Summary / learning points

- acute pancreatitis can occur as a complication of falciparum malaria
- persistent and severe abdominal pain may be presenting manifestation of acute pancreatitis in *P falciparum* infection
- serology of pancreatitis should be ordered routinely in falciparum malaria
- pancreatitis should be considered in the spectrum of disease associated with *P falciparum* infection

Box 3

The list of identifiable causes of pancreatitis is growing and pancreatitis should be considered in the spectrum of disease associated with *P falciparum* infection.

Final diagnosis

Acute pancreatitis complicating falciparum malaria.

Keywords: acute pancreatitis; malaria; *Plasmodium falciparum*

- 1 Banks PA. Acute pancreatitis. In: Haibrich WS, Schaffner F, Berk JE, eds. *Bockus Gastroenterology*, 5th edn. Philadelphia: WB Saunders Company, 1995; pp 2888–917.
- 2 Case records of the Massachusetts General Hospital (case 35–1989). *N Engl J Med* 1989;321:597–605.
- 3 Sheehey TW, Reba RC. Complications of falciparum malaria and their treatment. *Ann Intern Med* 1967;66:807–9.
- 4 Gurman G, Schlaeffer F, Alkan M, Heilig I. Adult respiratory distress syndrome and pancreatitis as complications of falciparum malaria. *Crit Care Med* 1988;16:205–6.
- 5 Steinberg W, Tenner S. Acute pancreatitis. *N Engl J Med* 1994;330:1198–1210.
- 6 World Health Organization. Severe and complicated malaria. *Trans R Soc Trop Med Hyg* 1990;84 (suppl 2):1–65.
- 7 White NJ, Breman JG. Malaria and babesiosis. In: Isselbacher KJ, Braunwald E, Wilson JD, et al, eds. *Harrison's Principles and practice of medicine*, 13th edn. New York: McGraw Hill Inc, 1994; pp 887–96.
- 8 Krogstad DJ. *Plasmodium* species (malaria). In: Mandell GL, Bennet JE, Dolin R, eds. *Principles and practice of infectious diseases*. 4th edn. New York: Churchill Livingstone, 1995; pp 2415–7.
- 9 Bradley D, Newbold CI, Warrell DA. Malaria. In: Weatherall DJ, Ledingham TG, Warrell DA, eds. Oxford: Oxford University Press, 1996; pp 835–63.
- 10 Marcial MA, Marcial-Rojas RA. Protozoal and helminthic infections. In: Kissane JM, ed. *Anderson's Pathology*, 9th edn. St Louis: CV Mosby Company, 1990; pp 205–6.
- 11 Boonpucknavig V, Boonpucknavig S. The histopathology of malaria. In: Wersdorfer WH, Mc Gregor IA, eds. *The principles and practice of malariology*. Edinburgh: Churchill Livingstone, 1988; pp 673–734.
- 12 Lichtman AR, Mohracken S, Englebrecht M, Bigalke M. Pathophysiology of severe forms of falciparum malaria. *Crit Care Med* 1990;16:205–6.
- 13 White NJ, Ho M. The pathophysiology of malaria. *Adv Parasitol* 1992;31:34–173.
- 14 Clark IA. Monokines and lymphokines in malarial pathology. *Ann Trop Med Parasitol* 1987;577–85.

Metabolic acidosis

M Souheil Darwich, Waddah Allaf

A 60-year-old woman on haemodialysis secondary to end-stage renal disease, was brought to the emergency room with recent onset of weakness, decreased consciousness and shortness of breath. She has a history of diabetes mellitus, hypertension and coronary artery disease.

Her medications on admission to the emergency room were: hydralazine, quinidine sulphate, catapres patch, lorazepam, dipyridamol, propulsid, nifedipine XL, metformin HCl, promethazine, and zolpidem tartrate. Physical examination revealed the following: respiratory rate 26 breaths/min and shallow, pulse 104, blood pressure 120/70 mmHg, afebrile. Physical examination was otherwise remarkable for only mild abdominal tenderness. Laboratory investigation revealed: sodium 141 mmol/l, HCO₃ 9 mmol/l, blood urea nitrogen 36 mg/dl, creatinine 9.7 µmol/l, glucose 172 mmol/l, amylase 168 mmol/l, alanine transaminase 19 IU/l, serum ketones 1:4 dilution, lactic acid 17.4 mmol/l; whole blood count was normal. Arterial blood gas: pH 6.88, pCO₂ 9.5, pO₂ 153, HCO₃ 1.8, SaO₂ 97.2 on room air.

During her stay in the emergency room, the patient became more lethargic and tachypnoeic, eventually requiring intubation and mechanical ventilation.

Question

What is the most likely diagnosis: sepsis, diabetic ketoacidosis, drug-related side-effect, uraemic acidosis, or salicylate overdose?

Department of
Medicine, Wright State
University, Good
Samaritan Hospital
and Health Center,
3535 Salem Ave,
Dayton, OH 45406,
USA
M S Darwich

50 Gibson Blvd, Apt#
B7, Valley Stream, NY
11581, USA
W Allaf

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Answer

The patient's illness is probably a drug-related side-effect.

Discussion

The patient has severe metabolic acidosis, most probably due to metformin. Metformin is a biguanide oral hypoglycaemic agent.¹ It can be used alone or in combination with sulphonylureas or insulin. The mechanism of action²⁻⁴ has been thought to be due to:

- increased glucose utilisation
- decreased glucose production
- increased glucose metabolism and lactate formation in the intestine
- reduced hepatic gluconeogenesis
- possibly reduced glucose absorption by the intestine.

Side-effects from metformin are rare, but potentially fatal. It can occasionally cause lactic acidosis.⁵ The half-life of metformin after oral administration is 4.0 to 8.7 hours. It is excreted by the kidneys. When creatinine clearance is decreased, the elimination of metformin is prolonged and may cause lactic acidosis. In end-stage renal disease its oral administration

is contraindicated. Metformin can also cause lactic acidosis in the presence of cardiovascular, pulmonary, and hepatic disorders. It is recommended that metformin be discontinued prior to surgery, administration of contrast dyes, sepsis, and acute cardiovascular and gastrointestinal events.

In the above case, metformin was discontinued, the patient underwent haemodialysis and an intravenous bicarbonate drip was initiated. Within 24 hours she improved dramatically with the lactic acid level dropping significantly and subsequent improvement in the metabolic acidosis. Physicians trained after 1976 may not be familiar with the side-effects of metformin and other biguanides. Efforts should be made to alert more recently qualified physicians to these potential side-effects, as these medications are regaining their popularity.

Final diagnosis

Severe metabolic acidosis, most probably due to metformin.

Keywords: lactic acidosis; metformin; renal failure; adverse drug reaction

1 Bailey CJ. Metformin: an update. *Gen Pharmacol* 1993;**24**:1299-309.

2 Sirtori CR, Pasik C. Re-evaluation of biguanide, metformin: mechanism of action and tolerability. *Pharmacol Res* 1994;**30**:187-228.

3 Fantus IG, Brosseau R. Mechanism of action of metformin: insulin receptor and postreceptor effects in vitro and vivo. *J Clin Endocrinol Metab* 1986;**63**:898-905.

4 Goo AK, Carson DS, Bjelajac A. Metformin, a new treatment option for non-insulin dependent diabetes mellitus. *J Fam Pract* 1996;**42**:612-8.

5 Lim PS, Huang CC, Wei JS. Metformin induced lactic acidosis. *J Formos Med Assoc* 1992;**91**:374-6.