

Herbal medicine-induced multiple pulmonary pseudotumors

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ABSTRACT

Japanese herbal medicines (HMs) cause adverse drug reactions (ADRs); however, solid nodule formation is uncommon. In this report, we aimed to show that ADRs with HM can mimic lung cancer. A 63-year-old man complained of back pain. His physician prescribed a traditional Japanese HM, Keishikajutsu, which alleviated his symptoms. After 4 weeks, a chest radiograph showed multiple lung nodules that were absent 6 months earlier; the patient did not have cough, fever, or dyspnea. Computed tomography (CT) showed multiple, bilateral lung nodules; however, blood tests and lung biopsy showed no abnormalities, ruling out interstitial pneumonia and lung cancer. Three months after the HM was discontinued, CT showed resolution of the lesions. Interstitial pneumonia was reported as a side effect of HM; however, no such side effect was reported for Keishikajutsu. When a patient presents with multiple lung nodules, a side effect of HM should be considered as a differential diagnosis.

Keywords: Adverse reaction, herbal medicine, lung nodule, pseudotumor

Introduction

Approximately 90% of Japanese physicians use traditional Japanese herbal medicines (HMs) with approval from the Japanese Ministry of Health, Labour and Welfare. Clinical practice guidelines published by medical societies in Japan recommend HM for several conditions.^[1] Adverse drug reactions (ADRs) associated with HM have been reported and vary in terms of clinical manifestations. The incidence of liver disorders is 0.16%^[2] and that of interstitial pneumonia is 0.08%.^[3] However,

the formation of solid nodules, which can be misdiagnosed as end-stage metastatic cancer, is uncommon. This case report aims to inform clinicians that ADRs with HM can mimic end-stage metastatic lung cancer. Ethical and institutional permission: This case report was approved by the Institutional Review Board of Tohoku University School of Medicine (No. 19272).

Case Report

A healthy 63-year-old man presented with spontaneous back pain. He was prescribed a traditional Japanese HM, Keishikajutsu, which is usually prescribed for neuralgia and arthralgia.^[4] Keishikajutsu contains the following crude drugs: JP Cinnamon Bark, JP Peony Root, JP Atractylodes lancea Rhizome, JP Jujube, JP Glycyrrhiza, JP Ginger, and JP Powdered Processed Aconite Root (JP: The Japanese Pharmacopoeia). His back pain was alleviated by HM. After 4 weeks, during a medical checkup of the patient, his chest X-ray revealed multiple solid nodules in both

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lungs. In a retrospective review of a chest X-ray 6 months earlier, no lung nodules were observed. During the entire treatment period, the patient did not have cough, fever, or dyspnea.

To further investigate the lesions, computed tomography (CT) scanning of the chest was performed; this revealed multiple irregular tumors in the bilateral lung. An irregular tumor with a diameter of 53 mm was observed in the S2 area of the right upper lung lobe. The tumor, with spicule formation, was connected to the interlobar pleura. Furthermore, right hilar lymph node enlargement indicated lymph node metastasis. The findings of the CT scan suggested stage-IV metastatic lung cancer [Figure 1a]. Based on bronchoscopic biopsy, the extracted specimen revealed no remarkable findings suggestive of malignancy; it only showed the infiltration of inflammatory cells [Figure 1b-d]. Other laboratory tests presented no findings suggestive of systemic inflammation (assessed using white blood cell count and analyses of serum amyloid A and C-reactive protein) or connective tissue diseases (assessed based on antinuclear antibody, rheumatoid factor, antineutrophil cytoplasmic antibody, and sialylated carbohydrate antigen KL-6). Based on the findings of the CT scan, the man was presumptively diagnosed with stage-IV metastatic lung cancer. However, the bronchoscopic biopsy revealed no malignancy, and the laboratory tests presented no findings of systemic inflammation or connective tissue diseases. At this point, an association with the HM was suspected.

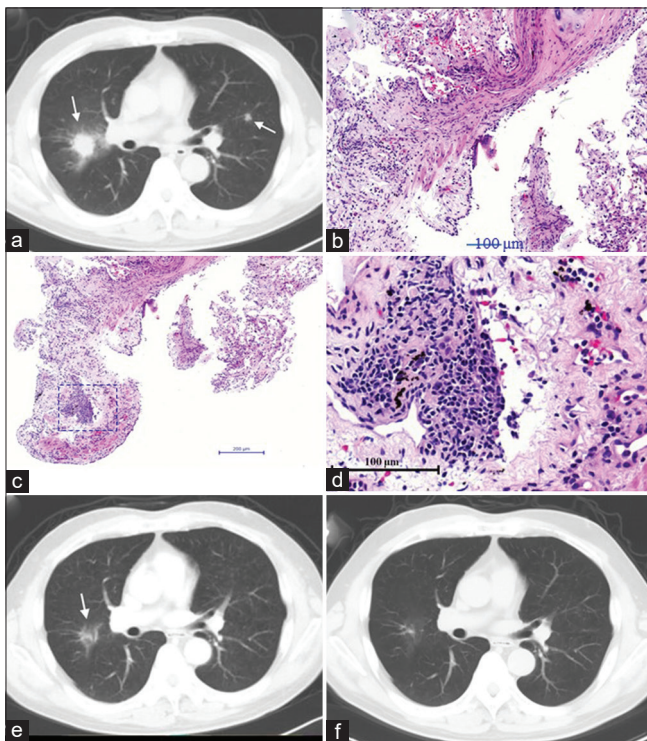


Figure 1: Computed tomography (CT) scans and stained histopathological sections of the chest before and after discontinuation of the suspected medicine. (a) CT scan during treatment with herbal medicine (HM). (b, c, and d) Hematoxylin and eosin-stained tissue from the bronchoscopic biopsy. (e) CT scan, 3 months after discontinuing HM. (f) CT scan, 6 months after discontinuing HM

The HM was discontinued; subsequently, the multiple nodules gradually decreased in size and some disappeared. The chest CT scan 3 months after the discontinuation of the HM revealed shrinkage of multiple nodular lesions [Figure 1e]. All the lesions fully disappeared, as observed in the latest CT scan of the chest 6 months after the discontinuation of HM [Figure 1f]. The definitive diagnosis was HM-induced multiple lung pseudotumor.

Discussion

Japanese physicians can prescribe 148 types of HM, which are covered under the National Health Insurance System. HMs cause a variety of clinical ADRs, although severe ADRs are not frequent. The most common ADR of HM is hypokalemia, caused by medicines containing licorice.^[5-7] The most severe ADR associated with HM is interstitial pneumonia, caused by the combination therapy of interferon- β and Shosaikoto (which contains the following crude drugs: JP Bupleurum Root, JP Pinellia Tuber, JP Scutellaria root, JP Jujube, JP Ginseng, JP Glycyrrhiza, and JP Ginger).^[4,8] A crude drug of Scutellaria root is suspected as a cause of HM-induced pneumonitis;^[9] however, Keishikajutsu does not contain Scutellaria root. Furthermore, HM-induced pneumonitis manifests as interstitial pneumonia, and there are no reports of multiple lung nodular lesions caused by HM. In this case, the histopathological evaluation of the bronchoscopically extracted specimen revealed no cellular dysplasia. The multiple lesions completely disappeared after discontinuing the suspected medicine, and nodular lesions were confirmed not to be metastatic lung cancer.

Primary care physicians have many opportunities to treat patients with lung nodules. They also have opportunities to prescribe HMs or treat patients who have taken HMs in clinical practice.^[10-14] If the patient started new drugs such as HMs before the appearance of lung lesions, an ADR should be one of the differential diagnoses. If physicians incidentally identify such multiple nodular lesions without clinical symptoms, systemic inflammation, or signs of malignancy in a patient, the history of drug use should be reviewed. In such cases, before considering surgical interventions, the suspected drugs should be discontinued. Based on this case report, we alert physicians to the fact that ADRs caused by HM can mimic end-stage metastatic lung cancer. When a patient presents with multiple lung nodules, a side effect of HM should be considered as a differential diagnosis.

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Conflicts of interest

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