

# A Case of Spontaneous Regression of Hepatocellular Carcinoma with Multiple Lung Metastases

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Spontaneous regression of hepatocellular carcinoma (HCC) is a rare phenomenon. We present herein the case of a patient with hepatocellular carcinoma with multiple lung metastases in whom malignancy spontaneously regressed after taking *Phellinus linteus Mycelium*. A 79-year-old man consulted our hospital complaining of epigastric discomfort. Abdominal MRI and CT revealed a 3 cm diameter tumor in the liver, and chest CT showed numerous nodular lesions. The levels of alpha-fetoprotein (AFP) and protein induced by vitamin K deficiency or antagonist-II (PIVKA-II) were very high. We diagnosed HCC with multiple lung metastases, and no therapy was performed. Independently he took exact from *Phellinus linteus Mycelium* for one month, and 6 months later the tumors appeared to be in complete regression. The mechanism underlying this intriguing phenomenon remains unknown.

**Key words:** cancer, hepatocellular carcinoma, computed tomography, magnetic resonance imaging, spontaneous regression, *Phellinus linteus Mycelium*

## INTRODUCTION

SPONTANEOUS REGRESSION OF MALIGNANT TUMOR IS considered a rare phenomenon, occurring in one of every 60,000–100,000 cases.<sup>1</sup> We present herein the case of a patient with hepatocellular carcinoma (HCC) with multiple lung metastases in whom malignancy spontaneously regressed after his taking *Phellinus linteus Mycelium*. A total of 47 cases of spontaneously regressed HCC have been reported, but the underlying mechanisms have yet to be elucidated.<sup>2</sup> More reports on such cases should help to clarify the mechanisms behind spontaneous regression of cancers and facilitate the establishment of novel anticancer therapies.

## CASE

Patient: A 79-year-old man  
Chief complaint: Epigastric discomfort

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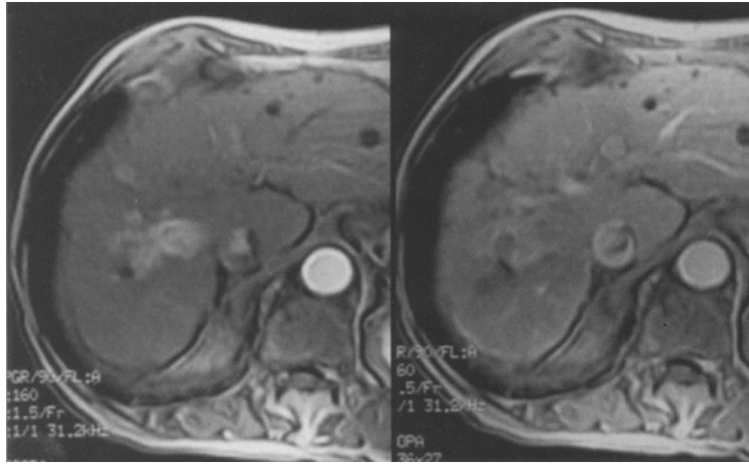
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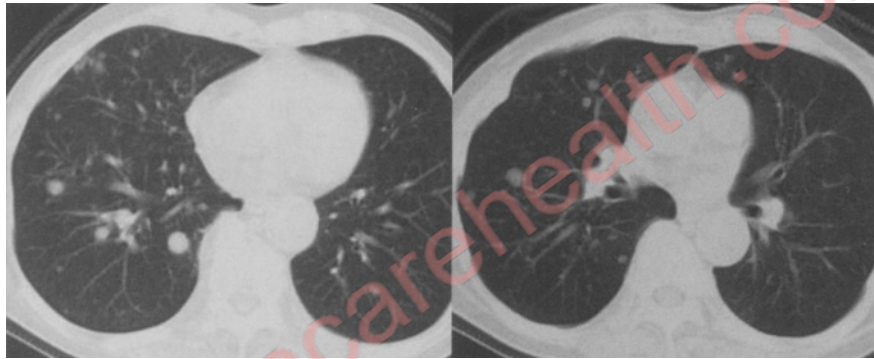
History of present illness: The patient suffered from chronic hepatitis C and liver cirrhosis. In 2000, HCC was detected in the S8 region, and percutaneous microwave coagulation therapy (PMCT) was performed. In 2002, HCC recurred in the same area, and PMCT was performed in April 2002, followed by transcatheter arterial chemoembolization (TACE) in August 2002. The patient was subsequently followed up, and recurrence was suspected in March 2003. The patient was referred to our department for thorough examination and treatment.

Laboratory data on initial presentation were as follows: RBC,  $401 \times 10^4/\mu\text{l}$ ; Hb, 13.2 g/dl; WBC, 3,600/ $\mu\text{l}$ ; PLT,  $11.9 \times 10^4/\mu\text{l}$ ; T-Bil, 0.7 mg/dl; GOT, 63 U/l; GPT, 49 U/l; LDH, 211 U/l; ChE, 69 U/l; TP, 7.8 g/dl; ALB, 4.1 g/dl; PT activity, 105%; and APTT, 25.3 sec; no ascites; no hepatic encephalopathy. Hepatic function was classified as Child A. Levels of hepatic tumor markers were markedly high: alpha-fetoprotein (AFP) was 10,101 ng/dl (reference value: 10.0 ng/dl), and protein induced by vitamin K deficiency or antagonist-II (PIVKA-II) was 5,114 AU/l (reference value: 40 AU/l). HBV antigen was negative, while anti-HCV antibody was positive.

Abdominal dynamic enhanced magnetic resonance imaging (MRI) showed that a 3 cm diameter tumor was present in the S8 region in the arterial phase, and a



**Fig. 1. Abdominal dynamic enhanced MRI.**  
**In the arterial phase, an intensely stained lesion with a diameter of approximately 3 cm is apparent.**  
**In the portal phase, a branch-like low-intensity area is observed, suggesting HCC accompanied with portal thrombus.**



**Fig. 2. Plain chest CT.**  
**Semicircular nodular lesions are apparent in both lung fields, suggesting multiple lung metastases.**

branch-like low intensity area was observed in the portal phase, suggesting HCC accompanied with portal thrombus (Fig. 1). Dynamic enhanced CT also showed findings that accorded with the MRI findings, compatible with HCC. Chest CT showed numerous well-defined nodules in both lung fields, thus suggesting multiple lung metastases (Fig. 2).

Based on the above findings, HCC with multiple lung metastases was diagnosed. The presence of multiple lung metastases contraindicated invasive therapy, and conservative therapy was recommended.

The patient underwent follow-up with a local physician, but received no therapy for HCC. Independently, the patient took exact from *Phellinus linteus* (*P. linteus*) *Mycelium* (Meshima EX powder, LS Medical, Tokyo, Japan) 3.3 g a day for one month. Six months later, abdominal dynamic enhanced MRI indicated disappearance of the tumor in the S8 region and no signs indicative

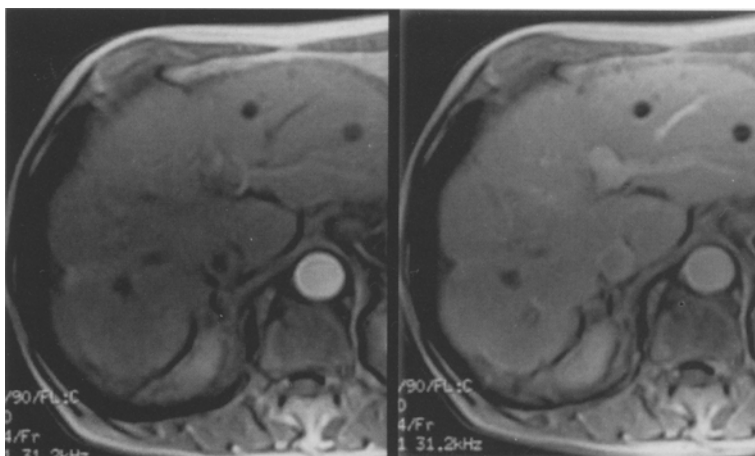
of HCC (Fig. 3). Similarly, dynamic enhanced CT also showed no signs of HCC, in accordance with MRI.

In addition, plain chest CT showed that the nodular lesions had disappeared (Fig. 4). Furthermore, levels of the HCC markers AFP and PIVKA-II were markedly high on the initial visit, but had decreased to 13.2 ng/dl and 18 AU/l, respectively, as of 6 months later, as the primary lesion and lung metastases regressed (Table 1).

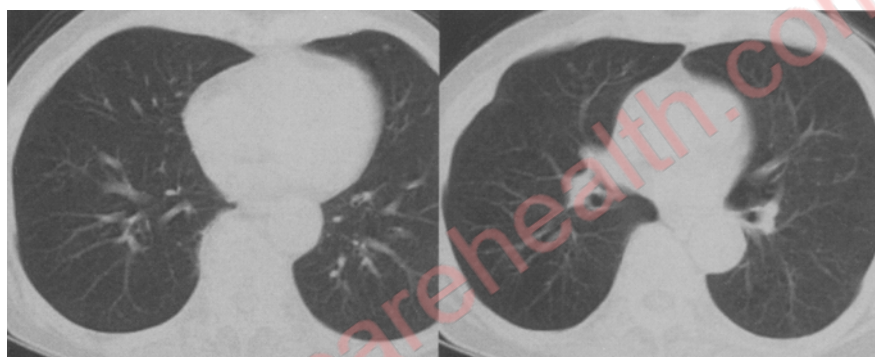
The patient is currently being followed up on an outpatient basis, and no imaging findings indicative of recurrent HCC or lung metastasis have been noted as of 10 months after his first visit to our hospital. Similarly, levels of the HCC markers have not increased.

## DISCUSSION

Spontaneous regression of malignant cancer was first proposed by Everson and Cole in 1966, and spontaneous



**Fig. 3. Abdominal dynamic enhanced MRI 6 months later.**  
**In the arterial phase, the intensely stained lesion in the S8 region has disappeared, and no signs indicative of HCC are apparent in the liver.**



**Fig. 4. Plain chest CT 6 months later.**  
**The multiple nodular lesions seen at the initial presentation have disappeared.**

**Table 1. Shifts in tumor markers**

	Mar 6, 2003	Aug 21, 2003	Mar 16, 2004	Sep 2, 2004
AFP (ng/ml)	10,101	13.2	13.6	12.9
PIVKA II (AU/ml)	5,114	18.0	16.0	18.0



Oral administration of *P. linteus*

While levels of tumor markers were markedly high on initial presentation, levels decreased almost to the normal range as the tumor regressed 6 months later. Levels of tumor markers have not increased since then.

regression of cancer was defined as a partial or complete disappearance of malignant tumor without any treatment thought to offer a potential cure for cancer. The incidence of spontaneous regression of malignant cancer is one in every 60,000-100,000 cases.<sup>1</sup> According to a 2004 study by Kato *et al.*, 47 cases of spontaneous regression of HCC had been documented, including their patient. In

7 of those cases, lung metastases also disappeared.<sup>2</sup> In 2001, Ikeda *et al.* reviewed 34 cases of spontaneous regression of HCC and reported that spontaneous regression of HCC tended to occur in men >60 years old with chronic liver disease, giant tumor, and increased levels of AFP.<sup>3</sup> Except for tumor size, the present patient satisfied all these characteristics.

In regard to the cause of spontaneous regression of HCC, external factors such as the followings may be involved: gastrointestinal bleeding; ischemic tumor changes due to catheterization during angiography; massive blood transfusion; steroid administration; discontinuation of hormone preparations, including oral contraceptives; use of herbs and Chinese medicine; trauma; surgery; and biopsy. However, the details of spontaneous regression remain unknown.<sup>4</sup>

Nakai *et al.* reported the case of a patient with HCC that increased in size after TACE and 16 months later regressed spontaneously without treatment. An immunological investigation was conducted into the relationship between spontaneous regression and increased NK cell markers.<sup>5</sup> In addition, Abiru *et al.* considered that relationships between spontaneous regression and increased IL-8 were attributable to enhanced T- and NK-cell activities.<sup>6</sup> In the present patient, the HCC that recurred after TACE regressed spontaneously without any anticancer therapy, suggesting the involvement of immunological mechanisms. In recent years, there have been many studies of tumor immunological mechanisms, and HCC resistance to apoptosis of hepatoma has been demonstrated. Expression of the Fas receptor, which may induce apoptosis, is thought to decrease or disappear. In addition to abnormality of the Fas receptor, in this case the activation of apoptosis may have contributed to the spontaneous regression.<sup>7</sup> In addition, spontaneous regression in the present patient may be attributable to the antitumor effects of *P. linteus Mycelium*, which the patient independently decided to take.

*P. linteus Mycelium* is a type of mushroom belonging to the black hoof fungus family that grows on mulberry trees, and the active ingredient is B-glucan. Different strains of *P. linteus* exist (strains PL2 and PL5 are considered most potent), and the mushroom is grown in different regions.<sup>8</sup> *P. linteus* is considered to possess some antitumor properties and to activate the immune system. In 1968, *P. linteus* was shown to suppress tumor proliferation in mice grafted with cancer cells. In addition, *P. linteus* reportedly acts to markedly activate cellular and humoral immunities by enhancing the function of macrophages, T lymphocytes, and B lymphocytes, to prevent cancer proliferation and metastasis in a non-toxic manner.<sup>9-11</sup> However, no relationship between *P. linteus* and the regression of HCC has been reported.

In recent years, the mass media have reported the use of folk remedies including *Agaricus*, *Curcuma*, and *Phellinus*, in patients with terminal malignant cancer, but no conclusive evidence supports the efficacy of these remedies. However, as with the present patient, some patients may respond to this type of therapy. Determination of the efficacy of folk remedies, identification of adverse reactions, and assessment of combined use with conventional treatments are required.

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## CONCLUSION

We have described herein the case of a patient in whom HCC with multiple lung metastases spontaneously regressed. Regression could have been attributable to the antitumor effects of *P. linteus*.

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