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Ursodeoxycholic acid dissolution of gallstones in cystic fibrosis

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ABSTRACT The dissolution of cholesterol gall stones is documented in two adults with cystic fibrosis.

Improved care of patients with cystic fibrosis has meant that most survive into adult life. Consequently extrathoracic complications are assuming greater importance, especially those of the hepatobiliary system. These include progressive biliary cirrhosis (25%) leading to portal hypertension and oesophageal varices (2–5%). Gall bladder abnormalities include microgallbladder (18%), a gall bladder that fails to opacify on oral cholecystography (15%), recurrent attacks of biliary colic or cholecystitis (5–10%), and cholesterol gall stones (12%).[1 2]

Poor respiratory function in cystic fibrosis patients puts them at considerable risk from a general anaesthetic,[3 4] and postoperative pain results in poor compliance with physiotherapy.

We report the first documented cases of dissolution of cholesterol gall stones in two adults with cystic fibrosis and recurrent attacks of biliary colic who were considered unfit for general anaesthesia.

Case reports

CASE 1

Cystic fibrosis was diagnosed in this patient at the age of 6 months. During adolescence she required intermittent treatment with intravenous antibiotics and daily nebulised antibiotics for respiratory infections due to *Pseudomonas aeruginosa*. She took 35 Pancrex V tablets with meals for documented steatorrhoea, and passed two to three formed stools a day. At the age of 18 years she developed insulin dependent diabetes mellitus, which was controlled with twice daily subcutaneous injections. Shortly after this she complained of recurrent attacks of right subcostal pain that radiated to her back. These episodes were sometimes accompanied by the passing of pale stools and dark urine. An oral cholecystogram showed a functioning gall bladder containing multiple small, radiolucent stones (fig 1). She had a forced expiratory volume in one second (FEV_1) of 1·01 (34% predicted) and a vital capacity (VC) of 1·81 (55% predicted). These values were sufficiently poor to preclude general anaesthesia and ursodeoxycholic acid 150 mg thrice daily was started. Her weight was 32 kg at the time, and her height 1·55 m. Occasional attacks of biliary colic occurred for several months but then resolved completely. An oral cholecystogram one year later showed complete dissolution of the gall stones and a normally functioning gall bladder (fig 2). Ursodeoxycholic acid has been continued at the same dose without side effects. She has subsequently changed from Pancrex to 12 capsules of Creon per day.

CASE 2

Cystic fibrosis was diagnosis in this patient at the age of 9 months. He remained relatively well until the age of 22 years, when he developed a respiratory infection due to *Pseudomonas aeruginosa*, which was treated with intravenous antibiotics. He was taking 20 Pancrex tablets before meals at that time to control steatorrhoea. Subsequently he reported episodes of severe right upper quadrant abdominal pain radiating to his back. An abdominal Ultrasound examination showed multiple gall stones. Oral cholecystography showed that the stones were radiolucent and that the gall bladder functioned normally. As his FEV_1 was only 0·61 (15% predicted) and VC 1·81 (38% predicted) ursodeoxycholic acid 150 mg thrice daily was started. His weight was 52·3 kg and his height 1·70 m. The attacks of pain diminished in duration and frequency over the next few months and one

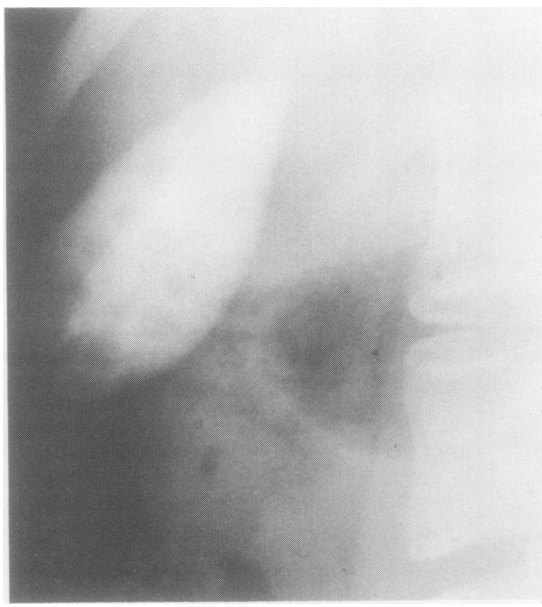

Fig 1 *Cholecystogram showing a functioning gall bladder containing small radiolucent stones (case 1).*

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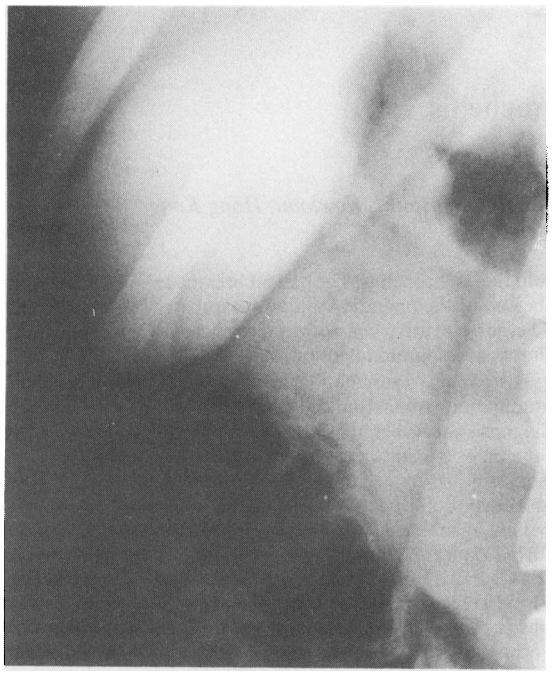

Fig 2 *Cholecystogram one year after figure 1 showing complete resolution of the gall stones.*

year later he is symptom free. A repeat ultrasound examination nine months after he started treatment showed considerable reduction in size of the stones; a repeat oral cholecystogram was not carried out. He has changed from Pancrex to 10 capsules of Creon a day.

There was no change in the weight of either patient following treatment with ursodeoxycholic acid.

Discussion

Gall stones can be dissolved in carefully selected cases, but they must be cholesterol stones as judged by radiolucency and the gall bladder must opacify on oral cholecystography, indicating a patent cystic duct and the ability of the mucosa to concentrate gall bladder contents.

It is not clear why patients with cystic fibrosis form cholesterol gall stones but two main factors are thought to play a part: cholesterol supersaturation of bile due to increased faecal losses of bile acids, with consequent interruption of the enterohepatic circulation,[5] and stone formation facilitated by the presence of mucin glyoprotein, which acts as a "nucleating factor."[6] Weizman *et al*,[7] however, were unable to find any difference in the lithogenic indices of bile of patients with cystic fibrosis with and without steatorrhoea, but this may have been due to the fact that the former group had been taking pancreatin up to 48 hours before the study. Previous experience suggests that optimal treatment with pancreatin is likely to prevent lithogenic bile.[8]

Stern *et al*[9] advocate cholecystectomy for patients with cystic fibrosis with symptomatic cholelithiasis, provided that pulmonary function is adequate. Our patients were clearly unsuitable candidates for surgery.

We have shown that administration of ursodeoxycholic acid to patients with cystic fibrosis and gall stones can result in complete dissolution or clinically useful size reduction.

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