

Augmented serum lactic acid combined with metabolic alkalosis : a case report

C. NIEWOLD (*), L. L. SZEGEDI (**), and T. F. JACOBS (**)

Abstract : Lactic acidosis is a common problem in the peri-operative period. During extensive surgery we frequently have an augmentation of lactic acid most often on the basis of hypoperfusion. Normally, a rise in serum lactate level causes a fall in blood pH, and this metabolic acidosis is accompanied by a high anion gap. In this case report a perioperative rise in lactic acid and an elevation in serum pH in a patient during meningeal tumour surgery is presented.

Key words : Lactic acid ; alkalosis ; meningioma.

INTRODUCTION

Metabolic acidosis can occur because of an increase in endogenous acid production (such as lactate), a loss of bicarbonate (as in diarrhoea) or an accumulation of endogenous acids (as in renal failure). Rises in serum lactic acid (LA) levels normally result in a high anion gap metabolic acidosis and occurs when there is an imbalance between the production and the clearance of lactate. The presence of hypoalbuminemia, however, can lower the anion gap and mask a high anion gap metabolic acidosis (1).

Accumulation in plasma of LA may be secondary to obvious tissue hypoxia (type A, e.g. circulatory insufficiency, severe anaemia) or to more occult disorders (type B, e.g. seizures, diabetes mellitus, hepatic failure, malignancy) (1).

Lactate is produced in all tissues, but the skeletal muscle, the brain and the red blood cells account for the majority of its production. Lactate is a metabolic end product of the anaerobic glycolysis and is excreted by the kidney or it can be converted in the liver and returned to the muscles, as described in the Cori cycle. The liver and the kidney are the two most important LA consuming organs (1).

As stated above, lactic acidosis occurs whenever production of LA exceeds its utilization. Lactic acidosis associated with sepsis and circulatory failure is a common pre-terminal event in many malignancies. In the absence of hypoxemia, lactic acidosis may occur in patients with leukaemia,

lymphoma or solid tumours (1). Extensive involvement of the liver by the tumour is apparent in most of these cases. Alteration of the liver function may be responsible for the LA accumulation (1). We hereby describe the anaesthetic course of a 64 year old patient, undergoing surgery for brain tumour removal, in which metabolic alkalosis was present despite of a continuous rise in serum lactate levels.

CASE REPORT

A 64 year old female patient (weight 53 kilograms, height 159 cm) was scheduled for resection of a meningioma located in the right fronto-temporal part of the brain. The patient didn't have any important medical history ; she only recalled a mild allergy (skin rash) to penicillin.

One day before elective surgery she had a partial embolisation of the medial meningeal artery under general anaesthesia. After this procedure she was fully awoken and alert.

Upon arrival into the operating room the mental status of the patient was normal, she only claimed of fatigue and a partial vision loss since two months.

Her laboratory results revealed a mild anaemia (Hct 34.6%) and thrombocytopenia (Platelet count of 105000/ μ l). Echocardiography showed no abnormalities.

Caroline Niewold, M.D. ; Laszlo L. SZEGEDI, M.D., Ph.D. ; Tom F. JACOBS, M.D.

(*) Resident in Anaesthesiology, Department of Anaesthesiology, Ghent University Hospital, Ghent, Belgium.

(**) Staff Anaesthesiologist, Department of Anaesthesiology, Ghent University Hospital, Ghent, Belgium.

Address for correspondence : Dr. Caroline Niewold, Ghent University Hospital, Department of Anaesthesiology, De Pintelaan, 185, 9000 Ghent, Belgium.
E-mail : caroline.niewold@skynet.be

Intraoperative monitoring consisted at the start of non-invasive arterial pressure, a five leads ECG, pulse-oximetry, capnography and a rectal temperature probe.

Two 20G peripheral venous catheters and a central venous line in the right internal jugular vein were inserted. The right radial artery was cannulated for continuous blood pressure monitoring and blood gas sampling. In order to monitor the diuresis an urethral catheter was inserted.

Anaesthesia was induced using a continuous infusion of remifentanyl ($0.15 \text{ mcg.kg}^{-1}.\text{min}^{-1}$), a bolus of propofol (loading dose 2 mg/kg) and a loading dose of cisatracurium (12 mg) to allow tracheal intubation. Anaesthesia was maintained with a variable rate continuous infusion of propofol and remifentanyl. A continuous infusion of cisatracurium was started to maintain neuromuscular block throughout surgery. The neuromuscular block was assessed by regular measurements of post-tetanic count during the procedure.

A cuffed tracheal tube n° 7.5 was inserted and volume controlled mechanical ventilation at constant flow with a mixture of 50% oxygen in air was started.

Surgery was in a half sitting position (45°) to lower the cerebral pressure, and lasted for over more than 16 hours.

At the beginning of surgery, in an attempt to lower the intracerebral pressure, the patient received a slow intravenous bolus of methylprednisolon (1000 mg) and 100 ml of mannitol 20%. Thereafter the surgeon asked to give 40 mg of furosemide.

As a consequence the patient developed a massive diuresis up to more than 1 litre per hour. Possibly there was also a factor diabetes insipidus participating.

The first seven hours, the patient remained hemodynamically stable, mainly due to aggressive fluid replacement to compensate for blood loss (estimated blood loss of 2000 ml) during surgery, and also for the initially massive diuresis. After seven hours surgery and anaesthesia, phenylephrine was administered ($0.3 \text{ } \mu\text{g.kg}^{-1}.\text{min}^{-1}$), and her blood pressure restored to starting levels and remained stable throughout the last part of surgery.

In total, over sixteen hours, she received 9 litres of crystalloids (2.5 litres Ringer lactate solution and 6.5 litres of Plasmalyte A), 3.5 litres of pentastarch solution and 7 units of packed cells. In order to restore coagulation, which became a problem near the end of surgery she also received 8 I.U. of thrombocytes and 2 I.U. fresh frozen

plasma. Peroperative laboratory testing revealed 52000 thrombocytes per μl and a Pt of 62% (INR of 1.40).

At the lowest the patient had an Hct of 24% and rose to 34% after transfusion.

Despite rigorous fluid replacement the patient's serum lactate augmented from 21 mg/dl at the start of surgery to 41 and 60 mg/dl after six, respectively eight hours of surgery. Nevertheless we observed a rise in serum pH from 7.43 to 7.55.

At the start of surgery there was a mild hyperventilation to reduce cerebral pressure. Partial carbon dioxide tension in arterial blood (PaCO_2) dropped from 38 to 32 mmHg and remained around that value throughout surgery.

Plasma bicarbonate was normal to even slightly augmented, ranging from 25 to 28 mmol/l . Serum glucose remained normal throughout surgery (160 mg/dl).

To exclude a possible epileptic insult which could cause an augmentation of lactic acid (although full muscle relaxation was provided by high dose of cisatracurium) the patient received 500 mg of phenytoin intravenously.

At the end of surgery, after approximately 16 hours, the lactic acid started to drop (LA levels of 50 mg/dl).

The patient was brought to the intensive care unit under propofol sedation and mechanical ventilation for 12 hours. Methylprednisolon (intravenously, $4 \times 250 \text{ mg/day}$) and phenytoin (intravenously, $3 \times 100 \text{ mg/day}$) was prescribed.

The next morning her LA dropped to 20 mg/dl with normalization in pH (7.4) and bicarbonate (25.7 mmol/l). The sedation was stopped, the patient was awakened and fully alert and the trachea was successfully extubated. After two days she was transferred to the neurosurgery high care unit, without complications.

Unfortunately after one day at the high care unit her neurological status deteriorated brutally. An emergency CT-scan showed extensive oedema of the right hemisphere. She quickly became unresponsive. Her trachea was intubated and she was urgently operated (surgical decompression), but three days later she died.

DISCUSSION

The anaesthetic course of a 64 year old female patient was reported, who while undergoing brain surgery, developed high levels of LA. In this

situation, one would expect metabolic acidosis, however this didn't occur. Thus, the above described case leaves us with two questions : why the patient presented an augmentation of LA levels, and why did the patient have metabolic alkalosis instead of becoming more acidic ?

Lactic acid is derived from the metabolism of pyruvic acid. This reaction is catalyzed by lactate dehydrogenase and involves the conversion of NADH into NAD⁺. Although LA is produced in all tissues, skeletal muscle, brain, red blood cells and renal medulla are responsible for the majority of the production. Both liver and kidney are important consumers of LA, and normally the liver takes up about 60% of the circulating lactate (1).

Lactic acid accumulation occurs whenever its production exceeds its utilization.

Epileptic seizures are a possible cause of transient increase in the production of LA (1, 2). It has been reported that intracranial meningiomas, more frequently those that have surrounding cerebral oedema, can very often be the cause of post-operative epilepsy (3, 4).

Although the patient in this case report didn't have a history of epileptic insults, brain surgery itself can be the provoking factor (4).

The patient received continuous curarisation during surgery, monitored by post tetanic counts, however at some point the surgeon complained about some movement in the brain. This could be attributed to a form of epileptic insult. She therefore received 500 mg IV over half an hour of phenytoin which was followed by 3 times 100 mg daily after surgery.

In most cases, however, there is evidence for overproduction and defective utilization as well.

Traditionally the classification of lactic acidosis is based on the presence of tissue hypoperfusion : type A is the group with impaired tissue oxygenation, type B is the group in which tissue oxygenation is maintained (1).

During surgery an impaired tissue oxygenation due to hypovolemia followed by tissue hypoperfusion would be the most obvious cause. However, in this case, hypoperfusion is to be excluded, as the patient's central venous pressure and systemic blood pressure were monitored and kept constant at normal values during the whole procedure.

Malignancy itself can be an important cause of the type B lactic acidosis.

There is evidence for altered carbohydrate metabolism in some cancer cells with increased glycolytic activity (1).

Central hyperventilation and increased brainstem tissue LA have been reported in malignant meningeal tumours (5). The patient, indeed, already had a slightly augmented LA at the beginning of surgery (20 mg/dl).

The last factor we think that could have played a role in the rise of LA is the continuous infusion of propofol at the rate of 6-7 mg.kg⁻¹.h⁻¹. There are several reports on the propofol infusion syndrome in adults after short-term propofol infusion of doses above 5 mg.kg⁻¹.h⁻¹. (6, 7). The full syndrome consists of cardiac failure, rhabdomyolysis, lactic acidosis and renal failure. It develops more frequently in combination with other drugs more specifically with steroids and catecholamines, which our patient received both. There has been a report in the past of a mild propofol infusion syndrome with only the development of a lactic acidosis without renal failure or cardiac depression (7). In the present case the patient had a normal renal and cardiac function, without signs of rhabdomyolysis (creatinine kinase was normal after surgery). An argument that also pleads against propofol infusion syndrome is that propofol infusion was continued at lower dose at the intensive care unit, however, during this time the serum LA was already lowered.

The second question we need to answer is why the patient developed an alkalosis although a severe rise in LA levels.

All changes in serum pH occur through changes in three variables : carbon dioxide, electrolyte concentration and total weak acid concentration (8). A rise in LA does not necessarily give an acidosis. Furthermore, a low serum albumin can mask the rise in negatively charged proteins. The patient had a drop in albumin, till a value of 1.6 g/dl. This means, that when lactic acidosis is associated with a respiratory or metabolic alkalosis, the arterial pH can be a non-sensitive indicator of lactic acidosis. The pH may therefore be normal or even elevated (1).

The patient of this case had an idiopathic respiratory alkalosis. To lower the cerebral pressure of the patient she was also hyperventilated. There are, however, reports of hyperventilation and respiratory alkalosis, due to central lactic acidosis caused by a meningeal tumour (5, 9).

A metabolic alkalosis was present, as shown by elevated bicarbonate.

Metabolic alkalosis is most often induced by diuretic therapy or the loss of gastric secretions due to vomiting or nasogastric suction. The patient received at the beginning of the surgery diuretics (40 mg intravenous bolus furosemide) which leads

to an inappropriate increase in renal acid loss and also a substantial volume contraction.

In this case report there were several events that may have influenced pH in the patient in addition to any changes in serum lactate levels. These events, including ventilation, medication such as diuretics, fluid and electrolyte administration, could have led to the accumulation of LA without an acidosis, but with the development of a lactic alkalosis.

References

1. Fall P. J., Szerlip H. M., *Lactic acidosis : from sour milk to septic shock*, J. INTENSIVE CARE MED., **20**, 255-71, 2005.
2. Orringer C. E., Eustace J. C., Wunsch C. D., Gardner L. B., *Natural history of lactic acidosis after grand-mal seizures. A model for the study of an anion-gap acidosis not associated with hyperkalemia*, N. ENGL. J. MED., **297**, 796-9, 1977.
3. Lieu A. S., Howng S. L., *Intracranial meningiomas and epilepsy : incidence, prognosis and influencing factors*, EPILEPSY RES., **38**, 45-52, 2000.
4. Jenssen S., Potolicchio S.L., Sekhar L.N., *Do skull base lesions and their surgical treatment cause epileptic seizures ?*, CLIN. NEUROL. NEUROSURG., **109**, 406-8, 2007.
5. Bluher S., Schulz M., Bierbach U., *et al.*, *Central lactic acidosis, hyperventilation, and respiratory alkalosis : leading clinical features in a 3-year-old boy with malignant meningeal melanoma*, EUR. J. PEDIATR., **167**, 483-5, 2008.
6. Liolios A., Guérit J. M., Scholtes J. L., Raftopoulos C., Hantson P., *Propofol infusion syndrome associated with short-term large-dose infusion during surgical anesthesia in an adult*, ANESTH. ANALG., **100**, 1804-6, 2005.
7. Burow B. K., Johnson M. E., Packer D. L., *Metabolic acidosis associated with propofol in the absence of other causative factors*, ANESTHESIOLOGY., **101**, 239-41, 2004.
8. Kellum J. A., *Disorders of acid-base balance*, CRIT. CARE MED., **35**, 2630-36, 2007.
9. Leverve X. M., Guignier M., *Hyperlactataemia : Acidosis or Alkalosis ?*, J. CLIN. CHEM. CLIN. BIOCHEM., **24**, 273, 1986.