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Perioperative Intractable Severe Lactic Acidosis in a Spine Patient: Is it Always Type A?

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Abstract

Perioperative lactic acidosis following major surgeries is usually attributed to oxygen debt resulting from tissue hypoxia. Lactate metabolism is more complex than initially appreciated and peri-operative physicians should recognize that causes of hyperlactatemia are myriad, and treatment can be highly disparate. We present a case of severe lactic acidosis which developed in a 67-year-old diabetic man during posterior cervical spine fixation surgery. The plasma lactate level peaked to 16 mmol/L, was fluid and vasopressor unresponsive, with negative urinary ketones, and progressively resolved within 24 hours without significant patient morbidity. This report emphasizes the importance of evaluating elevated lactic acid thoughtfully coupled with the entire clinical picture, and not as mere isolated biomarker of shock induced low flow state.

Keywords: ***Hyperlactatemia; Acidosis; Hyperglycemia; Ketoacidosis; Spine; Diabetic***

1. Abbreviations

LA: Lactic acidosis; MA: Metabolic acidosis; SCI: Spinal cord injury; C: Cervical spine; B.P: Blood pressure; H.R: Heart rate; ABG: Arterial blood gas; DKA: Diabetic ketoacidosis; P.O: Post operative; BS: Blood sugar; U.O: Urine output; (3-β-OH-B): 3-beta-hydoxy-butyrate; CPK: Creatinine phosphokinase.

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2. Introduction

Lactic acid is produced in physiologically normal processes, and as a common finding in disease states. When increased production is comorbid with decreased clearance, the severity of the clinical course escalates. Used synonymously, lactate or lactic acid levels are normally less than 2 mmol/L, with hyperlactatemia defined as lactate levels between 2-4 mmol/L, while severe levels of lactates are 4 mmol/L or higher. Other definitions for lactic acidosis (LA) include pH less than or equal to 7.35 and lactatemia greater than 2 mmol/L with a partial pressure of carbon dioxide less than or equal to 42 mmHg. No distinctive features are unique to pathological and persistent LA and signs and symptoms depend on the underlying aetiology [1].

Postoperative hyperlactatemia is generally considered to solely reflect hypoperfusion and tissue hypoxia and associated with poor surgical outcomes [2]. Pathological and persistent perioperative LA is a complex event determined by numerous variables, including shock (septic, distributive, cardiogenic), inadequate intraoperative rehydration, high dose vasopressors, mesenteric or limb ischemia, liver failure, medications induced (metformin, nucleoside reverse transcriptase inhibitors), propofol infusion syndrome, and metabolic disorders. Differentiating among all these causes can be challenging during a patient's initial presentation and must include the consideration of a multifactorial etiology [2,3].

This case highlights occurrence of intraoperative severe lactic and metabolic acidosis (MA) in a spine patient which was nearly refractory to targeted management, did not clearly fit into any subset of LA and reverted to normal levels within 24 hrs postoperative. The probable causes and pathophysiology are discussed with a dilemma whether lactate alone is sufficient to judge success or failure of treatment? A contemporary understanding of lactate balance is critical to the management of the postoperative patient with LA.

3. Case Report

A 67-year-old male presented with traumatic fracture subluxation at vertebral C 4-5 level sustaining cervical spinal cord injury (SCI). Neurological examination revealed sensory impairment below dermatome level C-4, 0 / 5 power in bilateral (b/l) lower limbs and 2/5 power in b/l upper limbs. His computed tomography and magnetic resonance image revealed ossified posterior longitudinal ligament from C-2 to C7-T1, focal disruption of anterior longitudinal ligament at C4-5-disc level with cord contusion and posterior disc protrusion at C4-5 level impinging thecal sac causing severe compromise of the spinal cord (FIG. 1).

There was no clinical or radiological sign of head, abdomen, or any other bony injury. He was non-smoker, non-alcoholic, physically fit for his age, and suffered from diabetes-2 for last four years on tablet glimepiride 2 mg OD. His presenting vitals included heart rate (H.R) of 52/min, blood pressure (B.P) of 142/80 mm Hg, respiratory rate of 14/min; and physical examination of respiratory and cardiac system was unremarkable. Other than high blood sugars (BS), glycosuria (3+) and HbA1C of 11%, rest laboratory parameters were acceptable (TABLE 1). Patient received intravenous fluids resuscitation, respiratory and oxygen therapy, thromboprophylaxis, proton pump inhibitors, subcutaneous insulin, and nasogastric tube feed in intensive care unit (ICU).

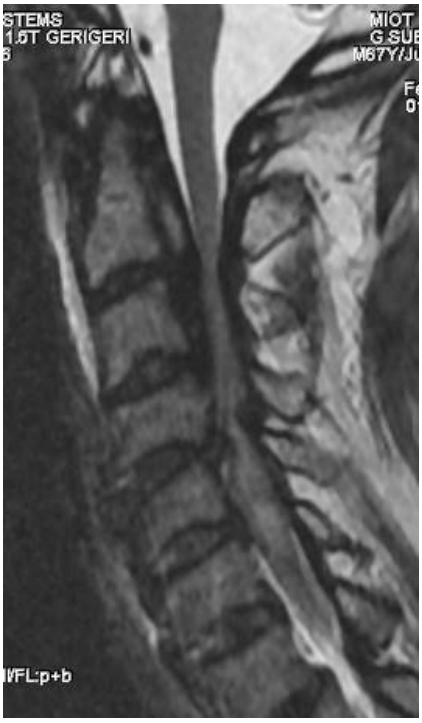

FIG. 1. **MRI Sagittal T-2 cervical spine shows ossification of posterior longitudinal ligament causing severe cord compression with cord oedema at C4-C5 and C5-C6 level.**

TABLE 1. **Perioperative laboratory parameters. Noticeably urinary ketones were negative during acute phase of lactic acidosis and appeared on postoperative day 2 when it had resolved. Serum 3-β-OH-B is moderately elevated (> 3 mmol/L being the cut off for diagnosing DKA or seeking urgent medical attention).**

INVESTIGATIONS	VALUES Pre-op	Post-surgery Day 0	Day 1	Day 2	BIOLOGICAL REFERENCE
HAEMOGLOBIN (g/dl)	12.9	12.6	11.8	12.2	14-17
LEUKOCYTE COUNT (cell/Cumm)	6420	10650	15950	12010	4400-1100
PLATELETS (cell/Cumm)	211000	237000	30400	22800	150000-450000
UREA (mg/dl)	27	30	29	35	20-40
CREATININE (mg/dl)	0.5	0.5	0.6	0.5	0.6-1.2
SODIUM (mEq/L)	137	140	151	146	136-142
POTASSIUM (mEq/L)	4.0	3.2	3.9	4.2	3.5-5.1
BICARBONATE (mEq/L)	21	12	22	23	21-28
CHLORIDE (mEq/L)	102	114	113	114	95-105
BILIRUBIN (mg/dl)	0.3	0.6			0-0.8
AST (IU/L)	24	23	24	26	10-34
ALT (IU/L)	20	24	26	22	10-40
HbA1C (%)	11.5				4-5.6
URINE KETONES	0	0	0	+++	
URINE GLUCOSE	++++	+++	+++	+++	
SERUM (3-β-OH-B) (mmol/L)		1.34			0-0.6

He was planned for C-2 laminectomy and decompression, posterior stabilization C2-7 and post operative on-table tracheostomy due to weak cough effort. Patient received uneventful awake fibreoptic nasotracheal intubation with spray-as you-go technique (2% lignocaine with adrenaline 1:200000), a right subclavian central venous and radial arterial catheter. Anaesthesia was maintained with oxygen, air, and sevoflurane with intravenous (I.V) fentanyl-vecuronium infusion. The patient was carefully pronated with help of Mayfield's tongs on soft abdominal rectangular frame while carefully padding chest, pelvis and limbs. Additionally, I.V insulin, glycopyrrolate 0.2 mg, tranexamic acid 1 gm, cefuroxime sodium 1.5 gm and dexamethasone 8 mg were administered. Intra-operative transient hypotensive episodes were managed by fluid boluses and intermittent IV ephedrine, while low dose adrenaline (3 mg/50 ml) infusion was commenced at 1-2 ml/hr for sinus bradycardia. Surgery lasted for 4 hrs and the patient received 4 L crystalloids, 1 L colloids, 1 unit of packed cell, and poured 570 ml urine output (U.O), while sustaining approximately 600 ml blood loss. Towards the end of surgery, patient started developing progressive hypotension, necessitating aggressive fluid therapy, and hiking adrenaline infusion. Arterial blood gas (ABG) analysis at this point revealed severe metabolic and lactic acidosis, hypokalaemia, and hyperglycaemia (FIG. 2). Post operatively patient was supinated, further fluid resuscitated, adrenaline infusion was discontinued and replaced with noradrenaline, and IV hydrocortisone 100 mg administered. Additionally, IV sodium bicarbonate 100 mEq and potassium chloride 30 mEq were administered followed by infusions respectively. Assuming undiagnosed diabetic ketoacidosis (DKA) insulin infusion was increased, and urinary ketones (acetoacetate) re-assessed which were surprisingly negative for ketonuria (nitroprusside method).

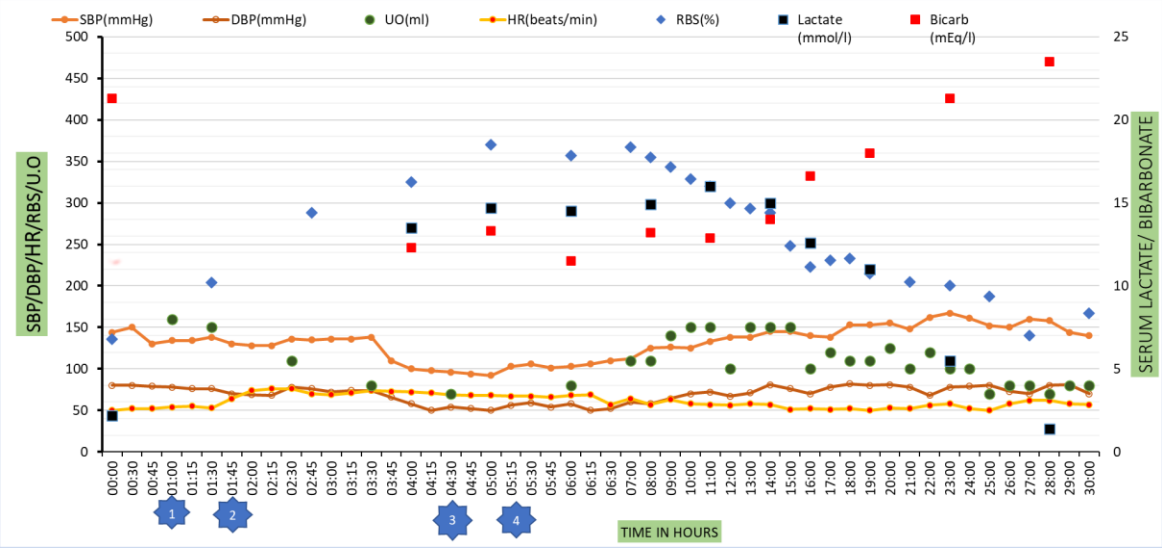

FIG. 2. **Graph depicting haemodynamic and laboratory parameters intraoperatively and post-operatively. X axis depicts time in hours format starting from anaesthesia induction. Primary Y axis (left of graph) shows systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), urine output (UO) in ml and random blood sugar (RBS) in gm/dl. Secondary Y axis (right of graph) depicts serum lactate (mmol/L) and bicarbonate (mmol/L).**

1. Incision 2. Low dose adrenaline infusion started 3. ABG reveals acidosis 4. Completion of surgery

Post tracheostomy patient was transferred on ventilator to ICU on norepinephrine, insulin, potassium, bicarbonate, and fentanyl infusions. Abdominal ultrasound revealed no signs of liver or bowel ischemia, venous and arterial doppler of b/l lower limbs were negative for thrombosis, U.O ≥ 1 ml/kg/hr with no signs of myoglobinuria, and all peripheries were clinically well perfused. Fresh laboratory parameters revealed persistent hyperglycaemia (BS ≥ 300), serum ketone 3-beta-hydoxy-butyrate (3-β-OH-B) level of 1.3 mmol/L, and escalating LA and MA (TABLE 1). By around post-operative (PO) 5 hours, the haemodynamic stabilized with gradual de-escalation of vasopressors and IV fluid requirements corresponding to peaking of lactates at 16 mmol/L (FIG. 2). Concomitantly bicarbonate and insulin infusions were steadily reduced and discontinued around PO 19-hours. The following day mechanical ventilation was liberated to spontaneous breathing tracheostomy mask, and nasogastric feeding was instituted. Sliding scale insulin was re-initiated with adequate glycaemic control. PO routine laboratory parameters were acceptable except PO-day-2 urine examination, which revealed urine ketones (3+) with normal serum pH and bicarbonate levels (table 1). PO-day-3 he was transferred to step down ICU and discharged on day 7.

4. Discussion

Lactate is an endogenous non-toxic molecule and an energetic substrate of gluconeogenesis. Current lactate measurement includes only L-Lactates isomer which has been the focus of all studies. While any accumulation of lactate results in LA, it is the combination of excessive accumulation with a diminished metabolic clearance which is by far the most serious. Hyperlactatemia is always an expression of adverse biochemical changes and anaerobiosis due to a low flow state represents just one possibility [4]. Although often used in the context of evaluating and prognosticating shock, lactates levels can be elevated for various reasons in the presence of adequate tissue perfusion i.e. liver disease, malignancy, medications (metformin, epinephrine), total parenteral nutrition, HIV, thiamine deficiency, mitochondrial myopathy, congenital lactic acidosis, trauma, excessive exercise, diabetic ketoacidosis, and ethanol intoxication. The elevated level in such cases stems from dysfunction of cellular metabolism, therefore approach and treatment are different [3]. Following the initial resuscitation, it is necessary to identify and treat additional contributors to ongoing hyperlactatemia. Elevated lactate in the setting of inadequate perfusion has classically been termed type A lactic acidosis because of the association with MA. Hyperlactatemia with adequate perfusion is termed type B lactic acidosis; although type B hyperlactatemia is more appropriate term since MA is not always present [1].

Retrospectively, we strongly believe that towards the end of surgery, probably LA and MA were the cause of worsening hypotension rather than vice versa. As most of clinicians we also initially assumed hypovolemia and neurogenic shock induced vasodilatation were the drivers of type-A LA and instituted appropriate intravenous resuscitation combined with vasopressors. Spine surgery in prone position is known to cause hypotension due to blood loss, anaesthesia, abdominal compartment syndrome, and malleable spine compressing inferior vena cava further decreasing venous return [5]. With ascending hyperlactatemia, we tried to rule out and engage other possible causes for LA; propofol infusion syndrome, visceral and liver ischemia, compression of major limb vessels, high dose adrenaline infusion or acute adrenal insufficiency. Abdomen and limb positions were reassessed, adrenaline infusion was replaced by noradrenaline, and additional intravenous steroids were administered. Rather than global hypoxia, transient episodes of low flow states and unidentified regional tissue ischemia may occur intraoperatively. Post-operative normal liver transaminases, absent clinical signs of bowel ischemia and unremarkable abdominal ultrasound ruled out hepatic and gut hypoperfusion as the cause. Blood samples were processed within 5 min, to

prevent artifactually elevated concentrations of lactate derived from erythrocytes and leukocytes and rechecked in another analyser to rule out equipment culpability. While we kept on checking and re-assessing hyperlactatemia assuming occult or cryptic shock, surprisingly haemodynamics were quite acceptable with adequate urine output, subtly signifying satisfactory perfusion. Inadequate perfusion may be global, regional, or microcirculatory. Unlike septic shock, the role of microcirculatory dysfunction has not been extensively studied in neurogenic spinal shock. SCI has been connoted to be associated with significant decrease in microvascular blood flow in liver, spleen, and muscles, and may cause regional tissue hypoxia and hyperlactatemia [6]. Endothelial inflammation and sepsis can impair the critical oxygen extraction ratio, which increases anaerobic metabolism and lactic acid formation despite fair organ oxygen delivery and perfusion [7].

We had a strong clinical suspicion of DKA as the perpetrator of LA and MA as supported by hyperglycaemia, polyuria, and hypokalaemia due to surgical stress. Surprisingly negative urine ketones, and serum 3-β-OH-B levels <3.0 mmol/L do not support the proposition of overt DKA causing definite LA. Postoperative hyperglycaemia, intravenous steroids, and surgical stress might have precipitated ketosis and ketonuria on PO-day-2, while insulin infusion prevented overt euglycaemic or DKA as showed by normal blood pH and bicarbonate levels (TABLE 1). We did not check serum 3-β-OH-B level at this occasion (PO-day-2) since urine ketones were already clinically significant (3+). Osmotic diuresis due to hyperglycaemia and intravenous volume loading resulted in respectable peri-operative U.O in our case. Semiquantitative urine ketones (acetoacetate) values are a surrogate measurement of clinically relevant capillary ketones (3-β-OHB) and diuresis may under-represent serum values [8]. Patient was on feeds prior to surgery and did not fast for prolong time, therefore starvation ketoacidosis causing LA seems unlikely too. LA and MA may occur in severe rhabdomyolysis secondary to lactic acid production from ischemic muscles. Since, clinically there was absent abnormal muscle soreness or discolouration, myoglobinuria and acute kidney injury, we did not measure creatinine phosphokinase (CPK). Moreover, modest postoperative elevation of CPK is a known phenomenon following extensive spine surgeries [5].

Hyperlactatemia can also result from aerobic glycolysis where serum glucose is said to represent an independent biomarker of the stressed state [9]. In the hyperdynamic stage of sepsis, epinephrine-dependent stimulation of the β2-adrenoceptor augments the glycolytic flux both directly and through enhancement of the sarcolemmal Na+-K+ pump [10]. Surgical stress, systemic inflammation, tissue injury, epinephrine infusion, exogenous steroid along with diabetes could have contributed to hyperglycaemia leading to disproportionate LA in our case. In the setting of type B LA hyperglycaemia is interrelated to hyperlactatemia, levels of both rise and fall together akin to our case [9].

Benign postoperative hyperlactatemia is occasionally encountered (36%-68%) during neuro-spine surgeries in the absence of hemodynamic instability or critical illness which usually clears by PO-day-3 and is not associated with a poor outcome. It has been theoretically associated with tumour handling (Warburg effect), neuronal tissue manipulation releasing catecholamines, and local muscle ischemia without systemic hypotension or marked tachycardia [11]. It usually causes peak lactates around 3-5 mmol/L and does not fully explain our exaggerated hyperlactatemia even though might have contributed. Significant MA is frequently observed in at the end of major surgeries; however, the clinical significance and cause remains unclear. It may be linked to extent of tissue dissection, duration and type of surgery, excess intravenous saline administration, and patient

comorbidities. Postoperative hyperlactatemia acidosis is associated with worse outcomes as compared to other types of MA [12]. Other postoperative causes of hyperlactatemia like hyperventilation, seizures and shivering were absent in our case.

The effect of LA is governed by its severity and the clinical context. Almost every organ system can be affected by LA and clinicians needs to assess laboratory data and evaluate the patient repeatedly to ensure that perfusion is not compromised [1]. In principle, the main aim of therapy in severe LA should be to prevent the multiple deleterious effects of the acidosis i.e. decrease in cardiac contractility, cardiac output, blood pressure, and tissue perfusion; peripheral venoconstriction, pulmonary vascular changes and attenuation of the cardiovascular responsiveness to catecholamines. The severity of acidaemia is a better predictor of cellular dysfunction and clinical outcomes than hyperlactatemia. A normal anion gap does not rule out LA and it lacks sufficient sensitivity or specificity as a screening tool for LA [9].

We administered intravenous bicarbonate when acidosis peaked, and pH dropped to 7.03 to prevent further haemodynamic collapse. Even though renal replacement and alkali therapy appear, appealing in such settings but are unproven, controversial and do not seem to counter hyperlactatemia [1,9]. The liver, kidneys, muscles, and heart normally take up lactate from the circulation, but sufficiently severe ischemia and acidosis results in lactate production by these organs of which the liver may turn into a net lactate producing organ. The cellular dysfunction in hyperlactatemia is complex and concomitant intracellular acidosis causes impaired mitochondrial oxidation leading to overproduction and underutilization of lactates [9].

It seems that LA in our case was likely a combination of type A and B even though we still do not have the exact reasons for sustained LA and MA and how it settled post operatively. Possibly hypoperfusion, postsurgical MA, adrenaline infusion, hyperglycaemia due to steroids and surgical stress, covert DKA, and postoperative hyperlactatemia and acidosis were the contributing components of LA. Type-A LA will increase the lactate-pyruvate ratio while glycolysis will increase lactate production yet preserve the lactate-pyruvate ratio. Theoretically measuring the ratio might have helped us to decipher the abnormal physio-biochemistry and shed more light on the cause, but such measurements are experimental, not routinely performed and results can be imprecise [8]. Even though we did not attempt, pharmacological measures to improve microvascular blood flow (dobutamine, nitro glycerine) hypothetically might have helped in correcting low flow microcirculation. We would like to know more about microvascular flow derangements in human SCI shock in future.

Multiple reasons for hyperlactatemia can be present in a given patient, making interpretation challenging, therefore the condition is best managed by an interprofessional team that consists of anaesthesiologist, surgeon, endocrinologist, physicians and intensivist [1]. The reason why some patients express lactates more than others in such scenarios is not well understood. Given the variety of aetiologies of hyperlactatemia and the varied clinical importance, lactate is not necessarily specific for either diagnosis or prognosis unless thoughtfully coupled with the overall clinical picture [3]. In substance blood lactate level remains only a partially understood and not a stand-alone biomarker, which reveals much more than a cellular oxygen deficit [2]. Physicians should understand the complexity of lactate metabolism and the limitations of lactate measurements in patient management. For patients with adequate perfusion, hyperlactatemia and associated hyperglycaemia, the optimum management is still observation and continued reassessment [8].

5. Acknowledgement

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6. Conflict of Interest

None

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