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DOI:
10.14744/ejp.2023.4007

Pulmonary embolism as the first sign of hepatocellular carcinoma in a patient who was cured after five years

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Abstract:

Pulmonary embolism (PE) is a preventable cause of death associated with high morbidity and mortality rates. Cancer is a significant risk factor for PE. In this case report, we present a patient with PE who was diagnosed with hepatocellular carcinoma (HCC) one month later. The patient had an unresectable tumor in the liver that had invaded both the inferior vena cava and the right atrium. He underwent transarterial chemoembolization (TACE) and sorafenib treatment. After two years, he underwent stereotactic radiosurgery, and he was switched to regorafenib. After five years, he was cured. This case is unique in terms of long survival compared to the literature.

Keywords:

Hepatocellular carcinoma, long survival, pulmonary embolism

Introduction

Venous thromboembolism (VTE), manifested as deep vein thrombosis (DVT) or pulmonary embolism (PE), is the third most common acute cardiovascular syndrome, posing a significant risk of morbidity and mortality if not promptly treated.^[1] Cancer, particularly the presence of metastases, is categorized as a moderate risk factor for VTE, and sometimes VTE can be the initial manifestation of cancer.^[1] Liver cancer ranks as the fifth most prevalent cancer globally, with hepatocellular carcinoma (HCC) car-

rying the highest mortality rate among liver cancers. The presence of thrombi in the portal or hepatic veins indicates advanced liver cancer, while pulmonary thromboembolism (PTE) is a rare condition and only a few reported cases.^[2]

The mortality is very high in patients with HCC and PE and survival is limited in only a few months according to the published literature. However, in this report, we present a case of a patient diagnosed with acute PE and HCC, who not only survived for five years but also achieved a cure of the disease.

How to cite this article: Esendağlı D, Rahatlı S, Hekimoğlu K, Savaş Bozbaş Ş. Pulmonary embolism as the first sign of hepatocellular carcinoma in a patient who was cured after five years. *Eurasian J Pulmonol* 2023;25:141-144.

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Received: 15-05-2023
Accepted: 19-06-2023
Published: 12-07-2023

Case Report

A 67-year-old man was admitted to the emergency department with shortness of breath and swelling in his right leg. His vital signs were as follows: respiratory rate 22 breaths/minute, heart rate 96 beats/minute, mild hypoxemia (peripheral capillary oxygen saturation (SpO₂) 92%), and blood pressure 140/80 mmHg. Laboratory findings revealed a high D-dimer level (5.71 mg/mL, normal value <0.44), high troponin-I (0.317 ng/mL, normal value <0.034), and a total bilirubin value of 1.38 mg/dL (normal range 0.2–1.2), whereas the other values were normal. He had a history of diabetes mellitus, coronary artery bypass graft surgery, and cholecystectomy. PE was suspected, and a computed tomography scan (CT) was performed, which showed a massive thrombus in the right pulmonary artery and a partial thrombus in the left pulmonary artery. Dense thrombus was observed in both lobar and segmental branches [Fig. 1]. Echocardiography revealed a mean pulmonary artery pressure of 55 mmHg, and the right ventricle was dilated, associated with moderate impairment of systolic function. Venous Doppler ultrasound did not reveal deep venous thrombosis in the lower extremities. The patient received an unfractionated heparin infusion, and activated partial thromboplastin time (APTT) was monitored. He was discharged six days later with an adjusted dosage of warfarin.

After one month of oral anticoagulation, he complained of anorexia and weakness, and angiography of the abdomen and thorax (CT) was performed to detect additional pathology. A mass (44×14 mm) was noted in the right hepatic lobe, and thrombus formation in the right hepatic vein was observed. Magnetic resonance imaging (MRI) also showed thrombus in the inferior vena cava and right atrium [Fig. 2].

The patient's radiological findings were typical of HCC, and the tumor was considered inoperable. Serum alpha-fetoprotein (AFP) levels were elevated to 115.25 IU/ml (normal range 0.89–8.78). He was started on sorafenib treatment (2×400 mg/day), and anticoagulation was continued with low molecular weight heparin (LMWH). At follow-up, a normal AFP level was measured.

After two years of treatment, a growing lymphadenopathy was detected near the right renal artery, and this finding was defined as disease progression because the AFP increased to 76.95 IU/ml. Due to the progression of

the disease, the patient was switched from sorafenib to regorafenib and continued for 20 months. However, due to intolerance of the drug by the patient, the treatment was discontinued. After 16 months of follow-up without any treatment, radiological examinations showed no evidence of recurrence or disease progression. The AFP level was 2.98 IU/mL, and the patient is alive and well at the 60th month after HCC diagnosis.

Discussion

This case report presents a patient with PE as the first sign of HCC. Malignancy itself is a risk factor for PE, and studies have shown an increased risk of cancer, especially within one year of the diagnosis of DVT or PE, compared with the general population.^[1] Our patient had no history of liver disease, and DVT was not present at the time of PE diagnosis. Studies have shown that the presence of liver disease confers a twofold increased risk of cancer, and in particular, the presence of cirrhosis in patients with a history of VTE increases the risk of cancer within one year by 4.3% compared with noncirrhotic liver disease, which was calculated to be 2.7%.^[3,4]

On the other hand, the risk of cancer after unprovoked venous thrombosis was calculated to be 4.5–5.06% in the EPIGETBO and SOME studies.^[4,5] Early detection of cancer could allow for early treatment and a better prognosis. Therefore, there is still a fierce debate about whether advanced screening for occult tumors should be performed in all patients with unprovoked VTE.

The presence of PE in HCC patients is a rare condition, and according to our literature search, this condition is mainly highlighted by case reports, totaling 30 as of June 2022.^[6,7] The patients are predominantly male, and their ages range from 16 to 83 years.^[6]

Another condition associated with HCC is the presence of thrombus in the inferior vena cava (IVC) and right atrium (RA), which is also rare and reported in 1.4–4.9% of cases.^[8] Interestingly, our patient did not have a mass or thrombus on echocardiography at the time of the PE diagnosis, but it was discovered one month later. The prognosis for patients with IVC and RA thrombus is usually poor due to the risk of cardiac arrest and acute PE. The origin of the thrombus is usually considered to be a tumor thrombus because tumor cells have invaded the veins, and PE could

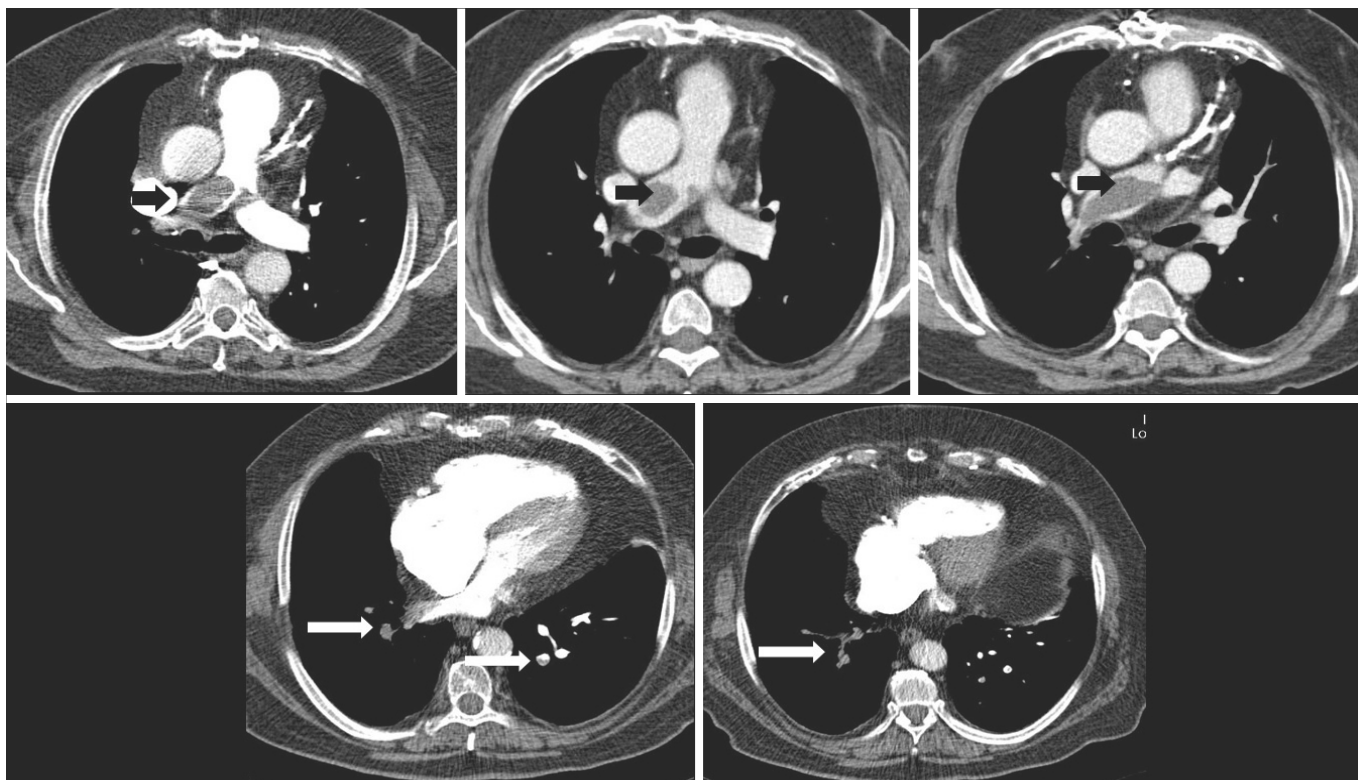


Figure 1: CT angiography showing the massive thrombus in the right pulmonary artery and bilateral segmental braches (black and white arrows, respectively)
CT: Computed tomography

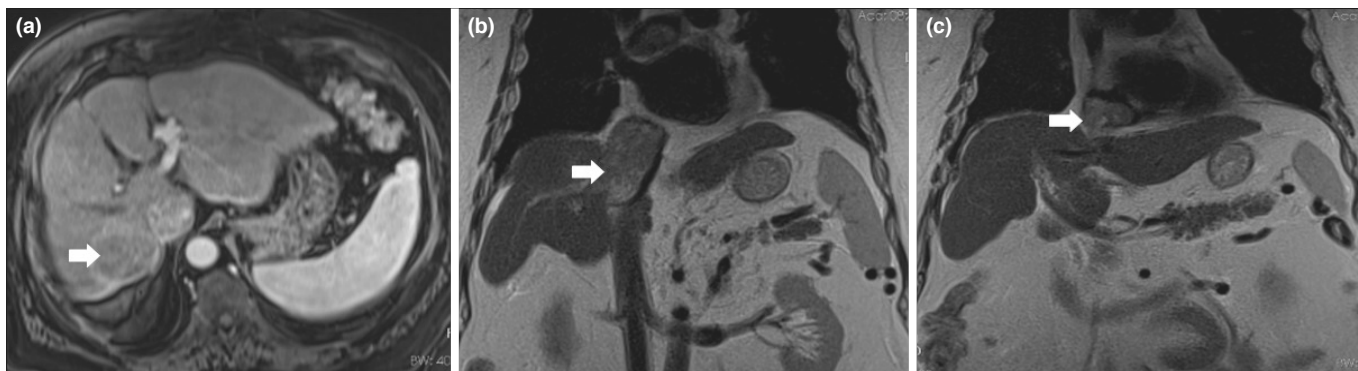


Figure 2: (a) The mass in the liver and (b) thrombus in the inferior vena cava, and (c) the right atrium

be a consequence of metastatic tumor embolism. On the other hand, cancer itself may cause a hypercoagulable state, leading to secondary tumor thrombosis.

The life expectancy of patients with HCC with vascular invasion is short (usually 1–5 months without surgery), and the longest reported survival^[2] was 26 months. There is still no standard therapy for HCC with IVC invasion, and surgery is not an option for most patients. Therefore, Transarterial Chemoembolization (TACE) is another

therapeutic option, especially in selected patients, with median overall survival of up to 14 months.^[9]

The recommended antiangiogenic drug is sorafenib, which acts on tyrosine kinase inhibitors, whereas regorafenib is an oral diphenylurea multikinase inhibitor that also targets many kinases involved in angiogenic and tumor growth-promoting pathways. Regorafenib has shown a significant survival benefit as second-line therapy in patients with unresectable HCC.^[10]

The patient is still alive with no evidence of recurrence or progression of cancer and continues to receive anticoagulation due to chronic thrombus in the inferior vena cava and branches of the pulmonary artery. This case report is the first to demonstrated such long survival in a patient with PE, HCC with hepatic vein, IVC, and right atrial invasion, highlighting the importance of early PE diagnosis and multimodal therapeutic treatment that could influence overall survival.

Informed Consent

Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

Conflicts of interest

There are no conflicts of interest.

Financial support and sponsorship

Nil.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept – D.E., Ş.S.B.; Design – D.E., Ş.S.B.; Supervision – Ş.S.B., S.R., K.H.; Funding – D.E.; Materials – Ş.S.B.; Data collection &/or processing – D.E., S.R., K.H., Ş.S.B.; Analysis and/or interpretation – D.E., S.R., K.H., Ş.S.B.; Literature search – D.E.; Writing – D.E., Ş.S.B.; Critical review – D.E., S.R., K.H., Ş.S.B.

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