Acute renal failure requiring haemodialysis after high doses percutaneous acetic acid injection for hepatocellular carcinoma

M. Van Hoof, J.-P. Joris, Y. Horsmans and A. Geubel

Department of Gastroenterology, Saint Luc University Hospital (UCL), 1200 Bruxelles, Belgium and Saint Luc Hospital, 5004 Bouge, Belgium.

Abstract

Recently, ultrasound-guided percutaneous acetic acid injection has been proposed in the treatment of hepatocellular carcinoma as an alternative to percutaneous ethanol injection. We report the case of severe renal failure requiring haemodialysis which occurred in a patient with 4 cm hepatocellular carcinoma treated adequately by high dose percutaneous acetic acid injection. The risk of such a serious side effect, likely related to a direct toxic effect of acetic acid, should be of concern when considering percutaneous treatment of hepatocellular carcinoma.

Acute renal failure has been reported as a complication of acetic acid poisoning, but to our knowledge, we report here the first case of acute renal failure following high dose percutaneous acetic acid injection. (Acta gastroenterol. belg., **1999**, 62, **49-51**).

Key words : hepatocellular carcinoma, acetic acid, renal failure, toxicology.

Introduction

Ultrasound-guided percutaneous acetic acid injection (PAI) has been recently proposed in the treatment of hepatocellular carcinoma (HCC) as an alternative to percutaneous ethanol injection (PEI) (1-3). Acetic acid seems to be equally or even more effective than ethanol in the treatment of small size HCC (3 cm or less in diameter) (1-3). Recently, efficacy of PAI has also been shown for the treatment of HCC larger than 3 cm (4). To date, there is no report of any significant side effect related to such a procedure (1-4).

We report the case of a patient in whom percutaneous injection of high doses of acetic acid for HCC resulted in severe renal failure requiring haemodialysis.

Case report

In May 1994, a 69-year-old man was referred for evaluation and treatment of recently detected diabetes mellitus. Work-up led to the diagnosis of cirrhosis with portal hypertension, being likely of mixed viral (HCV positive) and alcoholic origin. Serum α-foetoprotein (AFP) was normal (16 ng/ml) and neither ultrasound nor contrast enhanced computed tomography (CT) showed hepatic focal lesion.

In September 1995, follow-up blood analysis showed high AFP (5908 ng/ml). Repeat contrast enhanced CT (Fig. 1A) and magnetic nuclear resonance both demonstrated an apparently unique 40 mm diameter tumor located in hepatic segment VI, the tumor presenting

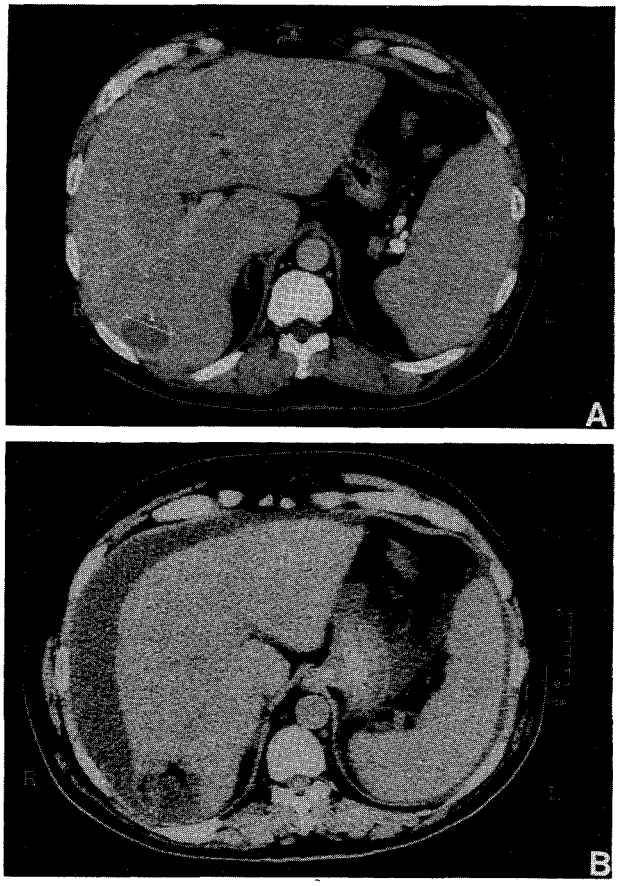

Fig. 1. — Contrast enhanced computed tomography (CT) showing splenomegaly and a 40 mm tumor of hepatic segment VI before treatment (A). Unenhanced CT performed 3 weeks after the second percutaneous acetic acid injection session showing ascites and an area of low attenuation with gas at tumoral site.

the usual radiological features of HCC. Poor hepatic functional reserve precluded surgical treatment and PAI was proposed because of the tumor size which was considered too large to achieve complete necrosis with PEI in a reasonable number of sessions (5-10).

At admission, the patient was in Child Class B with stable biochemical parameters (table I). A first PAI session was performed under ultrasound guidance and

Correspondence : Prof. André Geubel, Gastroenterology unit, Saint Luc University Hospital, Avenue Hippocrate 10, B-1200 Bruxelles, Belgium.

Table I.

Parameters	3/10/95*	16/10**	17/10	20/10	30/10	6/11	10/11	27/2/96
Leukocytes (4-10.000)	6700	8400	21600	11700	8600	6300	6300	6400
Urea mg/dl (15-45)	30	31	90	260	119	91	76	44
Creatinin mg/dl (0.7-1.4)	1.0	1.0	3.1	8.8	7.2	4.8	3.8	1.5
ALT U/l (< 29)	88	48	146	–	35	27	22	32
LDH U/l (160-320)	390	394	1304	–	483	444	383	275
Prothrombin time % (> 70)	78	73	–	68	71	–	70	–
Tot. Bilirubin mg/dl (0.1-1.1)	3.5	2.5	–	–	1.67	1.79	1.88	1.16
AFP ng/ml (< 16)	5908	–	–	–	–	174	–	44

* First PAI, ** Second PAI.

10 ml of 50% acetic acid solution were injected following the same procedure described by Ohnishi *et al.* (3,4). No serious complication was encountered although the patient experienced local pain during injection and a few hours after. Chest x-ray showed a slight right-sided pleural effusion with diaphragm hypomotility. The patient was discharged from hospital 24 hours after the procedure.

A second PAI session took place two weeks later. Home treatment was unchanged including only insulin therapy. At admission, blood analysis did not show any significant change in biological parameters, in particular renal function was normal (table I). For the second PAI session, 15 ml 50% acetic acid solution were used. Prior to the procedure the patient was given 5 mg midazolam by intramuscular route. A few hours after, he experienced transient fever (38.7°C) and 2 g paracetamol chlorhydrate (equivalent to 1 g paracetamol) were administered intravenously. Hydratation was normal. Blood pressure monitoring did not demonstrate hypotension and no clinical manifestation of hypotension was observed. Within 24 hours, he developed anuria. Biochemical work-up showed an elevated neutrophil leukocyte count, ALT and LDH, as well as renal function impairment (table I). Prothrombin time and bilirubin level remained unchanged. No biochemical sign of hemolysis was noted. Lactate level remained normal. Extensive urine analyses were repeatedly performed and did not show hemoglobinuria nor leukocyturia. Bacteriological work-up included six pairs of blood cultures, urine and sputum cultures, all remaining negative. No antibiotic was given at any time during the hospital stay. Acute renal failure required five haemodialysis sessions because of acidosis, hyperkaliemia and high blood urea level. The patient progressively recovered from renal failure. An unenhanced CT imaging (Fig. 1B) performed three weeks after the second PAI session showed at the tumoral site an area of much lower attenuation with gas, interpreted as necrosis. Moderate ascites was also noted. Four months after the second PAI session, the patient was asymptomatic, calculated creatinine clearance reached 46 ml/min, AFP level was strikingly decreased (44 ng/ml) and magnetic nuclear resonance showed signs of non-liquid necrosis of the tumor. Further evolution was characterized by absence of clinical event and unchanged radiological aspect of the lesion. At one year, AFP level raised to 127 ng/ml.

Discussion

Acute renal failure has been reported as a complication of acetic acid poisoning (11,12). Doses and concentrations of acetic acid ranged from 50 ml (12) to 400 ml (11) and from 9% (12) to 25% (11), respectively. In those cases however, renal function impairment was often associated with serious digestive caustic lesions and might also be related to other potential causes such as sepsis or shock.

In our case, the chronological relationship between acetic acid injection and renal failure as well as the negative bacteriological work-up and the favourable evolution without antibiotic treatment allow to exclude sepsis as the cause of renal impairment. In addition, the presence of gas is not uncommon after PAI (1) and should not be interpreted as a sign of infection. Arguments for a direct toxic effect of acetic acid thus include the absence of other cause of renal impairment such as sepsis, use of nephrotoxic medication or shock. The occurrence of transient acidosis could not be excluded.

The mechanism of acetic acid-induced renal failure remains unknown. Direct injection of the drug in the liver of this old patient could have induced an hypotension of short duration sufficient to provoke renal failure. Other mechanisms which have been evoked in case of renal complications following acetic acid ingestion are the occurrence of hemolysis followed by hemoglobinuria (13) and an elevation of serum lactate concentration (14). These mechanisms were not observed in this case.

To our knowledge, we report here the first case of acute renal failure following high doses PAI. The total amount of acetic acid solution used during the two PAI sessions was markedly greater than that reported in the first trials (1-4). Ohnishi *et al.* used 7 ml of acetic acid as the maximum dose at one session (4) while we used 15 ml of the same solution, an amount which was felt necessary to adequately treat a HCC of more than 4 cm in diameter with a small number of sessions, and which might have played a role in the development of renal failure. Fifty percent concentration of acetic

acid was chosen according to studies in rats (1) showing that hepatic necrotizing effect increased as the concentration of acetic acid increased to reach a plateau at a concentration of 50%. Recent data (3) confirmed that the use of 40% or 50% acetic acid is preferable for the treatment of small HCCs in terms of reduced number of PAI sessions. Thus, being aware of its potential serious complication, one should probably advise to use smaller amounts of acetic acid with more sessions. Finally, considering morphological changes of the lesion at CT, the striking decrease of AFP level and the further evolution, PAI seemed to have been an effective therapy in our patient.

Conclusions

Our observation emphasizes the potential risk of renal toxicity following efficient percutaneous acetic acid injection in the treatment of HCC of more than 3 cm in diameter.

References

1. OHNISHI K., OHYAMA N., ITO S., FUHIWARA K. Small hepatocellular carcinoma : treatment with US-guided intratumoral injection of acetic acid. *Radiology*, 1994, **193** : 747-52.
2. OHNISHI K., YOSHIOKA H., ITO S. *et al.* Prospective randomized controlled trial comparing percutaneous acetic acid injection and percutaneous ethanol injection for small hepatocellular carcinoma. *Hepatology*, 1998, **27** : 67-72.
3. OHNISHI K., NOMURA F., ITO S. *et al.* Prognosis of small hepatocellular carcinoma (less than 3 cm) after percutaneous acetic acid injection : study of 91 cases. *Hepatology*, 1996, **23** : 994-1002.
4. OHNISHI K., YOSHIOKA H., ITO S. *et al.* Treatment of nodular hepatocellular carcinoma larger than 3 cm with ultrasound-guided percutaneous acetic acid injection. *Hepatology*, 1996, **24** : 1379-1385.
5. EBARA M., OHTO M., SUGIURA N. *et al.* Percutaneous ethanol injection for the treatment of small hepatocellular carcinoma. Study of 95 patients. *J. Gastroenterol. Hepatol.*, 1990, **5** : 616-26.
6. SHIINA S., TAGAWA K., UNUMA T. *et al.* Pecutaneous ethanol injection therapy for the treatment of hepatocellular carcinoma. *AJR*, 1990, **154** : 947-51.
7. TANIKAWA K., MAJIMA Y. Pecutaneous ethanol injection therapy for recurrent hepatocellular carcinoma. *Hepatogastroenterol.*, 1993, **40** : 324-27.
8. LIVRAGHI T., SALMI A., BOLONDI L. *et al.* Small hepatocellular carcinoma : percutaneous alcohol injection-results in 23 patients. *Radiology*, 1988, **168** : 313-17.
9. SHEU J.C., SUNG L.L., HUANG G.T. *et al.* Intratumor injection of absolute ethanol under ultrasound guidance for the treatment of small hepatocellular carcinoma. *Hepatogastroenterol.*, 1987, **34** : 255-61.
10. CASTELLS A., BRUIX L., BRU C. *et al.* Treatment of small hepatocellular carcinoma in cirrhotic patients : a cohort study comparing surgical resection and percutaneous ethanol injection. *Hepatology*, 1993, **18** : 1121-26.
11. BOSENIUK S., RIEGER C. Akute orale Essigsäureintoxikation-fallbericht. *Anaesthesiol. Reanim.*, 1994, **19** : 80-82.
12. KAWAMATA M., FUJITA S., MAYUMI T. *et al.* Intoxication by rectal administration. *J. Toxicol. Clin. Toxicol.*, 1994, **32** : 333-36.
13. TEIXEIRA F., MORGAN J., KIKERI D. *et al.* Hemolysis following 80% acetic acid ingestion. *Vet. Hum. Toxicol.*, 1992, **34** : 340.
14. LINDEN R.E., BERNER L.M., KULIG K. *et al.* Acid ingestion : toxicity following systemic absorption. *Vet. Hum. Toxicol.*, 1983, **25** : 282.