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WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

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CASE REPORT

Sarcoidosis mimicking metastases in an echinoderm microtubuleassociated protein-like 4 anaplastic lymphoma kinase positive nonsmall-lung cancer patient: A case report

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Abstract

BACKGROUND

Rearrangements of the anaplastic lymphoma kinase (ALK) gene (ALK-positive) represent an oncogenic driver in approximately 3%-5% of non-small-lung cancer (NSCLC) patients. Sarcoidosis is a multisystem disease, and its reported incidence in Asia is 1 or less per 100000 people per year. The co-occurrence of sarcoidosis and ALK-positive NSCLC is rare, and ALK-positive lung cancer is likely to spread quickly. Therefore, the co-occurrence of sarcoidosis is more easily misdiagnosed as metastatic lung cancer by radiological examination.

CASE SUMMARY

A 50-year-old man had a nodule in the left superior lobe, many small nodules in left superior and right lungs, and enlarged bilateral hilar, mediastinal, and right supraclavicular lymph nodes. Computed tomography-guided pulmonary biopsy of the nodule in the left superior lobe revealed echinoderm microtubuleassociated protein-like 4 gene-ALK positive NSCLC with concomitant noncaseating granuloma. This patient was treated with crizotinib. Thirty days later, a chest computed tomography scan revealed a dramatic decrease in the size of the left superior lobe nodule; however, the lesions in the right lung progressed. The right supraclavicular lymph nodes showed granulomas, and no tumor cells were



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identified in the specimens. The angiotensin-converting enzyme level was high. After 1 wk of methylprednisolone treatment, a significant response of all lesions was revealed. Following radical resection of the lung cancer, noncaseating granulomas were observed in both lung tissues and lymph nodes, which resulted in a diagnosis of echinoderm microtubule-associated protein-like 4-ALK positive NSCLC accompanied with sarcoidosis.

CONCLUSION

Our experience illustrates that pathological evidence is needed to confirm metastatic disease, especially when some suspected metastatic lesions are negative for malignancy.

Key Words: Lung cancer; Sarcoidosis; Anaplastic lymphoma kinase; Echinoderm microtubule-associated protein-like 4 anaplastic lymphoma kinase; Metastasis; Case report

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Core Tip: The co-occurrence of sarcoidosis and echinoderm microtubule-associated protein-like 4 anaplastic lymphoma kinase (ALK)-positive non-small-cell lung cancer is rare. Here, we present one case of sarcoidosis mimicking metastases in an echinoderm microtubule-associated protein-like 4-ALK positive non-small-cell lung cancer patient. From this case, our experience illustrates that ALK-positive lung cancer is likely to spread quickly; therefore, the co-occurrence of sarcoidosis is more easily misdiagnosed as metastatic lung cancer by radiological examination. We suggest that pathological evidence is needed to confirm metastatic disease, especially when some suspected metastatic lesions are negative for malignancy or when the post-treatment follow-up evaluation results are unexpected.

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INTRODUCTION

Rearrangements of the anaplastic lymphoma kinase (ALK) gene (ALK-positive) represent an oncogenic driver in approximately 3%-5% of non-small-cell lung cancer (NSCLC) patients^[1,2]. The most common ALK partner is the echinoderm microtubuleassociated protein-like 4 gene (EML4) and generates EML4-ALK fusion transcripts^[3]. ALK tyrosine kinase inhibitors, including crizotinib, ceritinib, and alectinib, are the standard first-line treatment for advanced ALK positive NSCLC patients.

Sarcoidosis is a multisystem disease characterized by persistent granulomatous inflammation, affecting the intrathoracic region and lungs in over 90% of cases^[4]. The reported incidence of sarcoidosis in Asia is 1 or less per 100000 people per year^[5,6]. The co-occurrence of sarcoidosis and ALK positive NSCLC is rare. Here, we present one interesting case of sarcoidosis mimicking metastases in an EML4-ALK positive NSCLC patient.

CASE PRESENTATION

Chief complaints

A 50-year-old man was admitted to our hospital for chest tightness and a productive cough.



History of present illness

The patient reported that the chest tightness and productive cough have lasted 2 wk.

History of past illness

The patient had no history of past illness.

Personal and family history

The patient was a former heavy smoker and a former heavy drinker.

Physical examination

There were no physical findings to note.

Laboratory examinations

TSPOT-tuberculosis test was negative. His tumor marker levels were as follows: carcinoembryonic antigen 2.1 (0.0-5.0 ng/mL), carbohydrate antigen 199 2.3 (0.0-37.0 ng/mL), cancer antigen 125 115.9 (0.0-35.0 ng/mL), neuron-specific enolase 15.8 (0-30.0 ng/mL), C-terminus of cytokeratin 19 7.0 (0-7.0 ng/mL), squamous cell carcinoma antigen 0.9 (0.0-1.5 ng/mL), and cancer antigen 724 20.8 (0.0-16.4 ng/mL).

Imaging examinations

Chest computed tomography (CT) showed a 2.3 cm × 2.7 cm nodule in the left superior lobe, many small nodules in left superior and right lungs, and enlarged bilateral hilar and mediastinal lymph nodes (Figure 1A and B). Fluorine-18 fluoro-deoxyglucose (FDG) positron emission tomography (PET)-CT revealed hyper-metabolic activity in the left superior lobe nodule [maximum standardized uptake value (SUVmax) = 11.8], bilateral pulmonary small nodules (SUVmax = 20.3), and left sacrum (SUVmax = 6.3) as well as lymphadenopathy (right supraclavicular (SUVmax = 8.3) and bilateral hilar and mediastinal lymph nodes (SUVmax = 10.6), suggesting a neoplasm with extensive metastasis (Figure 1C).

Further diagnostic work-up

The left upper lung nodule was diagnosed as adenocarcinoma with concomitant noncaseating granulomas by CT-guided biopsy (Figure 1D). The diagnosis was clinical stage IVa (cT3N3M1b) adenocarcinoma. EML4-ALK fusion was detected using the amplification refractory mutation system method. Thus, the patient began receiving crizotinib 250 mg twice daily. CT was repeated 30 d later and revealed that the left upper lung nodule decreased dramatically in size; however, the lesions in the right lung progressed, and the mediastinal lymph nodes did not show a significant reduction except for the lymph nodes in station 5 (Figure 1E and F).

Therefore, this patient was admitted to our hospital for further evaluation. An elevated level of angiotensin-converting enzyme (ACE) (194 U/L, normal value, 24-139 U/L) was noted. Purified protein derivative skin tests and serum calcium levels were normal. The right supraclavicular lymph node was diagnosed with noncaseating granulomatous inflammation with negative acid-fast bacillus staining. Bronchoscope showed multiple nodular infiltrations in the right middle lobe (Figure 1G), and the pathological diagnosis was granulomas. The endobronchial ultrasound images showed enlarged lymph nodes in stations 4R, 7, and 11L, but no tumor cells were identified by endobronchial ultrasound-guided transbronchial needle aspiration.

Therefore, he was diagnosed as lung adenocarcinoma accompanied by sarcoidosis (stage II). As the disease progressed within 1 mo, he was administered oral methylprednisolone 8 mg twice daily as well as crizotinib. One week later, repeat chest CT revealed a significant response in all lesions in both lungs (Figure 1H and I). PET-CT showed a dramatic decrease in FDG uptake in all pulmonary lesions (Figure 1J) and no abnormal metabolic activity in the left sacrum. A magnetic resonance imaging scan of the left sacrum was also normal.

FINAL DIAGNOSIS

The final diagnosis was stage IIIA (cT1N2M0) lung adenocarcinoma accompanied by sarcoidosis (stage II).

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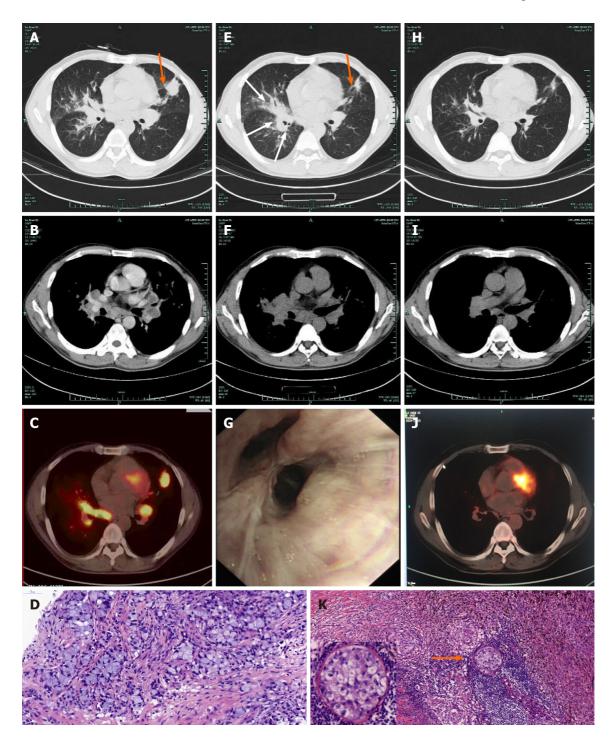


Figure 1 Thoracic computed tomography-scan, positron emission tomography- computed tomography, flexible bronchoscopy, and histopathological images. A and B: Computed tomography (CT) image obtained on August 7, 2018, showing a 2.3 cm × 2.7 cm nodule (orange arrow) in the left superior lobe, small nodules of varying sizes in the left superior lobe and right lung, and enlarged bilateral hilar and mediastinal lymph nodes; C: Positron emission tomography-CT image obtained on August 8, 2018 showing hypermetabolic activity in the left superior lobe nodule and lymphadenopathy, suggestive of a neoplasm; D: Histopathological images obtained showing an adenocarcinoma sample from the superior lung nodule obtained by CT-guided pulmonary biopsy (hematoxylin and eosin, × 40); E and F: CT image obtained on September 7, 2018 after 30 d of treatment with crizotinib showed a dramatic decrease in the size of the left superior lobe nodule (orange arrow); however, the lesions in the right lung progressed (white arrows); G: Flexible bronchoscopy image showing multiple nodular infiltrations in the right middle lobe; H and I: CT image obtained on September 19, 2018 after 1 wk of methylprednisolone showing a significant response of all lesions in both lungs; J: Positron emission tomography-CT image obtained on November 15, 2018 showing a dramatic decrease in fluorodeoxyglucose uptake in pulmonary lesions; K: Histopathological image showing changes within the adenocarcinoma (orange arrow) with concomitant noncaseating granulomatous inflammation in samples from the parabronchial lymph nodes obtained by video-assisted thoracic surgery (hematoxylin and eosin, × 20).

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TREATMENT

The multidisciplinary team therefore considered that the patient was suitable for surgery, and the patient underwent radical resection of left superior pulmonary carcinoma by video-assisted thoracic surgery. The intraoperative findings showed a hard nodule approximately 2 cm in diameter on the left superior lobe and enlarged hilar and mediastinal lymph nodes.

The pathologic findings revealed a small cluster of heteromorphic cells in the nodule and that the remaining lung tissues had granulomatous inflammation. One of eight parabronchial lymph nodes and one of one lymph node in station 5 contained metastases with concomitant granulomatous inflammation (Figure 1K). The pathologic diagnosis was stage IIIA (ypT1N2M0) lung adenocarcinoma accompanied by pulmonary sarcoidosis.

OUTCOME AND FOLLOW-UP

This patient refused chemotherapy and radiotherapy after surgery. He continued to receive crizotinib and methylprednisolone. Methylprednisolone was gradually tapered to a maintenance dose of 4 mg daily. The serum ACE activity was reexamined 9 mo after the diagnosis of sarcoidosis and the level was normal. To date, he has been followed-up for 24 mo and remains recurrence-free.

DISCUSSION

This is one case of sarcoidosis mimicking metastases in an EML4-ALK positive NSCLC patient. ALK-positive patients tend to be younger, have little to no smoking history, and have histologic characteristics of adenocarcinoma^[7]. Sarcoidosis is more common in young adults, African Americans, and women^[4]. The exact etiology of sarcoidosis remains largely unknown. However, both environmental and genetic factors, including specific occupations and exposures, human leukocyte antigen class II, and cytokine polymorphisms, are likely to define the risk of developing the disease^[4,8]. Furthermore, a history of ever smoking instead is protective against sarcoidosis^[8]. Therefore, both ALK-positive NSCLC and sarcoidosis tend to occur in younger patients, but no other common susceptibility factors exist between the two diseases.

Sarcoidosis can develop as local sarcoid reactions that are induced by lung cancer^[9] or medical treatments including chemotherapy^[10], tyrosine kinase inhibitors^[11], or immune check-point inhibitors^[12]. In this case, the primary lung cancer lesion was in the left upper lobe, but granulomas were found even in the nonneoplastic right lung and supraclavicular lymph node. Moreover, the serum ACE level was high. These findings suggest that the granulomas were more likely to be coincidental, true sarcoidosis rather than sarcoid reactions in respond to lung cancer.

Apart from affecting the lungs and lymph nodes, both sarcoidosis and lung cancer can affect bone. Bone involvement is moderately rare in sarcoidosis, occurring in 3%-13% of patients^[13]. Earlier studies demonstrated that the small bones of the hands and feet are typically affected^[13]. However, axial bone involvement including spine and pelvis was found to be more frequent with the usage of magnetic resonance imaging and PET-CT scanning^[14,15]. In contrast, bone metastases are a common complication in lung cancer^[16], and sacrum involvement is frequently observed^[17]. In this case, the lesions in the sacrum were initially assessed as a sign of extensive metastasis based on the PET-CT findings, and the pathological findings of concomitant granulomas obtained by CT-guided biopsy were ignored by us at first. Moreover, the use of PET/CT led to a false-positive result in this case due to the absorption of fluorine-18 FDG by the inflammatory lesions associated with sarcoidosis^[18,19]. As such, this case illustrates that when found in cancer patients, sarcoidosis can easily be misdiagnosed as metastatic lesions.

CONCLUSION

Herein, we described a case of sarcoidosis mimicking metastases in an EML4-ALK positive NSCLC patient. From this case, we can learn that sarcoidosis is easily misdiagnosed as metastatic lesions of lung cancer by radiological examinations and



that pathological evidence is needed to confirm metastatic disease, especially when some suspected metastatic lesions are negative for malignancy. Moreover, further examinations are needed when posttreatment follow-up evaluation results are unexpected.

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