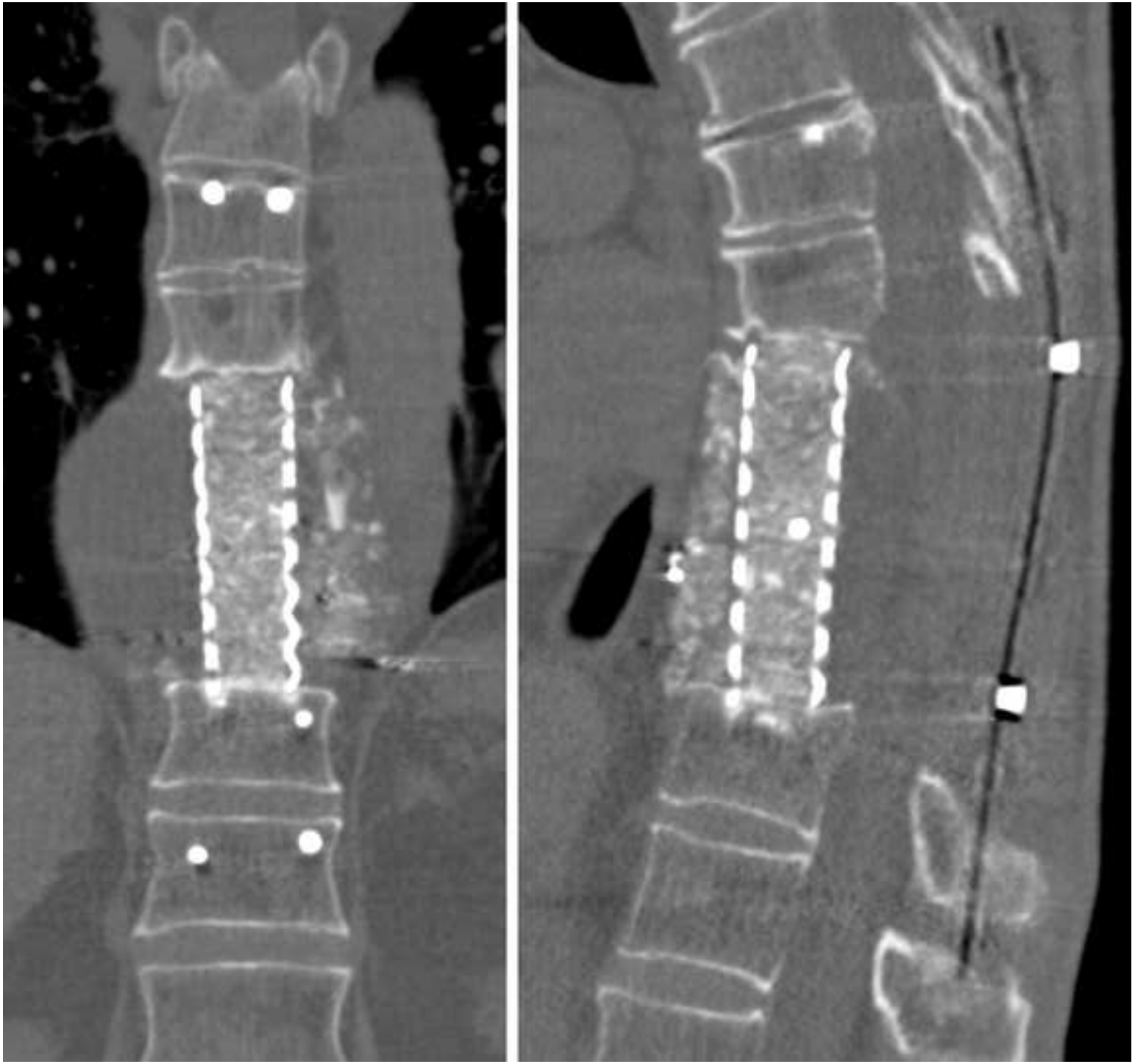

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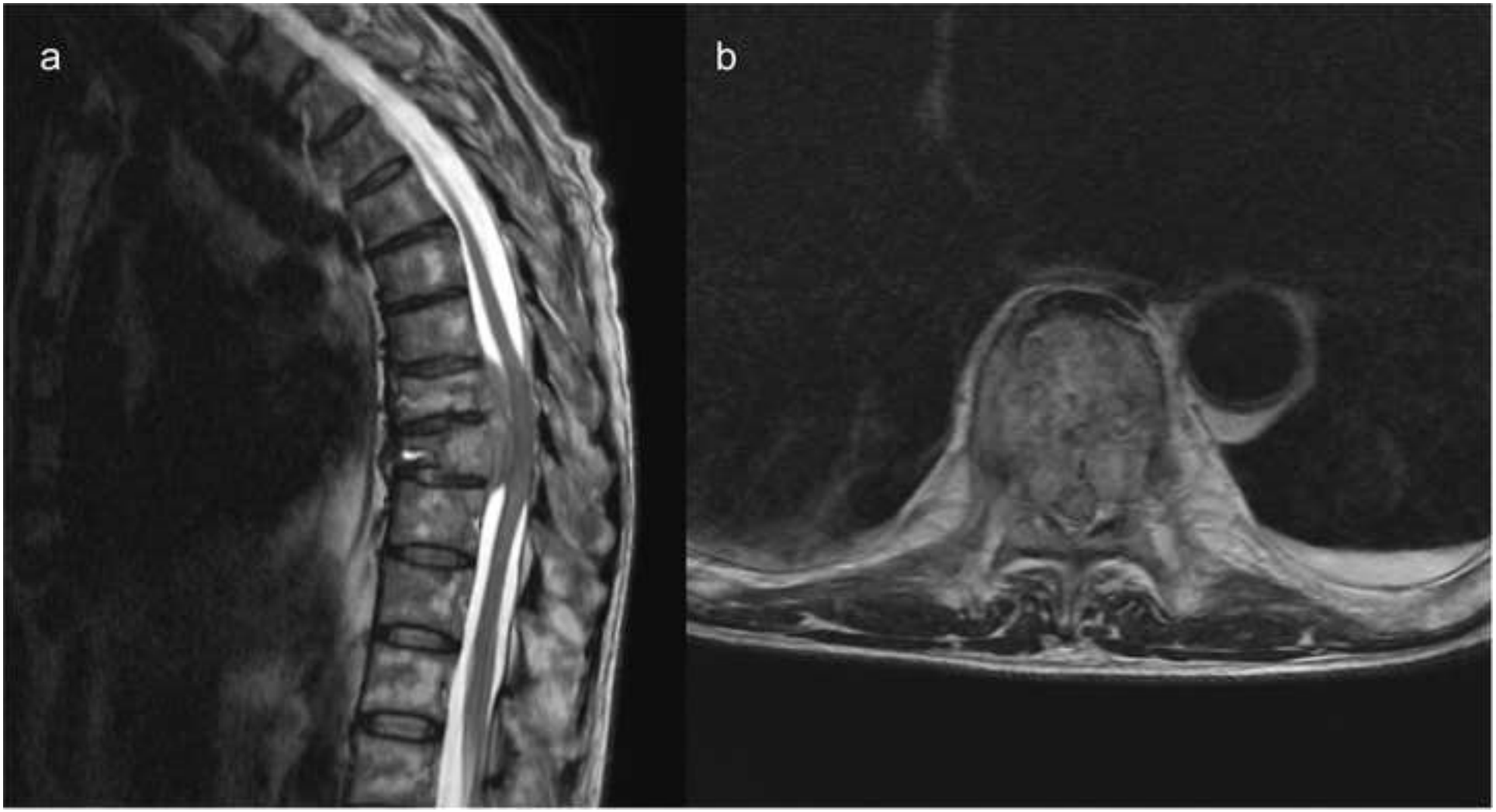

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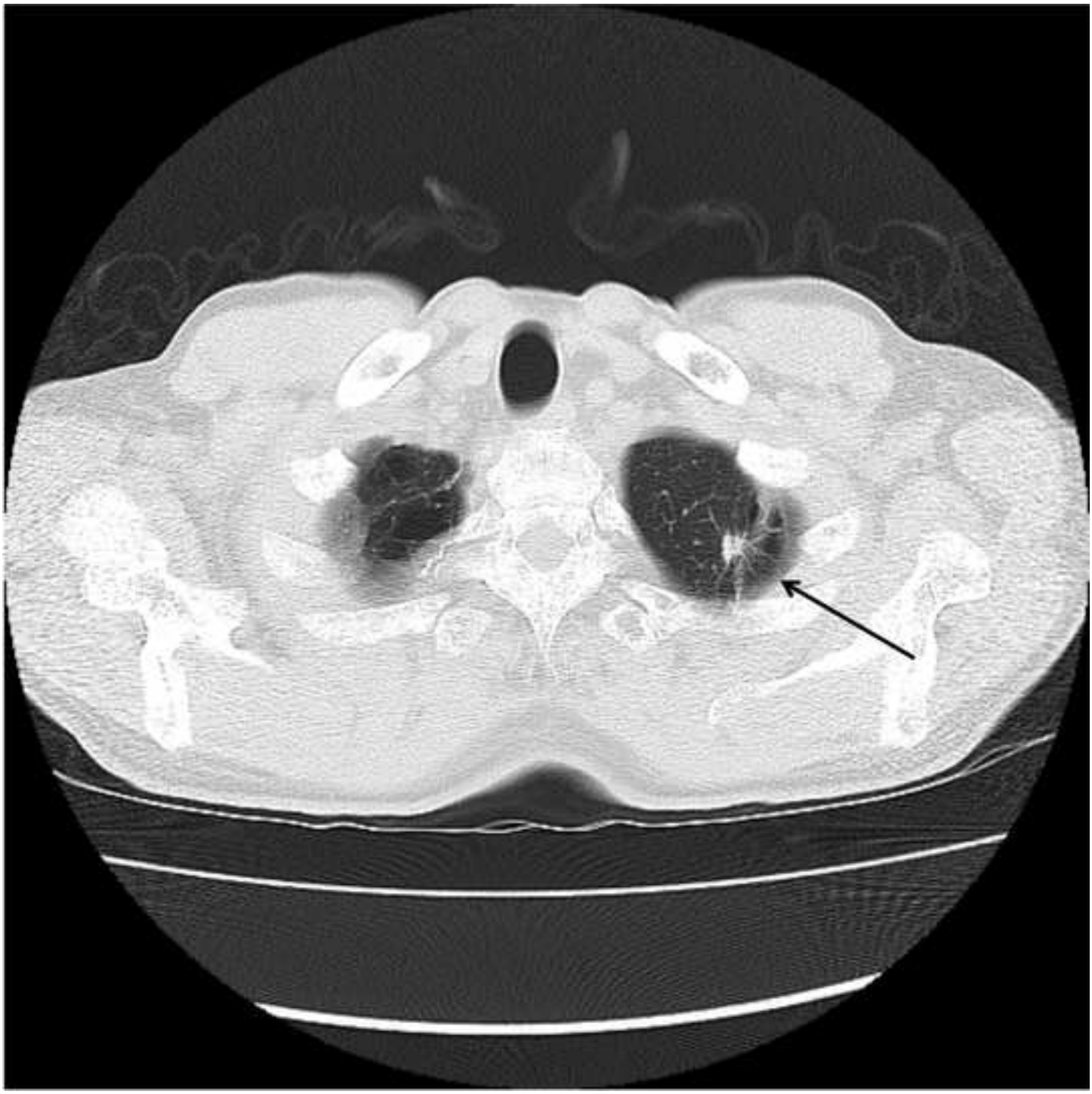

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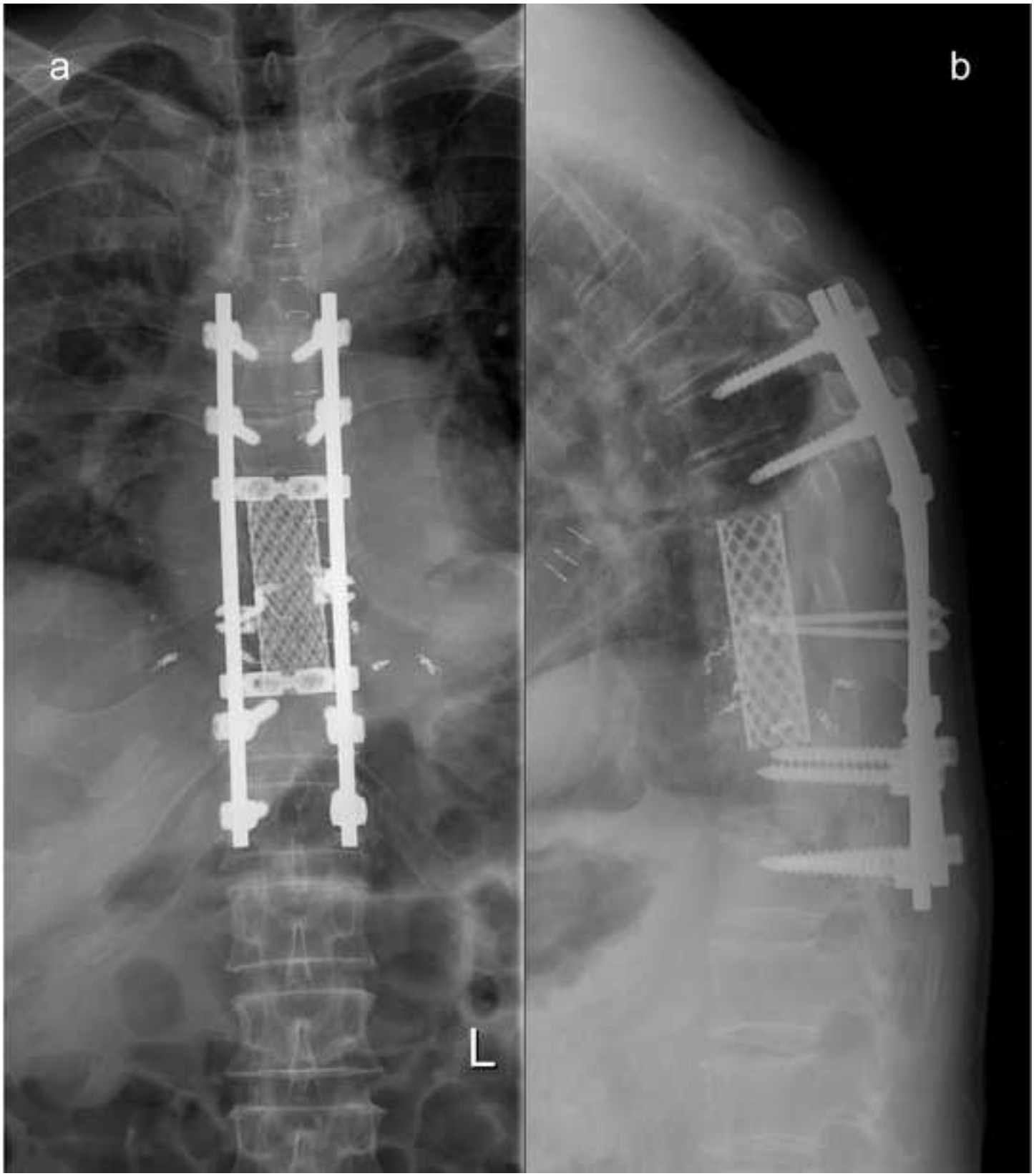

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