week. We noticed that large haemoptyses occurred shortly after the nebulised salbutamol. After substitution of the salbutamol by nebulised isotonic saline there was a pronounced reduction in haemoptysis with only streaks of blood in the sputum thereafter. To substantiate these observations nebulised salbutamol was reintroduced and caused a further large haemoptysis (300 ml). Bronchodilator treatment was therefore subsequently maintained with oral prednisolone and the nebulised salbutamol discontinued. The episodes of haemoptysis gradually subsided over the next 48 hours. There was no recurrence when inhaled salbutamol 200 μg four times daily was reinstituted one week later.

Comment

Although intermittent haemoptysis may occur in bronchiectasis and be exacerbated by intercurrent infection, in our patient the continued use of nebulised salbutamol appeared to increase the degree of haemoptysis. This effect may be dose related, since before admission and during two previous admissions for haemoptysis the patient had used a salbutamol inhaler 200 μg four times daily as well as an ipratropium inhaler without any apparent adverse effect. During the two previous admissions when nebulised salbutamol was not used the haemoptysis was much less severe, less persistent, and disappeared within 48 hours. We therefore suggest that nebulised salbutamol and other similar nebulised drugs should be used with caution in patients with chronic reversible airflow obstruction and haemoptysis.

Neither Allen and Hanburys Ltd nor the Committee on Safety of Medicines had any record of this side effect of nebulised salbutamol being notified to them.

1 Crofton J, Douglas A. *Respiratory diseases*. 2nd ed. Oxford: Blackwell Scientific, 1975:382.
2 Gibson DG, Coltart DJ. Haemodynamic effects of intravenous salbutamol in patients with mitral valve disease; comparison with isoprenaline and atropine. *Postgrad Med J* 1971;**47**,suppl:41.
3 Paterson JW, Woolcock AJ, Shenfield GM. Bronchodilator drugs. *Am Rev Respir Dis* 1979;**120**:1166.

(*Accepted 30 December 1982*)

Chest Unit, Heathfield Hospital, Ayr KA8 9DZ
M I ULLAH, MRCP, consultant physician
O FEGAN, SRN, ward sister

Correspondence to: Dr M I Ullah.

Exacerbation of chronic liver disease due to hepatitis B surface antigen after delta infection

Carriers of the hepatitis B surface antigen (HBsAg) appear to be at high risk of developing δ infection.[1] The δ agent is highly pathogenic and causes acute and chronic liver disease.[2] δ Antigen is detectable in serum only in acute hepatitis and indicates recent δ infection[1]; in chronic hepatitis δ antigen may be identified in liver specimens, but in the serum only the antibody to it (anti-δ) may be identified.[1] Results of recent studies[3] suggests that the δ agent is a factor in fulminant hepatitis in asymptomatic carriers of HBsAg; it could also be responsible for serious infections in patients with chronic HBsAg liver disease.

We report on three patients with a history of chronic HBsAg liver disease whose clinical condition worsened suddenly and who died; sera from the three patients were tested for the presence of markers of hepatitis B virus and the δ agent.

Patients, methods, and results

We examined three men admitted to hospital with jaundice. Their histories showed them to have been HBsAg carriers for at least two years with raised activity of alanine transaminase (from two to four times normal), slightly raised bilirubin concentration, serum albumin concentration >30 g/l, and gammaglobulinaemia < 20 g/l. They had not had ascites, bleeding, or periods of disturbed consciousness. Only one had undergone liver biopsy: histology had shown chronic persistent hepatitis. None had had previous treatment, and none was alcoholic.

During admission alanine transaminase activity was three to five times normal and they had hyperbilirubinaemia (six or more times normal concentrations), low serum albumin concentrations, hypergammaglobulinaemia, prolonged prothrombin times, ascites, bleeding, and disturbed consciousness progressing to hepatic coma. Death occurred three to five weeks after admission.

Sera of the three patients were tested for markers of hepatitis B virus and δ agent. HBsAg, antibody to HBsAg (anti-HBs), total antibody to hepatitis B core antigen (anti-HBc), hepatitis B e antigen (HBeAg), and antibody to HBeAg (anti-HBe) were estimated with commercial radioimmunoassays (Ausria II, Ausab, Corab, Kit HBe; Abbott, Chicago, Illinois). Anti-HBc of IgM class (IgM anti-HBc) was detected with a solid phase radioimmunoassay using the method described by Lavarini *et al*[4] (the HBc reagent was kindly provided by Dr Rizzetto, and we used anti-HBc iodine-125 from kit Corab, Abbott). Serum δ antigen and anti-δ were detected with solid phase enzyme linked immunosurbent assay based on the technique described by Crivelli *et al*[5] (IgG anti-δ conjugated with immunoperoxidase was kindly provided by Dr Rizzetto).

The three patients were positive for HBsAg, total anti-HBc, and anti-HBe and negative for anti-HBs, IgM anti-HBc, and HBeAg; they were positive for δ antigen and negative for antibody to it.

Comment

The δ agent is highly pathogenic; in asymptomatic carriers of HBsAg it usually produces acute hepatitis that can occasionally be fulminant and often becomes chronic. In the three cases described the δ agent did not produce the classical picture of acute hepatitis with very high alanine transaminase activity. The patients in fact had suffered for at least two years from an HBsAg hepatitis that had evolved slowly, as is usually observed in our area, and then their condition deteriorated unexpectedly, leading to death. The infection with hepatitis B virus was not recent since their sera were positive for anti-HBe and negative for IgM anti-HBc; the presence of δ antigen in the sera indicated current infection by the δ agent.

We therefore presume that in these three cases the δ agent played an important part in the sudden and fatal exacerbation of the patients' liver disease.

1 Rizzetto M. Biology and characterization of the delta agent. In: Alter H, Mayonard J, Szmuness W, eds. *Viral hepatitis*. Philadelphia: Franklin Institute Press, 1982:355-60.
2 Rizzetto M, Shih JWK, Gocke DJ, Purcell RH, Verme G, Gerin JL. Incidence and significance of antibodies to delta antigen in hepatitis B virus infection. *Lancet* 1979;ii:986-90.
3 Smedile A, Farci P, Verme G, *et al*. Influence of delta infection on severity of hepatitis B. *Lancet* (in press).
4 Lavarini C, Crivelli O, Smedile A, *et al*. Radioimmunoassay detection of IgM antibodies to the hepatitis B core antigen in HBsAg liver disease. *Boll Ist Sieroter Milan* (in press).
5 Crivelli O, Rizzetto M, Lavarini C, Smedile A, Gerin JL. Enzyme-linked immunosorbent assay for detection of antibody to the hepatitis B surface antigen-associated delta antigen. *J Clin Microbiol* 1981;**14**:173-7.

(*Accepted 9 December 1982*)

Institute of Internal Medicine, Hepatology Section, University of Messina, Policlinico Messina, Italy
G RAIMONDO, MD, lecturer
G LONGO, MD, senior lecturer
G SQUADRITO, MD, professor of clinical medicine

Correspondence to: Dr G Raimondo.

Chlormezanone poisoning

Chlormezanone is a tranquilliser with muscle relaxant properties that was first introduced into clinical practice in 1958. There is, however, only one published report of an overdose due to this drug.[1] We report a further case of chlormezanone intoxication.

Case report

A 36 year old woman was admitted to hospital after ingesting 7 g chlormezanone (Trancopal) five hours previously. On admission she was comatose (grade 3, Edinburgh scale) and hypotensive (95/60 mm Hg) and had a positive gag reflex, equal and reactive pupils, normal fundi, flaccid muscle tone, and reflexes that were generally difficult to elicit. Over the next 15 hours she regained consciousness and her blood pressure rose to 115/70 mm Hg. No evidence of respiratory depression was observed, and renal and hepatic function remained normal. The patient made an uneventful recovery.

The figure shows plasma chlormezanone concentrations, estimated by a