

Case Report

Primary mediastinal adenocarcinoma originating from a calcified nodule

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Abstract: Primary mediastinal adenocarcinoma is rare, but its originating from a calcified nodule is even more unusual. We present herein a 55-year-old female with a superior mediastinal mass, first discovered 2 years prior that changed dramatically from its original appearance as a calcified nodule. The mass was completely resected, and histopathological examination revealed a primary adenocarcinoma. The patient has been disease-free for over 13 months since surgery. To the best of our knowledge, this is the first reported case of mediastinal adenocarcinoma to demonstrate such a surprising course of development.

Keywords: Mediastinal adenocarcinoma, calcified nodule, surgery

Introduction

Primary mediastinal adenocarcinoma is a rare malignancy that can arise from normal or ectopic tissue in the mediastinum [1]. Only a few cases are reported in the literature. In general, calcifications found in the mediastinum are benign and associated with granulomatous disease, especially when the patient is from a tuberculosis-endemic country. We present a patient with mediastinal adenocarcinoma containing calcifications, whose malignancy arose from a calcified nodule over the course of 2 years; this case illustrates a unique course of development for this malignancy.

Case report

A 55-year-old Chinese woman was referred to our hospital for a superior mediastinal mass that had been present on computed tomography (CT) for 2 years. She did not complain of chest pain, fever, wheezing, hemoptysis, or any symptoms of superior vena cava syndrome. On a routine examination 2 years ago, a calcified nodule was found in the superior mediastinum (**Figure 1A**). Because of the calcification and the benign appearance of the nodule, she was not treated but advised to return for re-examination 3 months later. At that time, follow-up CT

showed moderate shrinking of the nodule, which had a more dense appearance (**Figure 1B**). The nodule was judged to be benign and no treatment was given. The patient was advised to continue routine follow-up; however, she did not have another CT for 2 years. One month prior to her presentation to us, she underwent a routine systemic examination and the calcified nodule was found to have enlarged dramatically, now appearing to be a soft-tissue mass with punctate calcifications. CT-guided percutaneous puncture biopsy revealed the presence of adenocarcinoma. She received a single cycle of chemotherapy with docetaxel and cisplatin, with no effect on tumor size. At this point, she was transferred to our department for further surgical treatment. Her medical history was significant for 10 years of well-controlled hypertension. At the age of 49, she underwent a hysterectomy with bilateral oophorectomy because of an ovarian cystadenoma. She had no personal smoking history and no family history of cancer. A review of systems was noncontributory, and physical examination was unremarkable. On admission, her peripheral blood count, serum chemistry analysis, and urinalysis were normal.

Enhanced chest CT revealed a huge mass in the superior mediastinum, involving the superior vena cava and containing both punctate and

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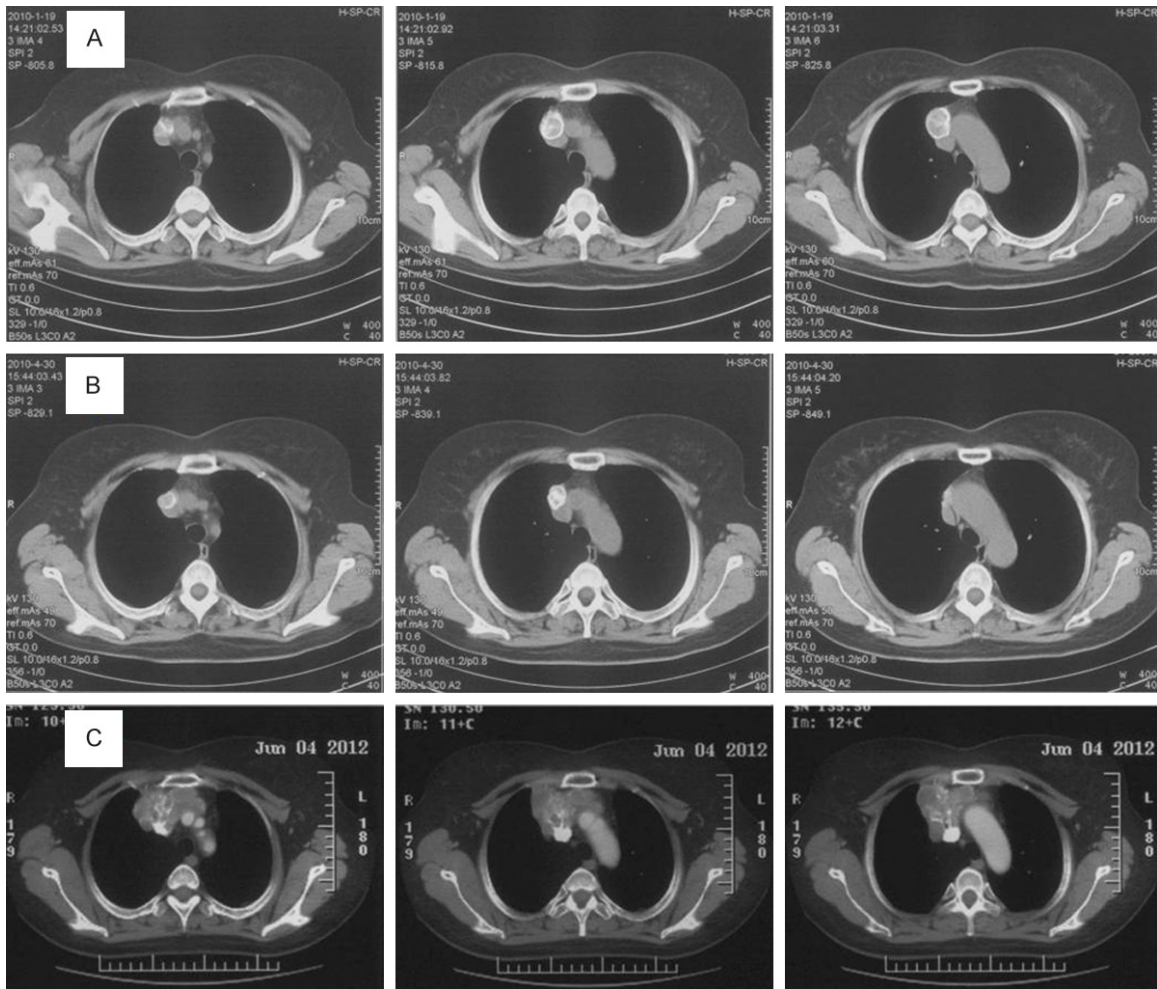


Figure 1. A. Computed tomography (CT) from January 19, 2010, showing a nodule with rim- and linear calcifications. B. CT from Apr 30, 2010, showing a smaller, denser, calcified nodule. C. CT from Jun 4, 2012, showing a soft-tissue mass with punctate calcifications in the superior mediastinum, invading the superior vena cava.



Figure 2. Gross examination: the tumor is irregularly shaped; the cut surface is shiny, yellowish, and multilobular, with focal, punctate, light yellow calcifications.

plaque calcifications (**Figure 1C**). Compared with the 2-year-old chest CT, it seemed that the

soft tissue within the calcified shell had enlarged, crushing and digesting the shell. There were no abnormal findings in the lung fields. The results of abdominal CT, brain magnetic resonance imaging, bone scan, and bronchoscopy were all normal.

The mass was surgically removed on June 19, 2012. After administration of general anesthesia, venous bypass was established between the right internal jugular vein and the right femoral vein. A standard median sternotomy was chosen for surgical exploration in order to adequately expose the mass and the bilateral innominate veins. The irregular tumor was located in the superior mediastinum and was found to invade the superior vena cava, the left and right innominate veins, part of the pericardium, a portion of the right upper lung, and the

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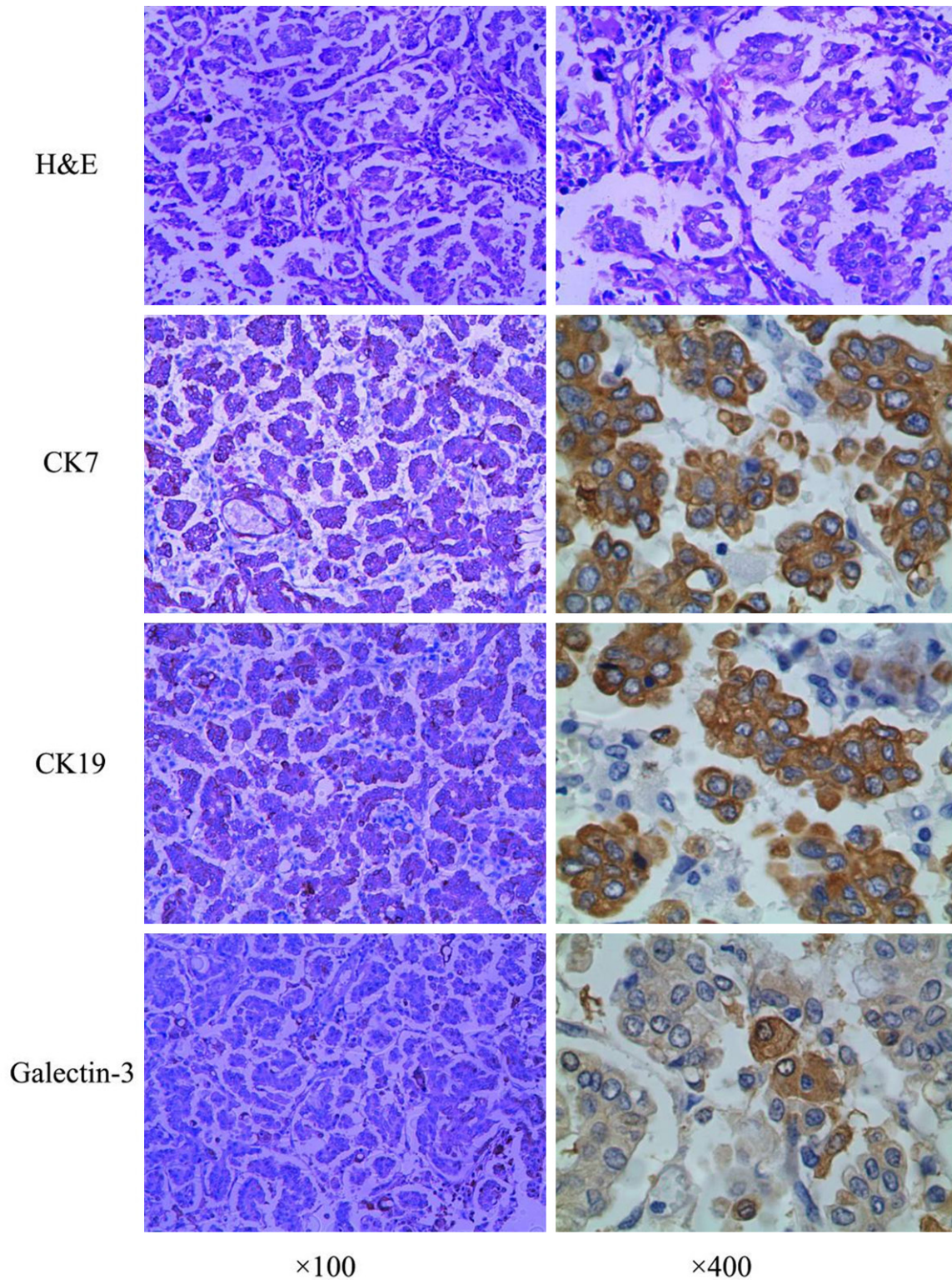


Figure 3. Hematolylin and eosin (H&E) staining and immunohistochemical analysis. The tissue is positive for cyto-keratin 7 (CK7) and CK19, partially positive for galectin-3, and negative for thyroglobulin (Tg) and thyroid transcrip-tion factor 1 (TTF-1).

right phrenic nerve. The tumor was removed en bloc, together with mediastinal lymph nodes,

the entire length of superior vena cava and por-tions of bilateral innominate veins, and part of

the pericardium. Tumor invasion also necessitated wedge resection of the right upper lung. Finally, artificial grafts were used to reconstruct the left innominate vein to connect with the right auricle, and the right innominate vein to connect with the superior vena cava.

Grossly, the tumor had an irregular surface and measured 8 cm × 7 cm × 6 cm. The cut surface was shiny, yellowish, and multilobular, with focal, punctate, light yellow calcifications (**Figure 2**). Immunohistochemical analysis was positive for cytokeratin 7 (CK7) and CK19, partially positive for galectin-3, and negative for thyroglobulin (Tg) and thyroid transcription factor 1 (TTF-1) (**Figure 3**). The final histological diagnosis was adenocarcinoma, micropapillary subtype.

The patient's postoperative course was uneventful; warfarin was prescribed for routine anticoagulation. Adjuvant chemotherapy and radiotherapy were given after surgery. Over 13 months after surgery, the patient has no evidence of local recurrence or distal metastasis.

Discussion

Primary mediastinal adenocarcinoma is extremely rare. Most adenocarcinomas in the mediastinum are metastases from the lung, gastrointestinal tract, pancreas, kidney, or even the pituitary gland [2-4]. Primary mediastinal adenocarcinoma can arise from normal organs in the mediastinum, such as the thymus and the lymph nodes, or from pathologic situations such as cystic teratomas, enteric cysts, bronchial cysts, and lymphoepithelial cystic lesions. It can also arise from the rare situation of ectopic organs (ectopic pancreas has been reported) in the mediastinum [5] and ectopic thyroid adenoma [6].

In our patient, the adenocarcinoma originated from the calcified nodule that was previously considered to be a calcified lymph node from tuberculosis infection. Surprisingly, the nodule originally decreased in size over a 3-month period without any treatment, strengthening the original diagnosis of a calcified lymph node. Thereafter, the patient was not compliant with the recommendation for chest CT every several months. Carcinomas of unknown origin can arise from lymph nodes. Nakano et al [7] reported a patient with multistation mediasti-

nal lymph node adenocarcinoma with no primary lesion, developing over a 4-year period. The authors speculated that the tumor might have been a metastasis of minimal lung cancer or a malignant transformation of aberrant benign epithelial tissue in the lymph nodes. Sawada et al also reported a patient with mediastinal lymph node adenocarcinoma of unknown origin. It is interesting that, in both this patient and our patient, the mediastinal lymph nodes spontaneously decreased in size over 3 weeks of initial observation. Sawada et al purport that tumor-infiltrating lymphocytes and a sarcoid reaction may be immunological responses to cancer and may cause transient tumor regression in the lymph nodes. However, our patient's immunohistochemical studies were negative for Tg and TTF-1, a finding that does not support metastasis from the thyroid or the lung. Systemic examination failed to find a primary lesion in any other organ. One can therefore speculate that the adenocarcinoma in our patient may be the result of malignant transformation of aberrant benign epithelial tissue in the calcified lymph node, itself the result of previous tuberculosis. However, a definite pathologic diagnosis of the calcified nodule was not determined.

Calcifications in the mediastinum are generally benign and usually associated with granulomatous disease, especially in China, where tuberculosis was once widespread. Even today, tuberculosis is still a major public health problem in our country. Lymph nodes are often completely calcified in patients with tuberculosis, whereas in sarcoidosis, another granulomatous disease, the calcifications are often described as focal, popcorn-like, or eggshell-like, becoming larger and more dense over time. Other benign and malignant mediastinal masses may demonstrate calcifications on CT, and these must be included in the differential diagnosis. For example, up to 40 percent of thymomas may present with focal, scattered, ring-like, or linear calcifications [8]. Calcifications in mature teratomas often represent osseous or dental elements, included in a combination of fluid, tissue, and fatty components [9]. Occasionally, mediastinal goiter can present with coarse, punctuate, or ring-like calcifications [8]. Rarely, circumscribed and patchy-type calcifications have been described in mediastinal leiomyomas. Matsuguma et al [10] described a patient

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with localized mediastinal lymph node amyloidosis that enlarged and calcified over time; the authors concluded that the calcifications in amyloidosis may be described as coarse, punctate, speckled, or progressive. Osaki et al [11] reported a patient who underwent surgical removal of a mediastinal cystic tumor with rim calcification. The tumor was thought to probably represent a multilocular thymic cyst, but the lining epithelial cells were absent because of dystrophic calcification resulting from chronic inflammation. Sugimoto et al [12] reported a similar case. Mediastinal lymphoma may present with calcifications after chemotherapy or radiotherapy because of fibrous healing and scar formation [13]. Rarely, coarse calcifications inside a discrete mediastinal mass are seen with untreated lymphoma. Calcified metastatic mediastinal lymph nodes from mucinous breast carcinoma and papillary serous ovarian carcinoma are also reported in the literature.

In our patient, the possibility of a malignant tumor with calcifications in the mediastinum should not have been overlooked. The tumor could have been easily removed via thoracoscopy 2 years earlier, before it invaded the superior vena cava. When facing a mediastinal mass in which the possibility of malignancy cannot be excluded, early surgical intervention should be employed.

In conclusion, we report a patient with mediastinal adenocarcinoma containing calcifications, arising over the course of 2 years from a calcified nodule. To the best of our knowledge, this is the first reported case of mediastinal adenocarcinoma with such an unusual course of development. The presence of calcifications on radiographic evaluation of a newly diagnosed mediastinal mass does not completely exclude a malignant tumor; although rare, adenocarcinoma should be included in the differential diagnosis.

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The patient granted written informed consent for publication of this manuscript and the accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Disclosure of conflict of interest

The authors have no competing interests to declare.

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