Results of liver function tests, showing peak biochemical values. (Normal ranges are shown in parentheses)

Case No	Age (years)	Duration of fever on admission (days)	Time when jaundice noted	Serum bilirubin ($\mu\text{mol/l}$) (5-17 $\mu\text{mol/l}$)	Alkaline phosphatase (3-13 KAU)	Serum alanine transference (3-30 U/l)	Total duration of fever (days)
1	19	20	23rd day of fever	133	20.0	675	51
2	17	4	On admission	125	17.5	237	18
3	12	7	11th day of fever	65	18.0	195	18
4	15	15	On admission	58	34.0	255	24
5	26	12	On admission	75	80.0	45	23

Conversion: SI to traditional units—Bilirubin: 1 $\mu\text{mol/l} \approx 58.5 \mu\text{g/100 ml}$.

Blood culture grew *Salmonella typhi* in the first four cases. In case 1 the organism was resistant to chloramphenicol. In case 5 a culture was not drawn but a Widal test showed a characteristic rising titre, from *S typhi* O negative and H 1/50 to O 1/50 and H 1/250. Liver function tests showed hepatocellular jaundice in four cases and a cholestatic picture in one (table). All patients were negative for hepatitis B surface antigen, and no biliary stones were seen on a plain abdominal x ray film. Oral cholecystography was performed after the jaundice had subsided in cases 1 and 5 and did not show any stones. Percutaneous liver biopsy in cases 2, 3, and 4 showed fatty infiltration of hepatocytes with lymphocytic infiltration of portal triads. In cases 2 and 3 granulomas were seen, but in case 4 no definite granulomas could be made out.

Patients were treated with either co-trimoxazole or chloramphenicol in standard doses. In case 1 the organisms were resistant and required treatment with gentamicin and ampicillin. Corticosteroids were not used. The fever took an average of 15.2 days to respond to treatment. The jaundice subsided with the fever.

One patient (case 1) developed overt hepatic failure with bleeding diathesis; another (case 2) had an asymptomatic prolongation of prothrombin time; and a third (case 5) suffered an anicteric relapse three weeks after discharge, which responded to amoxycillin. There were no deaths.

Comment

Jaundice due to a hepatitis like syndrome in typhoid fever is uncommon. "Hepatitis typhosa" was reported in six out of 530 patients from Iran,¹ 0.4% of 3476 patients from Chile,² and five out of 92 cases from Sri Lanka.³ The present study was not a systematic study of typhoid fever, and an exact incidence cannot be given. During this period, however, 925 patients were treated in this hospital with a diagnosis of typhoid fever.

As a group these patients were young and severely ill and had a prolonged and persistent fever even after starting specific chemotherapy. Blood cultures were positive in all patients in whom they were done, and in one case the organism grown was resistant to chloramphenicol. This was also reported by Rowland.¹ It is noteworthy that none of the patients had received specific treatment before admission, which is distinctly unusual in India. This may explain the severity of their disease.

The pathogenesis of typhoid hepatitis is unclear. Although typhoid endotoxin was once considered to be the cause of many of the manifestations of typhoid fever, more recent evidence indicates that systemic endotoxaemia is unlikely to have any major role.⁴ At the site of multiplication of *S typhi*, however, as in the liver, high concentrations of endotoxin may provoke a granulomatous or mononuclear inflammatory response. Tolerance to this local reaction does not occur as it does for systemic reactions to endotoxin.⁵ It should be remembered, however, that the liver disease described in typhoid fever may occur in other ulcerative diseases of the intestine—for example, Crohn's disease, amoebiasis, and ulcerative colitis.³ In conclusion, typhoid must be kept in mind as an unusual cause of a hepatitis syndrome, especially in endemic areas.

¹ Rowland MAK. The complications of typhoid fever. *J Trop Med Hyg* 1961;64:143-52.

² Faerman D, Ross FA, Seckler SG. Typhoid fever complicated by hepatitis, nephritis and thrombocytopenia. *JAMA* 1972;221:60-1.

³ Ramachandran S, Godfrey JJ, Perera MVF. Typhoid hepatitis. *JAMA* 1974;230:236-40.

⁴ Butler T, Bell WR, Levin J, Link NN, Arnold K. Typhoid fever—studies of blood coagulation, bacteremia and endotoxemia. *Arch Intern Med* 1978;138:407-10.

⁵ Hornick RB, Greisman S. On the pathogenesis of typhoid fever. *Arch Intern Med* 1978;138:357-9.

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Inadvertent self administration of superglue: a consumer hazard

Tissue bonding is a hazard of using cyanoacrylate adhesive (super-glue) both in industry and the home. Recently, a new hazard, first reported in America, has been defined¹: the similarity between the bottles used as containers for certain superglues and those used for therapeutic eye drops has led to people inadvertently instilling the adhesive into their eyes.

Case report

A 47 year old man presented as an emergency. A short time previously he had placed drops into his left eye from a bottle that he had assumed contained Clearine eye drops (Optrex). He had in fact picked up a bottle of cyanoacrylate (Super Glue, Bostik Ltd). There was immediate pain and blepharospasm with watering; he then found that he could not open his eye and came straight to the hospital.

Close similarity between bottles of Super Glue (left) and eye drops (right).

On examination his left lids were totally adherent apart from a small defect medially. Hardened adhesive coated his lid margins and lashes. So that the adhesive would separate from the ocular tissues we filled the conjunctival sac through the small defect with chloramphenicol eye ointment. The eye was then padded, and he was given an analgesic and asked to return the next day. On his return the lashes were carefully cut and the adhesive between his lid margins was divided with scissors. A hardened shell of adhesive could then be gently lifted from the conjunctival sac.

A large underlying corneal and conjunctival epithelial defect healed progressively during the next week, and the eye recovered fully without any further complications.

Comment

Super Glue is a cyanoacrylate monomer made by condensation of formaldehyde and a cyanoacetate. It undergoes rapid anionic polymerisation in the presence of even trace amounts of weakly basic substances; the reaction proceeds unless acid is encountered.² It thus bonds tissue in seconds. Higher alkyl derivatives (butyl, decyl) have lower tissue toxicity and have found therapeutic use in the fashioning of temporary tarsorrhaphies and in the temporary patching of corneal defects.^{2,3}

The figure shows the similarity between the bottle of adhesive and the bottle of eye drops. Indeed, both containers were made by the same manufacturer. Other bottles in our ward drug store were also similar. This surely represents an unnecessary hazard, especially for patients with deficient eyesight, which is easily avoidable.

The manufacturers of the adhesive (Bostik), who have not heard of a case similar to ours, were asked to comment and to consider changing their packaging. They responded, "It so happens that we are . . . planning changes to the bottle for other reasons and in doing so we shall certainly take the point made . . . into consideration."

We would like to see a ban imposed on the sale of non-pharmaceutical chemicals in small plastic dropper bottles, as many alternative packagings are available.

¹ Margo CE, Trobe JD. Tarsorrhaphy from accidental instillation of cyanoacrylate into eye. *JAMA* 1982;247:660-1.

² Refojo MF, Dohlman CH, Koliopoulos J. Adhesives in ophthalmology: a review. *Surv Ophthalmol* 1971;15:217-36.

³ Ellis RA, Levine AM. Experimental sutureless ophthalmic surgery. *Am J Ophthalmol* 1963;55:733-41.

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Primary liver cell carcinoma complicating secondary biliary cirrhosis

Over recent years there have been reports of primary liver cell carcinoma complicating most types of cirrhosis, including autoimmune chronic active hepatitis¹ and primary biliary cirrhosis,² but none in relation to secondary biliary cirrhosis. We report a case of primary liver cell carcinoma in a patient with secondary biliary cirrhosis due to a postoperative biliary stricture.

Case report

A 68 year old woman presented to this hospital in September 1982 with jaundice and gastrointestinal bleeding. She was a teetotaler and had never taken potentially hepatotoxic drugs. At the age of 40 she had undergone a cholecystectomy for gallstone disease. Over the next three years she had two further operations in which attempts were made to repair a benign stricture of the proximal common bile duct. She remained well until 1978, when she again developed recurrent bouts of cholangitis. On each occasion her symptoms settled with oral antibiotics.

In August 1982 she was admitted to her local hospital because of vomiting, increasing jaundice, itch, and abdominal distension. Examination showed gross ascites and peripheral oedema but none of the peripheral stigmata of chronic liver disease. Haemoglobin concentration was 9.8 g/dl, and red cells showed morphological features of iron deficiency. Liver function tests yielded bilirubin concentrations of 147 μ mol/l (8.6 mg/100 ml) (normal < 23 μ mol/l (< 1.3 mg/100 ml)); serum aspartate transferase activity 157 IU/l (normal < 50 IU/l); serum alanine transferase 67 IU/l (normal < 50 IU/l); alkaline phosphatase 256 IU/l (normal < 110 IU/l); γ glutamyltransferase 157 IU/l (normal 0-40 IU/l); albumin concentration 25 g/l (normal > 35 g/l); lactate dehydrogenase activity 686 IU/l (normal < 300 IU/l); and prothrombin time 70%. Autoantibodies and hepatitis B surface antigen were not detected. Abdominal paracentesis yielded an evenly bloodstained transudate that was negative on cytological examination. Ultrasound examination of the liver showed mild dilatation of the intrahepatic ducts. After treatment with diuretics had reduced her ascites a percutaneous liver biopsy showed established cirrhosis, with regenerative nodules of parenchyma separated by broad bands of fibrous tissue containing numerous bile ducts and acute and

chronic inflammatory cells. This was thought to be consistent with biliary cirrhosis.

Her clinical course was complicated by haematemesis, which was shown by endoscopy to be due to oesophageal varices. Further investigation showed portal hypertension (splenic pulp pressure 16 mm Hg) and patent splenic and portal veins. A percutaneous transhepatic cholangiogram established that biliary drainage was completely blocked at the level of the proximal common bile duct. As variceal bleeding persisted portosystemic shunt surgery was performed to achieve decompression. Her postoperative course was compli-

Postmortem liver biopsy specimen showing hepatocytes separated from tumour cells by a broad band of fibrous tissue. Haematoxylin and eosin $\times$ 99.

cated by increasing jaundice. Resuscitation was slowly reduced when the preoperative serum α fetoprotein concentration was found to have been 74 mg/l, and she died one week later. Necropsy disclosed a small cirrhotic liver with multifocal primary liver cell carcinoma invading intrahepatic vascular channels (figure) and a benign stricture of the proximal common bile duct.

Comment

Primary liver cell carcinoma as a complication of secondary biliary cirrhosis has not been reported previously. Though Purtilo and Gottlieb described 10 cases of malignant liver disease (primary liver cell carcinoma and cholangiocarcinoma) complicating unspecified biliary cirrhosis, they included patients with cholangiocarcinoma in whom the tumour may have been the cause of the cirrhosis. Moreover, serological evidence that might have excluded primary biliary cirrhosis was not available in most of their patients.

The diagnosis of secondary biliary cirrhosis and primary liver cell carcinoma in this patient was supported by the consistent clinical history of biliary surgery and recurrent biliary sepsis; the presence of a benign stricture of the proximal common bile duct, which was confirmed radiologically and histologically; compatible hepatic and tumour histology; and an appreciably raised serum α fetoprotein concentration.

It appears that primary liver cell carcinoma may complicate the clinical course of any patient with cirrhosis. Thus this diagnosis should be considered in patients with secondary biliary cirrhosis in whom hepatocellular function deteriorates without obvious cause.

¹ Jakobovits AW, Gibson PR, Dudley FJ. Primary liver cell carcinoma complicating auto-immune chronic active hepatitis. *Dig Dis Sci* 1981;26:694-9.

² Krasner N, Johnson PJ, Portmann B, Watkinson G, MacSween RNM, Williams R. Hepatocellular carcinoma in primary biliary cirrhosis: report of four cases. *Gut* 1979;20:255-8.

³ Purtilo DT, Gottlieb LS. Cirrhosis and hepatoma occurring at Boston City Hospital (1917-1968). *Cancer* 1973;32:458-62.

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