SHORT REPORTS

Anaphylactic shock induced by diclofenac

Diclofenac is a non-steroidal anti-inflammatory agent used in degenerative joint disease, rheumatoid arthritis, and allied conditions. Its most important untoward effects include gastrointestinal disorders, rashes, peripheral oedema, and abnormalities of serum transaminase activity. More rarely, melena and haematemesis, myoclonic encephalopathy, and myoclonus of the lower limbs may occur. We report a case of anaphylactic shock induced by diclofenac, which as yet is an unreported complication of treatment with this agent.

Case report

An 80 year old man with mild diabetes was treated with diclofenac 50 mg three times a day for degenerative osteoarthritis. Six months later in January 1981 his treatment was changed to ibuprofen 0.2 g three times a day. In March 1981 his pain was worse and he restarted treatment with diclofenac. Twelve hours after the first dose he consulted his doctor with a fever of 38.5°C and vomiting. He was treated with paracetamol and his symptoms subsided in 36 hours. After 36 hours he took another tablet of diclofenac and six hours afterwards was referred to our department because of a temperature of 38°C and vomiting. Laboratory tests were: haemoglobin, 12 g/dl; white blood cell count, 17 x 10⁹/l with a normal differential count; serum aspartate transaminase (AST), 90 IU/l (normal, 20-45 IU/l); serum lactate dehydrogenase, 337 IU/l (normal, 160-220 IU/l); serum alkaline phosphatase, 263 IU/l (normal, 20-95 IU/l); serum bilirubin, 35.9 µmol/l (2-1 mg/100 ml (direct, 18.9 µmol/l (1.1 mg/100 ml)); and serum creatinine 205-2 µmol/l (3.0 mg/100 ml). Urine analysis was normal. Sputum, urine, and blood cultures were negative. A chest radiograph showed a mild cardiomegaly and electrocardiogram at rest showed a right bundle branch block with left axis deviation.

Although no causative agent or possible source of infection was found, the patient was treated for septic shock. He received isotonic fluids, crystalloid, penicillin 10 million units, and gentamicin 240 mg a day. His temperature subsided within 10 days, and the liver and kidney function tests returned to normal. He was readmitted after four months when rigors, vomiting, and fever (38°C) followed a single dose of 25 mg of diclofenac by mouth. Blood pressure on admission was 100/60 mm Hg and the remainder of the physical examination was normal. Laboratory findings were: erythrocyte sedimentation rate (Westergren), 72 mm/first hour; haemoglobin, 12.2 g/dl; white blood cell count, 9.6 x 10⁹/l with a normal differential count; serum aspartate transaminase, 65 IU/l; serum lactate dehydrogenase, 280 IU/l; serum alkaline phosphatase, 165 IU/l; serum bilirubin, 2.9 µmol/l (14 mg/100 ml); serum creatinine, 123.7 µmol/l (1.4 mg/100 ml); serum complement—C3, 0.98 g/l (normal, 0.57-1.2 g/l), C4, 0.38 g/l (normal, 0.2-0.5 g/l). Protein immunoelectrophoresis and urine analysis were normal. Sputum, blood, and urine cultures were negative. Macrophage migration test was inhibited by diclofenac but not by ibuprofen. Mast cell degranulation test was negative for both drugs. X-ray examination of the chest and total body radioscopc scan with gallium 67 did not show signs of focal infection. At this stage a hypersensitivity reaction to the drug was suspected and no antimicrobial treatment was given. Fever subsided gradually within four days and the patient was discharged in good health with normal kidney and liver function tests.

Comment

Hypersensitivity reactions to non-steroidal anti-inflammatory drugs, mainly by diclofenac, aspirin, and ibuprofen, have been described. These reactions have been attributed to prostaglandin synthetase inhibition. Anaphylactic shock and urticaria have been reported in patients with idiopathic reaction to pyrazolone drugs, and this type of hypersensitivity seems to have an immunological background.

Our patient developed a shock like syndrome, accompanied by a high grade fever, which is similar to that described in patients with idiосyncrasy to pyrazolone drugs. The concomitant appearance of shock and diclofenac ingestion on three different occasions confirms their causal relation.

Both the clinical picture and the positive macrophage migration test suggest a type of hypersensitivity reaction.

We should, however, emphasise that in all three instances in our patient the drug induced anaphylaxis was preceded by ibuprofen ingestion. When the patient took diclofenac for the first time treatment with ibuprofen anaphylaxis did not occur. Thus the role of this drug in the induction of hypersensitivity is still to be determined.


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Rifampicin and adrenal crisis

Rifampicin, a potent inducer of hepatic enzymes, increases the metabolism of glucocorticoids. We report two cases of adrenal insufficiency secondary to tuberculous in which acute adrenal crisis was apparently precipitated by rifampicin.

Case reports

Case I—A 65 year old man presented with a productive cough and weight loss. Examination showed generalised skin pigmentation. The chest radiograph showed minimal infiltration in the left upper lobe, and after weeks of incubation the sputum continued a scanty growth of acid-fast bacilli. The serum sodium concentration was 135 mmol(l/1)g, potassium concentration 5.14 mmol(l/1)g, and urea concentration 6 mmol(l/1)g (35.7 mg/100 ml) and the blood pressure 140/90 mm Hg. Treatment was started with rifampicin 600 mg, isoniazid 300 mg, and ethambutol 1 g daily. Because of the pigmentation arrangements were made to investigate possible adrenal insufficiency. Blood was tested before and after admission, however, he presented with dizziness and lethargy. He was clinically dehydrated and had a blood pressure of 100/60 mm Hg. The serum sodium concentration had fallen to 115 mmol/l and the potassium and urea concentrations increased to 5.4 mmol/l and 8.0 mmol/l (14.8-2 mg/100 ml), respectively. A tetracosactrin (Synacthen) challenge test was immediately performed and subsequently confirmed adrenal insufficiency: serum cortisol values were 95 mmol/l (3.4 µg/100 ml) before and 85 mmol/l (3.1 µg/100 ml) 30 minutes after 0.25 mg tetracosactrin. The patient was treated with intravenous saline and hydrocortisone, his condition rapidly improved, and the electrolyte values returned to normal. He subsequently remained well initially taking 37.5 mg cortisone acetate and 0.1 mg hydrocortisone daily. Plasma cortisol concentrations remained low (85 mmol/l two hours after cortisone acetate), however, and these doses were therefore doubled. The 65-hydroxycortisol excretion rate was 4379µg/day.

Case 2—A 73 year old man with extensive pulmonary tuberculosis was admitted complaining of nausea, vomiting, and weight loss seven weeks after beginning treatment with rifampicin 600 mg, isoniazid 300 mg, and ethambutol 800 mg daily. He was clinically dehydrated. Blood pressure was 120/70 mm Hg and serum sodium concentration 127 mmol(l/1)g, potassium concentration 4.3 mmol(l/1)g, and urea concentration 17.8 mmol(l/1)g (107 mg/100 ml). Chemotherapy was discontinued. After 400 mg of hydrocortisone his general condition slowly improved, and four weeks later the antituberculous chemotherapy was reinstated. Within 14 days he was again complaining of nausea and vomiting. There was mild generalised pigmentation, clinical dehydration with a blood pressure of 100/60 mm Hg, and the serum sodium concentration was 127 mmol(l/1), potassium concentration 5.2 mmol(l/1), and urea concentration 23.3 mmol(l/1) (140 mg/100 ml). The basal cortisol value was 213 mmol(l/1) (7.7 µg/100 ml) with no response to challenge with tetracosactrin. After treatment with intravenous saline and hydrocortisone he rapidly improved and subsequently remained well taking 37.5 mg cortisone acetate and 0.1 mg hydrocortisone daily.