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www.wjgnet.com
wjg@wjgnet.com

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*CASE REPORT*

# Patient with hepatocellular carcinoma related to prior acute arsenic intoxication and occult HBV: Epidemiological, clinical and therapeutic results after 14 years of follow-up

Teresa Casanovas-Taltavull, Josepa Ribes, Ana Berrozpe, Sara Jordan, Aurora Casanova, Concha Sancho, Carles Valls, F Xavier Bosch

Teresa Casanovas-Taltavull, Ana Berrozpe, Sara Jordan, Department of Gastroenterology , Hospital Universitari de Bellvitge, Feixa Llarga s/n, 08907 L'Hospitalet de Llobregat, Barcelona, Spain
Josepa Ribes, F Xavier Bosch, Epidemiology and Cancer Registration Unit, Institut Català d'Oncologia, Hospital Universitari de Bellvitge, Feixa Llarga s/n, 08907 L'Hospitalet de Llobregat, Barcelona, Spain
Aurora Casanova, Department of Microbiology, Hospital Universitari de Bellvitge, Feixa Llarga s/n, 08907 L'Hospitalet de Llobregat, Barcelona, Spain
Concha Sancho, Carles Valls, Department of Radiology. Hospital Universitari de Bellvitge, Feixa Llarga s/n, 08907 L' Hospitalet de Llobregat, Barcelona, Spain
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Correspondence to: Dr. Teresa Casanovas-Taltavull, Department of Gastroenterology, Hospital Universitari de Bellvitge, IDIBELL, Feixa Llarga s/n, 08907 L'Hospitalet de Llobregat, Barcelona, Spain. teresacasanovas@csub.scs.es
Telephone: +34-93-2607909 Fax: +34-93-2607603
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## Abstract

Little is known about the long-term survivors of acute arsenic intoxication. We present here a clinical case report of a man with chronic hepatitis B virus (HBV) infection who developed hepatocellular carcinoma four years after acute arsenic poisoning. HBsAg was detected in serum in 1990 when he voluntarily donated blood. In 1991, the patient suffered from severe psychological depression that led him to attempt suicide by massive ingestion of an arsenic-containing rodenticide. He survived with polyneuropathy and paralysis of the lower limbs, and has been wheelchair-bound since then. During participation in a follow-up study conducted among HBV carriers, abdominal ultrasound detected a two-centimeter liver mass consistent with hepatocellular carcinoma. The tumor was confirmed by computed tomography (CT) and magnetic resonance image (MRI). Because of his significant comorbidity, the patient received palliative treatment with transarterial lipiodol chemoembolization (TACE) on three occasions (1996, 1997 and 1999). At his most recent visit in May 2005, the patient was asymptomatic, liver enzymes were normal and the tumor was in remission on ultrasound.



**Key words**: HBV carriers; Occult HBV; HCC therapy; Arsenic intoxication

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## INTRODUCTION

Arsenic is a recognized human carcinogen established by the International Agency for Research on Cancer[1]. Chronic arsenic intoxication has been associated with skin lesions (such as hyperpigmentation, hyperkeratosis and carcinoma) and liver disease (non-cirrhotic portal hypertension, hepatocellular carcinoma and angiosarcoma). Moreover, chronic arsenic exposure is associated with a higher frequency of diabetes mellitus, ischemic heart disease and hypertension[2-4]. Epidemiological studies mainly involving cohorts of chronic arsenic-exposed subjects suggest that chronic arsenic intoxication increases the risk of developing liver cancer as compared with non-exposed populations[5,6].

Patients who survive the initial effects of acute arsenic exposure may develop peripheral neuropathy and encephalopathy[7]. Hepatic injury is uncommon but is associated with severe liver disease and high mortality[8]. Little is known about the long-term survivors of acute arsenic intoxication.

We present here a clinical case report of a Caucasian man with chronic hepatitis B virus (HBV) infection who developed hepatocellular carcinoma four years after acute arsenic poisoning.

## CASE REPORT

The man born in 1947 was obese with no HBV carriers

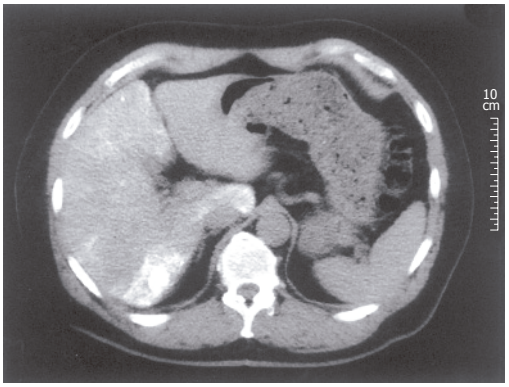


**Figure 1** Non-contrast CT one month after arterial chemoembolization with iodized oil (Lipiodol) and doxorubicine emulsion. CT shows a 2-cm nodule with dense Lipiodol enhancement in segment VI (arrow), consistent with hepatocellular carcinoma.

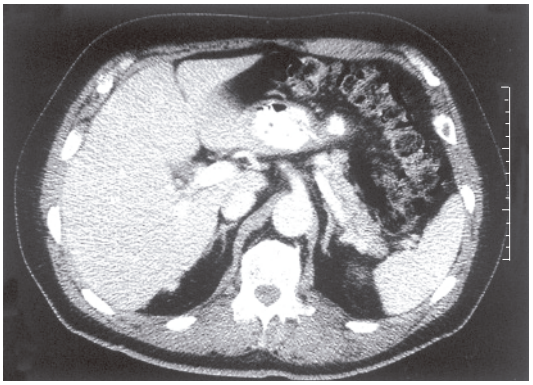

**Figure 2** Follow-up contrast-enhanced CT five years later from 1995 shows a small hypervascular lesion (arrow) in segment VI consistent with residual tumor. Tumoral Lipiodol retention was absent and the size of the lesion was significantly decreased.

in his family and no previous hepatitis or parenteral drug use. He was a heavy smoker and alcohol consumer before 1987. HBsAg was detected in serum in 1990 when he voluntarily donated blood.

In 1978 he had self-limited cardiac arrhythmia because of stress and in 1991 arrhythmia due to atrial fibrillation that reverted with cardioversion. In 1991, the patient suffered from severe psychological depression that led him to attempt suicide by massive ingestion of an arsenic-containing rodenticide. He developed acute renal failure and generalized paralysis and was hospitalized for 11 days in the intensive care unit, requiring assisted ventilation and chelation therapy with dimercaprol. He survived with polyneuropathy and paralysis of the lower limbs, and has been wheelchair-bound since then. In 1994 and 1995 he suffered from several transient ischemic attacks that were managed with chronic decoagulation therapy. In 2000 diabetes was diagnosed. He also required long-term treatment for sleep apnea-hypoapnea syndrome with automatic continuous positive airway pressure.

In November 1995 he was invited to participate in a follow-up study conducted in HBV carriers[9]. The viral serology results were negative for HBsAg, anti-HBs, HBeAg, IgM-anti-HBc, and positive for anti-HBe, IgG-anti-HBc. Serum HBV-DNA was negative by PCR technique, while anti-HDV, anti-HCV and anti-HIV were all negative. ALT was 1.36 μKat/mL (normal <0.5 μKat/mL), AST and alpha-fetoprotein were normal. Abdominal ultrasound detected a pattern suggestive of chronic liver disease and a liver mass two centimeters in diameter consistent with hepatocellular carcinoma. The tumor was confirmed by computed tomography (CT) scanning and magnetic resonance imaging. Because of his comorbidity, the patient was not considered eligible for liver transplant or hepatectomy. Palliative treatment with transarterial lipiodol chemoembolization (TACE) was performed on three occasions (1996, 1997 and 1999) (Figure 1) with clinical, analytical and imaging follow-up studies (Figure 2). At his last visit in May 2005, he was asymptomatic, liver enzymes were normal and the tumor was in remission on ultrasound imaging.

## DISCUSSION

To the best of our knowledge, this patient is the first known case of liver tumor developed after acute arsenic exposure. Standard chelation treatment for acute intoxication could not remove arsenic from intracellular sites because of its lipophobic nature, suggesting that this treatment cannot protect cells from long-term clinical consequences[10]. As has been described, the presence of intracellular arsenic may be related to the development of diabetes, arterial hypertension, ischemic arterial disease and liver cancer in such patients. It should also be taken into consideration that intraindividual variability in arsenic methylation can increase susceptibility to arsenic-induced cancer[11].

Given the fact that the patient was obese and had occult HBV infection (his anti-HBc and anti-HBe positive status could indicate integration of the virus in the host genome) prior to arsenic intake, we are not sure that some hepatic injury is not due to these risk factors[12,13]. The presence of these risk factors may enhance the hepatic lesion and the development of liver cancer.

Angiosarcoma is the type of liver tumor most often related with chronic arsenic exposure[5]. In our case, histological confirmation of the liver tumor could not be performed due to the anticoagulant treatment (Sintrom®). However, the features of the tumor on CT and TACE are consistent with hepatocellular carcinoma, particularly when the tumor characteristics are considered after lipiodol uptake during and after TACE[14]. Even though the most effective therapy for hepatocellular carcinoma is liver transplantation or partial hepatectomy[15], our patient remains asymptomatic after nine years of TACE treatment. This fact is consistent with the increasing survival rates of patients receiving this palliative treatment[16].

In conclusion, this is the first patient with occult HBV infection who developed hepatocellular carcinoma after acute arsenic exposure, and his tumor remitted after palliative treatment with TACE. The clinical implication of our observation is that periodical liver studies should be undertaken in patients who survive after acute arsenic exposure.

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