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Warburg Effect and Tumour-Associated Hyperlactatemia in a Non-Descript Dog

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Abstract

An eight-year-old male non-descriptive dog was presented to Madras Veterinary College Hospital, Chennai, with a history of severe respiratory distress and open-mouth breathing. Clinical examination revealed hyperthermia, SpO2 98%, tachypnea, and small multiple skin masses, and a large ulcerated mass on the left medial thigh region. Haematological evaluation showed leukocytosis with neutrophilia, while biochemical parameters were within reference limits. Radiography revealed normal lung parenchyma with no effusions. Arterial blood gas analysis revealed a normal pH with reduced bicarbonate concentration, decreased partial pressure of carbon dioxide, and markedly elevated lactate levels, indicating metabolic acidosis with a compensatory respiratory component.. Fine needle aspiration cytology was collected from the small skin masses and from the left thigh mass which revealed a mast cell tumour and fibrosarcoma, respectively. The dog was stabilized with fluid therapy, antipyretics, antibiotics and supportive medications.

Keywords: Warburg effect, Tumour, Lactate levels, Blood gas analyser

Respiratory distress in dogs is commonly attributed to primary cardiac or pulmonary disorders; however, metabolic causes are often overlooked (DiBartola, 2012). Tumour-associated hyperlactatemia may result in metabolic acidosis and secondary respiratory compromise (de Groot et al., 2011). The Warburg effect is one of the most important metabolic characteristics of cancer cells (Hanahan and Weinberg, 2011). This article presents a case of tumour associated hyperlactatemia in a non-descript dog.

An eight-year-old male non-descriptive dog was presented to Madras Veterinary College, Chennai, with a history of severe respiratory distress, open-mouth breathing, and drooling of saliva. On clinical examination, the patient's rectal temperature was 105.4^{0}F, oxygen saturation was 98%, open-mouth breathing, tachypnea, enlarged lymph nodes, normal mentation, and multiple small cutaneous masses and a large ulcerated mass in the left medial thigh region were noted (Fig. 1, 2). Haematology and serum biochemistry revealed leucocytosis, with other parameters within the normal range (Table 1). Thoracic and abdominal radiography revealed normal lung parenchyma with no effusions, and a severely distended stomach with gas (Fig. 3, 4). No abnormality could be detected through AFAST and TFAST. Arterial blood gas analysis revealed metabolic acidosis with a compensatory respiratory component & hyperlactatemia (Table 2). Fine needle aspiration cytology was collected from the small skin masses and from the left thigh mass which revealed a mast cell tumour and fibrosarcoma, respectively.

The dog presented with marked respiratory distress in the absence of cyanosis, suggesting that the dyspnea was not primarily caused by pulmonary or cardiac insufficiency. DiBartola, (2012) reported, in which compensatory hyperventilation develops secondary to systemic acid–base imbalance rather than an intrinsic respiratory disease in animals and humans with metabolic acidosis. The peripheral oxygen saturation (SpO_2) of 98% further supported adequate oxygenation and reduced the likelihood of hypoxemic respiratory failure. Nelson and Couto (2020) reported that aerophagia and gastric dilatation have been associated with excessive respiratory effort and compensatory hyperventilation in animals with metabolic acidosis and systemic stress. A marked increase in blood lactate concentration was also observed, indicating severe hyperlactatemia. Malignant tumours are known to induce aerobic glycolysis, commonly referred to as the

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Warburg effect, in which neoplastic cells preferentially convert glucose into lactate despite adequate oxygen availability (Liberti and Locasale, 2016). This excessive lactate production contributes to metabolic acidosis and may result in secondary respiratory compensation, manifesting clinically as tachypnea or respiratory distress. The pet was managed symptomatically with fluid therapy, mild sedation, and antibiotic administration. However, despite supportive treatment, the patient died during therapy, indicating the severity of the systemic metabolic derangement and advanced neoplastic disease. Previous studies have shown that severe lactic acidosis associated with malignancy often carries a grave prognosis due to rapid progression of metabolic failure and underlying tumour burden (de Groot *et al*., 2011). Arterial blood gas and lactate analysis were crucial in identifying the metabolic derangement and should be considered valuable diagnostic tools in critically ill oncology patients for accurate diagnosis and prognostic evaluation

Fig.1: Open mouth breathing, abdominal distension

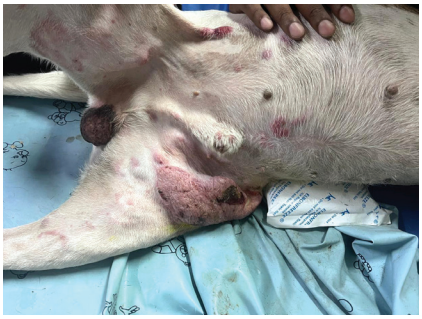

Fig. 2: Multiple small masses over the skin, large ulcerated mass at thigh region

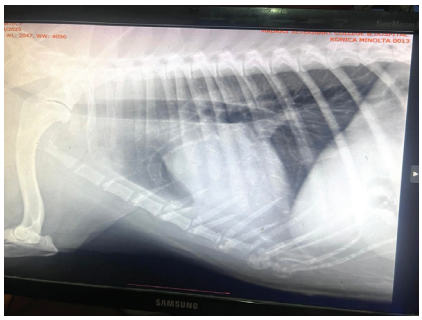

Fig. 3: Normal lung praenchyma with no effusions

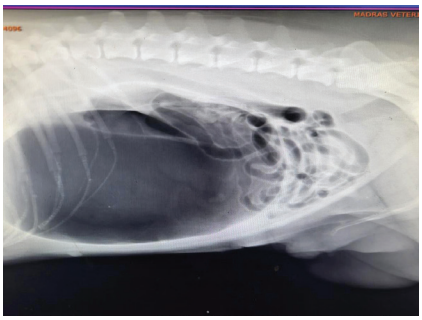

Fig. 4: Distended stomach with gas due to aerophagia

Table 2: Arterial Blood Gas Analysis

GASES		CHEMICAL		METABOLIC	
Ph	7.4	Na	145	Glucose	121 mg/dl
PCO_2	31.2	K	3.7	Lactate	10.37mmol/l
$P0_2$	73.8mmHg	Cl	117	BUN	17 mg/dl
$CHCO_3$	17.8mmol/l	Ca	1.22	Creatinine	0.9mg/dl
BE (ecf)	-5.6mmol/l	Tco_2	18.7	Urea	6.0 mmol/l
CSO_2	81.6%	A gap	14	Bun/Crea	18.6

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