

# CONCOMITANT HEPATOCELLULAR CARCINOMA AND LIPOSARCOMA IN A PETROCHEMICAL INDUSTRY WORKER: A CASE REPORT

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**ABSTRACT** This case report presents a unique and unreported association between synchronous hepatocellular carcinoma (HCC) and liposarcoma in a 30-year-old male petrochemical industry worker. The patient's main concerns were asymptomatic hyperferritinemia and isolated high gamma-glutamyl transferase levels. Clinical findings revealed mild hepatic steatosis, nonspecific nodular images, and fibrosis grade F4 on imaging and elastography. Further investigations confirmed the presence of HCC and subsequent liposarcoma in different organs. The patient underwent SIVB-VI hepatectomy followed by a nephrectomy to remove the tumors. The case report adds to the scientific literature by presenting a clinical scenario that has never been described before—the synchronous occurrence of HCC and liposarcoma in a patient with occupational risk exposure to aromatic organic compounds. The patient's occupation, along with other risk factors such as alcohol consumption, cirrhosis, and dyslipidemia, may have contributed to the development of these tumors. This report underscores the need for further research with larger sample sizes and extended follow-up periods to better understand the underlying mechanisms and outcomes associated with multiple primary neoplasms. The findings emphasize the significance of environmental and occupational chemical exposure as potential risk factors for developing HCC and numerous primary malignancies. Enhanced knowledge in this area can improve clinical understanding and inform optimal treatment approaches for patients with similar presentations.

**KEYWORDS** Hepatocellular Carcinoma, Liposarcoma, Multiple Primary Malignancies, Case Report

## Introduction

Hepatocellular carcinoma (HCC) represents a significant burden in global cancer incidence, representing 70-80% of primary liver neoplasms, and is one of the most common malignant tumors in the world[1]. Common risk factors associated with HCC include liver cirrhosis, chronic infection with hepatitis B and C viruses, chronic alcohol consumption, and hemochromatosis[2]. More-

over, individuals exposed to chemical compounds, such as those working in the petrochemical industry, may be at an increased risk of developing liver cancer due to their occupational exposure to arsenic products, vinyl chlorides, formaldehyde, and organic solvents[3-5].

In recent years, there has been a growing recognition of Multiple Primary Malignancies (MPMs), defined as two or more malignancies without subordinate relationships detected in different organs of an individual patient[6]. The emergence of MPMs has been attributed to various factors, including advancements in cancer detection, improved survival rates, and aging populations[7,8]. As a result, there has been an observed increase in the prevalence of multiple primary malignancies (MPMs) in Western countries by 10%[9]. Notably, studies have shown that liver cancer was frequently diagnosed alongside other primary malignant tumors, constituting a substantial proportion of

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MPM cases[10]. Despite the growing prevalence of MPMs with hepatocellular carcinoma, the concomitant association between hepatocellular carcinoma and liposarcoma has never been reported in the literature. This case report presents a 30-year-old male petrochemical industry worker with a previous medical history of alcohol consumption, dyslipidemia and mild hepatic steatosis, initially evaluated for asymptomatic hyperferritinemia. Subsequent investigations led to the unexpected discovery of synchronous hepatocellular carcinoma and liposarcoma. This case report highlights a clinical scenario that has never been described, contributing valuable insights into understanding multiple primary neoplasms and exploring optimal treatment approaches for patients with similar presentations. The present study adheres to the CARE guidelines.

## Case report

A 30-year-old male patient, a long-term petrochemical industry worker, with a previous medical history of alcohol consumption, dyslipidemia and mild hepatic steatosis, without a family history of cancer or hepatopathy, came up to the specialized hepatology service asymptomatic but with an isolated high level of gamma-glutamyl transferase (365 U/L) and hyperferritinemia (1650 ng/mL). No abnormalities in the physical examination were found. The Hemochromatosis Gene (HFE) test was negative. Further exams reported low serum ceruloplasmin levels (15 mg/dL). Hepatic transaminases, alkaline phosphatase, total bilirubin, and alpha-1-antitrypsin were within normal limits, and autoantibody screening was negative.

The first abdominal ultrasonography (USG) revealed mild hepatic steatosis without signs of hepatic iron overload and non-specific nodular images with slightly blunt margins and mildly undulating contours measuring approximately 1.5 centimeters (Figure 1). Acoustic Radiation Force Impulse (ARFI) Elastography revealed fibrosis grade F4, hepatic stiffness of 11 kPa, an indeterminate nodule measuring 1.7 centimeters and multiple hepatic cysts.

Therefore, to better evaluate the nature of the observed nodules and hepatic cysts, four months later, an abdominal computed tomography (CT) and hepatic biopsy were performed, which revealed a hypervascular nodule without washout measuring 2.1 centimeters, in segment IV, with slight capsular enhancement. Additionally, signs of chronic hepatopathy and incipient signs of recanalization of the paraumbilical vein were observed. New laboratory tests showed a slight decrease in hyperferritinemia (939 ng/mL) and gamma-glutamyl transferase (228 U/L), as well as the permanence of low serum ceruloplasmin levels (16 mg/dL), low serum copper (62 mcg/dL) and low free copper (9 mcg/dL). Five months after the first appointment, the patient underwent an upper gastrointestinal endoscopy (UGIE), which revealed no gastroesophageal varices and exanthematous gastritis further to investigate portal hypertension secondary to chronic liver disease. After discussion with a multidisciplinary team, it was proposed that an SIVB-VI hepatectomy be performed.

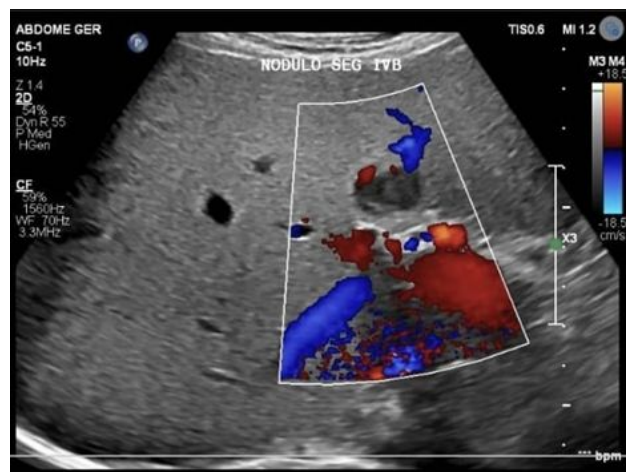
Six months after the first appointment, the patient underwent the procedure, which went well without complications. In the postoperative period, the patient experienced weight loss. The sample obtained during the process confirmed a well-differentiated HCC measuring 1.5 centimeters, without vascular or perineural invasion, and with clear margins of 0.2 centimeters. The hepatic parenchyma showed cirrhosis, mild interface activity, and portal and septal lymphomononuclear infiltrate. The

anatomopathological report described the lesion as trabecular and pseudoacinar HCC, biliary pattern cirrhosis, portal fibrosis with thick intraportal sept, and mild to moderate iron overload.

In the first postoperative month, the patient presented laboratory tests that showed mixed dyslipidemia, with no substantial changes in other tests compared to previous ones. Therefore, it was decided to prescribe Ezetimibe 10 mg in combination with Simvastatin 20 mg. For the postoperative evaluation, the patient performed an abdominal MRI that revealed a 4-centimeter renal nodule suspected to be a primary renal tumor (Figure 2). The patient was referred for a biopsy that revealed an undifferentiated liposarcoma. So, the patient underwent additional surgery to remove the cancer. The surgery underwent a nephrectomy without complications, and the liposarcoma, measuring 7 centimeters with involved margins, was removed.

In the fifth postoperative month of the first surgery, the patient performed a new abdominal MRI, which showed a residual lesion in the right kidney and a small arterial focus in segment VIII without representation in other phases (LIRADS 3). In addition, the laboratory tests showed significant decreases in ferritin levels (365 ng/mL) and gamma-glutamyl transferase (97 U/L).

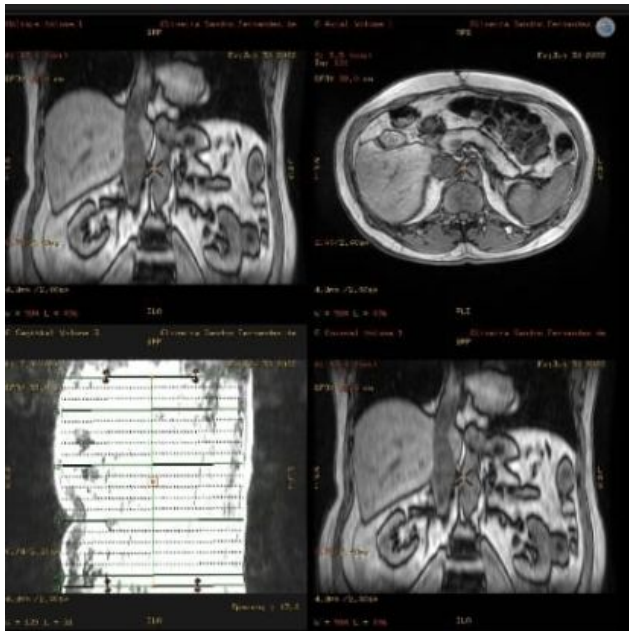
In the eighth postoperative month of the first surgery, the patient returned for a new consultation with a weight loss of 9 kilograms since the beginning of the follow-up. The abdominal ultrasound did not find nodules but identified signs of previous hepatic surgical manipulation, cholecystectomy, and nephrectomy. Laboratory tests were within normal ranges, except for increased serum creatinine (1.9 mg/dL). The patient is still alive and performing cancer screening annually.



**Figure 1:** Abdominal ultrasonography (USG) revealing suggestive findings of advanced compensated chronic liver disease and a mild hepatic steatosis compatible with the degree of F4 hepatic fibrosis by the METAVIR score, a hypoechoic nodule in the left hepatic lobe and a small cyst in the right hepatic lobe.

## Discussion

This case report demonstrates synchronous primary neoplasms in two different organs in a patient who works in a petrochemical company, thus having high exposure to aromatic organic compounds. This presentation of synchronous MPM of HCC and liposarcoma has not been described in the literature before, which makes the case even more relevant. Our first impression



**Figure 2:** An Upper Abdomen MRI evidencing a 4-centimeter expansive formation with a solid hypovascular appearance in the middle/lower third of the left kidney, with suspicious characteristics of a neoplastic lesion.

of a patient with a high risk of environmental exposure, alcohol consumption, compensated cirrhosis with no established cause, mild steatosis, hyperferritinemia without iron overload, and low serum ceruloplasmin levels. So, the patient's occupation significantly increases the likelihood of his condition's aetiology being related to benzene's carcinogenic effects (chronic benzene intoxication) or exposure to other harmful substances such as ethylene, propylene, and polyethylene[11,12].

According to the World Health Organization, approximately 80% of neoplasms are related to environmental factors[11] as well multiple primary malignancies (MPM) have also been associated with various factors environmental exposure factors[13]. Also, occupational exposure to chemicals is considered a potential risk factor for developing HCC[14]. However, due to the limited number of studies, uncertainties in accurately diagnosing liver cancer, and the influence of confounding factors like alcohol consumption, the exact contribution of occupational chemical exposure to HCC and MPM development remains unclear[14,15]. Therefore, contextualized with our study, even with work exposure, it's essential to consider that the patient presented multiple other risk factors, such as alcohol consumption, cirrhosis and dyslipidemia.

In recent years, there has been an increase in the publication of case reports and small studies on MPMs involving HCC[16–18]. However, previous studies have reported different patterns of extra-hepatic malignancies in patients with MPM and HCC, such as lung, colorectal, breast and thyroid cancers, which differed from the present study's findings [10,16,18–20]. Our patient showed up with HCC and synchronous renal dedifferentiated liposarcoma. Synchronous tumors occur when the second primary cancer is diagnosed within six months of initial cancer, while metachronous tumors occur when the second primary cancer is diagnosed more than six months after the diagnosis of the first primary cancer[21]. Renal presentation of liposar-

coma is a very rare and aggressive condition, which develops in 1–2% of sarcoma cases, where most published cases involve well-differentiated tumors[22]. Distinct areas of nonlipogenic sarcomatous tissue characterize dedifferentiated liposarcoma within a well-differentiated tumor[23]. Due to the limited number of cases in the literature, other features, such as predictors and prognosis of primary kidney dedifferentiated liposarcoma, have not been extensively studied[22].

One study with MPM patients who underwent radical resections for HCC describes a higher risk of HCC-related mortality, and the tumor size was identified as the sole independent predictor for overall survival (OS) in MPM patients[10]. Therefore, strict follow-up is crucial for patients who have recovered from their initial malignancy, as it can improve long-term survival prospects. Otherwise, screening for other potential malignancies in cancer survivors based on the most common sites is challenging. This difficulty arises from the variable distribution of extra-hepatic malignancies, the lack of statistical evidence supporting enrichment patterns, and the unexpected dedifferentiated liposarcoma in the kidney.

There is no standard treatment for MPM. So, we conducted the case by treating the two pathologies separately. Considering that curative therapies have significantly enhanced the expected survival rates of patients with HCC and cirrhosis[24], we first opted to perform an SIVB-VI hepatectomy in our case. Three months after the first diagnosis, a second diagnosis of renal liposarcoma came, and we chose a curative therapy with nephrectomy. Multiple primary tumor resections may be reasonable in this case. We must consider several limitations in our study. First, further investigations with larger sample sizes are necessary to provide more robust evidence. Secondly, even with a strong hypothesis of a working exposition, we could not give a detailed explanation for the mechanism of multiple primary tumors. Therefore, additional basic research is needed to elucidate the underlying mechanisms. Thirdly, the follow-up time for our patient was limited, and more extended follow-up periods were required to assess the long-term outcomes. Despite these limitations, our study improves the clinical understanding of multiple primary cancers by reporting this tumor association for the first time and identifying potential risk factors.

## Conclusion

This case report presents a unique and previously unreported association of synchronous hepatocellular carcinoma (HCC) and liposarcoma in a patient with occupational exposure to aromatic organic compounds. The patient's occupation, along with other risk factors such as alcohol consumption, cirrhosis, and dyslipidemia, may have contributed to the development of these tumors. Environmental and occupational exposures to chemicals are known to increase the risk of HCC, but the precise role of such disclosure in MPM development remains unclear. The findings emphasize the importance of comprehensive screening and follow-up for patients with HCC after surgical resection, as the occurrence of synchronous tumors in different organs can impact prognosis and treatment decisions. Further research with larger sample sizes and extended follow-up periods is needed to enhance our understanding of the underlying mechanisms and outcomes associated with multiple primary neoplasms.

## Informed Consent:

Written informed consent was obtained from all the participants.

## Ethics Committee Approval

According ethics consent.

## Conflict of Interest:

No potential conflict of interest relevant to this article was reported.

## Authorship Principles:

All authors contributed to the study's conception and design. MENA, BBF, GMN and PRO contributed to developing, acquiring data, drafting, and revising the manuscript. MENA and LRL wrote the first draft of the manuscript, and all authors commented on previous versions. All authors read and approved the final manuscript.

## Research involving human participants, their data or biological material:

This is an observational case report with complete deidentification. So, ethics approval was optional for this type of case report at our institution.

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