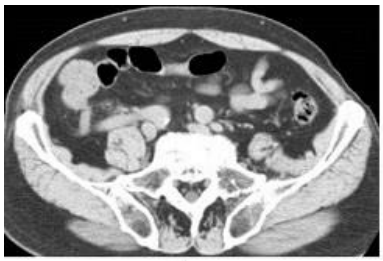
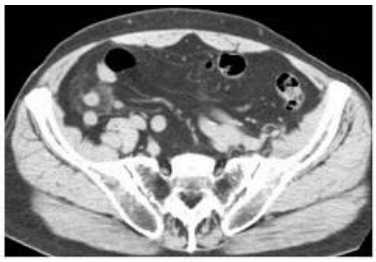
Clinical diagnosis

Case 32

5. Ceftriaxon infusion caused microlithiasis in bile and pancreatitis



A



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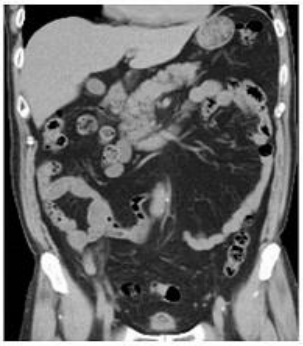
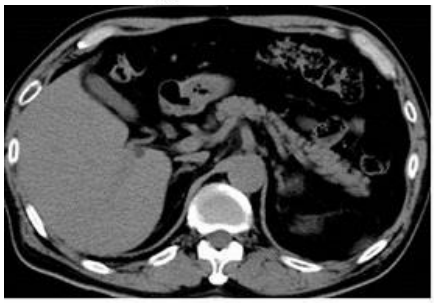
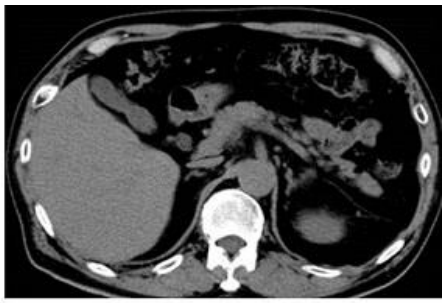


C

Fig. 1 Axial images (A, B) and coronal image (C) of CT depict focal peritonitis surrounding the swollen appendix.



A



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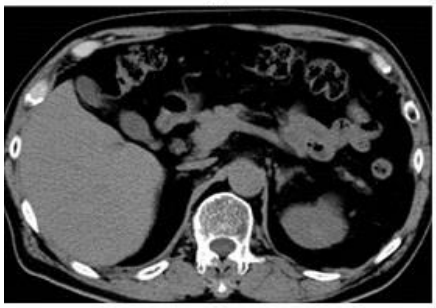
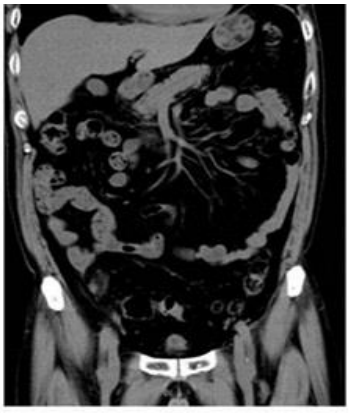


C

Fig. 2 Axial images (A, B, C) and coronal image (D) of CT depict the whole gallbladder with no high density stones



D

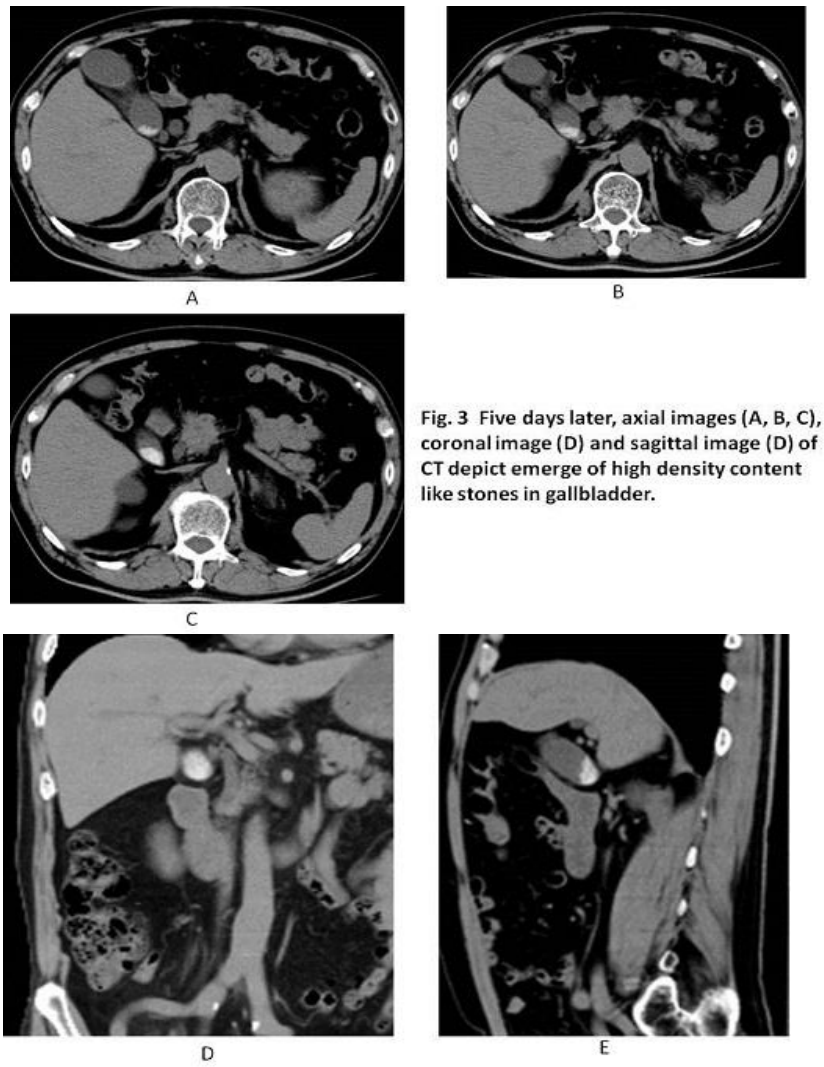


Fig. 3 Five days later, axial images (A, B, C), coronal image (D) and sagittal image (D) of CT depict emerge of high density content like stones in gallbladder.

【Progress】

After CT, ceftriaxon was discontinued and changed into the other antibiotics, meropen. Two days later, slight abdominal pain still continued but fever decreased. Laboratory test revealed the gradual decrease of amylase and still slight elevation of AST, ALT andγGTP. One week later, no abdominal pain was found and laboratory test revealed decrease of hepato-biliary enzymes to normal range. The patient was discharged and returned his healthy condition.

【Discussion】

The common causes of acute pancreatitis are alcohol abuse, gallstone disease and idiopathic, which together account for nearly 95 percent of cases (1). As idiopathic pathogenesis, microcrystal or bile sludge is reported to be the possible cause (1). Fewer than 5 percent of the cases of acute pancreatitis are caused by hypercalcemia, hyperlipidemia, and drugs (1). Ceftriaxon is listed as one of the drugs (2, 3). Other reported drugs are contraceptive steroids, postmenopausal estrogens, progesterone, octreotide (Sandostatin) (2).

Ceftriaxone is a third-generation cephalosporin which acts against broad spectrum of bacteria (3-6). About 30 % of the drug is excreted unchanged in bile and the greater excreted in case of renal disorder (3-5). Further, ceftriaxone is known to easily penetrate inflamed blood brain barrier (3). Because the tolerance is usually good, ceftriaxone is being prevailed to use in the various infections (5, 6), and often used for meningitis and hepatobiliary infection. In our case, cftriaxone was used to protect against the post-appendectomy infection.

With respect to the hepatobiliary side effect, the case with ceftriaxon-induced pancreatitis and/or cholecystolithiasis is recently encountering (7-11). Ceftriaxone is reported to complex with the calcium in bile salts to form biliary sludge or micro-gallstones (2-4). It is thought that, at doses < 1 g/day, precipitation of ceftriaxone with bile salts does not occur (7). The risk of this complication increases with high doses of ceftriaxone, prolonged administration, rapid bolus injection of the antibiotic, parenteral nutrition, and in patients with gallbladder emptying or renal failure (7, 8). In our case, the gallbladder immediately before appendectomy was nearly emptying (Fig. 1). After usage of 1g/day for 5 days after surgical appendectomy, the bile sludge or gallbladder microlithiasis appeared such as calcium milk on CT (Figs 2, 3)(11).

In general, gallstone formation is usually preceded by the presence of biliary sludge like viscous gel which composed of cholesterol and calcium bilirubinate (12). Biliary sludge becomes nucleus of gallstone. In short, cholesterol is insoluble in water but soluble in bile acid. The basic mechanism is oversaturation with cholesterol in bile exceeding the maximum solubility (12). As the cholesterol concentration increases, cholesterol crystal begins to form as the nucleus of gallstone. It is known that up to 90 percent of gallstones are cholesterol (more than 50 percent cholesterol) or mixed (20 to 50 percent cholesterol) gallstones (12). The remaining 10 percent of gallstones are pigmented stones (12). Ceftrixone binds calcium resulting in insoluble crystals in bile (2). Because this sludge is not relevant with cholesterol and promptly dissolution of the sludge after the disconnection of ceftrixone, ceftrixone-induced sludge is termed pseudolithiasis (11). However, this sludge is reported to be capable of being nucleus of gallstone and causing occlusion (8). In our case, ceftriaxone was stopped four days later, his abdominal pain nausea improved promptly and amylase and hepatobiliary enzymes returned to normal range.

【Summary】

We present a seventy five-year-old male who suffered from pancreatitis after he was given ceftriatxone of 1g/day for 4days for preventing post-appendectomy infection. CT before and 5 days after ceftriaxon administration showed emergence of biliary sludge of high density such as calcium milk in the gallbladder. Approximately 30 % of ceftriaxon is known to excrete bile and bind calcium, inducing ceftriaxon-induced sludge and causing pancreatitis. Empty gallbladder before administration of ceftriaxone such as in our case is one of the risk factors to form bile sludge because of possibility of ceftriaxone with high concentration binding calcium in bile. Clinicians and radiologists keep in mind that the early emergence of gallstones might imply the possible usage of ceftriaxone.

【References】

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