

LETTER

A falling row of dominoes

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To the Editor,

A 60-year-old man presented himself in the emergency room in a state of deep shock and severe metabolic acidosis (pH=6.654). He had an acute abdomen, initially attributed to intestinal ischaemia, based on abdominal pain, CT findings and high blood lactic acid levels (22 mmol/l). At exploratory laparotomy, though, only viable intestines were found. A solid mass at the mesenteric root was biopsied and would later prove to be a carcinoid tumour. This tumour led to chronic diarrhoea, which was attributed to other causes. Slowly and progressively his kidney function diminished, as the tumour further dehydrated him. Not drinking for hours during long-distance travel finally tipped the balance. The resulting hypovolemic shock cannot fully explain the deep acidosis or extremely high lactic acid level, so one final domino is missing...

It was the metformin. He suffered from type II diabetes, for which metformin is the cornerstone of the treatment, as it increases glucose-to-lactic-acid conversion (the result of intracellular redox potential shifting from aerobic to anaerobic), exchanging glucose (which diabetics have too much) for lactic acid. Under normal circumstances, the liver's capacity to metabolize lactic acid greatly exceeds lactic acid production, but when lactic acid production explodes, this may fail (1-2). His dehydrated body couldn't maintain adequate perfusion, leading to peripheral lactic acid production. His ever increasing metformin levels (the exact level remains unknown, as most laboratories – including ours – are unable to measure), no longer cleared by the progressively failing proximal renal tubules, gave the final blow.

Metformin-associated lactic acidosis (MALA) is a well-known entity (incidence < 0.1/1000 patient-years of metformin exposure), characterised by deep high-anion gap metabolic acidosis and extremely high blood lactic acid levels, in predisposed patients, suffering from renal dysfunction (insufficient metformin clearance), hepatic dysfunction or alcoholism (insufficient lactic acid clearance), heart failure or vascular disease (inadequate perfusion), ... (3) In that state, it doesn't take much to make the first domino fall; the rest will follow (Fig. 1).

MALA commonly presents insidiously, mimicking other illnesses present; with symptoms such as nausea, vomiting, abdominal pain, confusion, weakness, hypotension and tachypnoea easily attributed to other causes

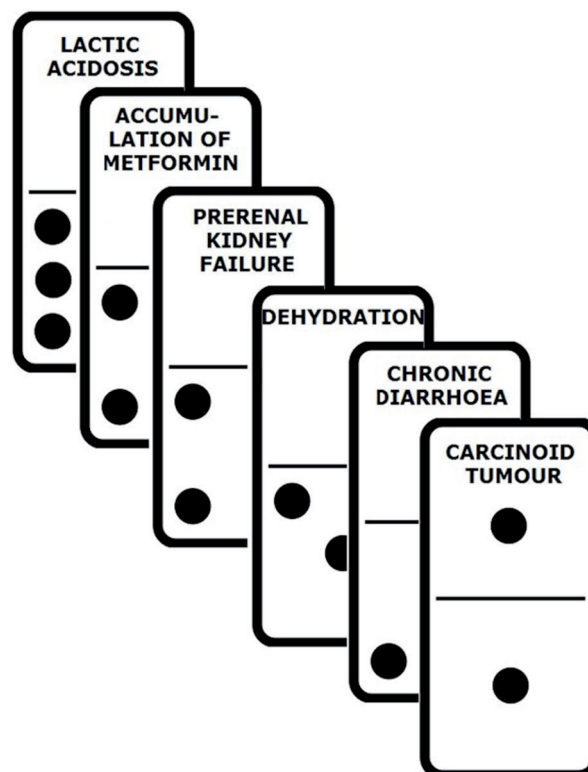


Figure 1. — “The row of dominoes”, Van Looy E.

– MALA rarely comes alone. Treatment is possible, in severe cases by haemodialysis, but mortality reaches 30-50%, once the final domino has fallen (4). Therefore we must prevent it by correctly educating patients on pausing it during acute illness, especially when dehydration is possible or likely. And carefully monitor kidney function regularly, as diabetes worsens it, and patients more often grow old with diabetes, ... and with metformin.

References

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