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CASE REPORT

Acute pancreatitis after a course of clarithromycin

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ABSTRACT

We present a case of acute pancreatitis after a course of clarithromycin. An 84-year-old woman died of suspected pneumonia and cardiac failure. Autopsy surprisingly revealed acute pancreatitis. Except for the use of clarithromycin no other cause for her acute pancreatitis was obvious. Pancreatitis induced by clarithromycin has been reported twice in the English literature so far. There are, however, a few reports on acute pancreatitis associated with other macrolide antibiotics, such as erythromycin and roxithromycin.

INTRODUCTION

Pancreatitis is usually caused by gallstones or excessive alcohol consumption, but may occasionally be precipitated by drugs. Among the antibiotics, tetracycline and sulphamethoxazole have been implicated most often. Acute pancreatitis is hypothesised to be due to the inappropriate intrapancreatic activation of proteases, which leads to digestion of cell membranes and further activation of other zymogens. Local effects include inflammation, oedema and ischaemia, which progress to local and regional necrosis. Mechanisms for drug-induced pancreatitis include pancreatic duct constriction; immunosuppression; cytotoxic, osmotic, pressure or metabolic effects; arteriolar thrombosis; and direct cellular toxicity.[1] Here we report a case in which clarithromycin, a macrolide antibiotic, may have induced pancreatitis.

CASE REPORT

An 84-year-old woman presented to the emergency department because of shortness of breath and loss of consciousness. A history was obtained from her daughter. She had been feeling ill for seven days prior to admission. She was short of breath and dysarthric. There was no cough or fever. She was not suffering from any pain. There were no pareses. Five days prior to admission her general practitioner prescribed clarithromycin 500 mg twice a day because of suspected respiratory tract infection. Since then her condition had worsened. She stopped eating and drinking properly and stayed in bed most of the time. The last few days her dyspnoea had increased. Urinary production came almost to a standstill. The morning of admission she lost consciousness.

Her past medical history was remarkable for transient ischaemic attacks, hypothyroidism and chronic obstructive pulmonary disease. A few months before admission she had visited our outpatient department with suspected deep vein thrombosis which was excluded by repeated ultrasound investigations. She was taking acetylsalicylic acid 80 mg, levothyroxine 125 μg, chlorthalidone 25 mg and valsartan 80 mg.

On arrival, ambulance nurses measured an oxygen saturation of 79% which improved with oxygen suppletion. In the emergency department, we saw an ill-looking woman who was talking incomprehensibly. Temperature was 36.0°C, blood pressure 150/70 mmHg and pulse 100 beats/min. Oxygen saturation was 94% with 10 litres of oxygen. There were no weaknesses. Auscultation of the heart was unremarkable and breath sounds were clear without crackles. Her abdomen was not tender and she did not seem to have any pain. Laboratory investigations revealed

a respiratory acidosis: pH 7.07, PO_2 17.1, PCO_2 14.5 and bicarbonate 29.3. Na was 134 mmol/l, K 4.8 mmol/l, glucose 7.4 mmol/l, asparate aminotransferase 819 U/l, alanine aminotransferase 658 U/l, alkaline phosphatase 109 U/l, γ-glutamyltransferase 57 U/l, lactate dehydrogenase 2066 U/l, creatinine 190 µg/l, urea nitrogen 23 mmol/l and creatinine kinase 89 U/l. No amylase determination was ordered. Haemoglobin was 8.0 mmol/l, leucocyte count 9.8 x 10^9 and platelets 187 x 10^9.
A chest x-ray showed pleural effusion on both sides. There were signs of congestive heart failure.
We considered pneumonia with an exacerbation of her chronic obstructive pulmonary disease to be the cause of her illness. Other possibilities were end-stage cardiac failure, pulmonary embolism or recent stroke. With her relatives' consent we decided not to admit her to the ICU. We lowered the oxygen supply and gave her amoxicillin/clavulanic acid. Intravenous high-dose furosemide elicited minimal urinary production. In the course of hours her saturation dropped and she became unconscious. Eventually she died the day after admission. Permission for autopsy was obtained. Surprisingly, autopsy revealed that she had severe acute pancreatitis with extensive necrosis around the pancreas. The heart was dilated and hypertrophic. The gallbladder contained multiple small stones but the common bile duct was not dilated and contained no stones.

DISCUSSION

Our patient had no history of alcohol abuse. Except for the stones in the gallbladder there were no other signs of biliary disorder. Acetylsalicylic acid is only known to cause pancreatitis in high doses. Chlorthalidone can cause pancreatitis but usually only shortly after initiation.[2] We do not know whether she was suffering from hypertriglyceridaemia. An important piece of information is that the patient had been on clarithromycin for five days. Clarithromycin is a macrolide antibiotic which is gaining popularity, especially among general practitioners, in the treatment of respiratory tract infections. At least four reports of acute pancreatitis associated with use of the older macrolide erythromycin have been published in English literature[3-7] and a few reports in French and Spanish literature. Often it is associated with high intravenous doses or intoxications. There is also one report of acute pancreatitis with roxithromycin therapy[8] and a report of a child who died from pancreatitis treated with valproic acid and azithromycin.[9]
As for clarithromycin there is one report of pancreatitis in English literature[10] and one recent report in French literature.[11] The Netherlands Pharmacovigilance Centre (LAREB) has not received any reports of a relationship between clarithromycin and pancreatitis. Direct action on the smooth muscle of the gut resulting in spasm of the sphincter of Oddi and bile reflux has been proposed as a mechanism.[1,4] Others suggest an allergic response.[1,5,7]
In this case it cannot be proven that clarithromycin was the cause of the pancreatitis, but since there was no other obvious cause, and because of the reports in literature, it is suggestive. Clarithromycin and other macrolide antibiotics are commonly used for respiratory infections. It is important to remain aware of the possible side effects.

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