Investigation vignette

A 38-Year-old Morbidly Obese Man With Chest Pain, Shortness of Breath and a Numb Lip

CASE REPORT

A 38 year old man presented to hospital with left chest pain and dyspnoea which had evolved over the day. The pain was intermittent and pleuritic in nature, with no accompanying cough, rigors or other acute features. He was 170 cm tall and was morbidly obese weighing 157 kg. His past medical history consisted of asthma, smoking, hypertension, angina, sleep apnoea, epilepsy and a lymphoma when he was a teenager which was treated with chemotherapy. A past sleep study showed significant sleep apnoea. The initial blood tests are shown in Figure 1.

The history and positive D-Dimer prompted a CT pulmonary angiogram, which was of poor quality but showed no gross pulmonary emboli. An ultrasound of his leg veins and an echocardiogram, both of which were reported as technically difficult were within normal limits. A gated heart pool scan showed a right heart ejection fraction of 30%. An abdominal CT revealed ascites.

A diagnosis of decompensated right heart failure, provoked by occult pulmonary emboli, obesity, severe sleep apnoea and obstructive airways disease was made. Warfarin, frusemide, spironolactone and fluid restriction were commenced. He failed to improve and complained of worsening dyspnoea, abdominal distension and exhaustion. He also complained of right lower lip and chin numbness. On day ten he was referred to the intensive care unit for initiation of nocturnal CPAP. His investigations were reviewed (Figure 1) and a new diagnosis was made.

	Day 1	**Day 10**		**Reference range**
Sodium	141	139	mmol/L	(136 - 145)
Potassium	4.0	4.3	mmol/L	(3.5 - 5.1)
Bicarbonate	29	25	mmol/L	(23 - 29)
Urea	6.0	8.9	mmol/L	(3.0 - 8.0)
Creatinine	0.108	0.163	mmol/L	(0.06 - 0.12)
Total Calcium	2.31	2.49	mmol/L	(2.10 - 2.55)
Urate	0.44	0.92	mmol/L	(0.21 - 0.42)
Total Bilirubin	9	9	μmol/L	(0 - 18)
GGT	28	47	U/L	(11 - 50)
ALP	57	61	U/L	(45 - 122)
ALT	26	51	U/L	(4 - 40)
AST	26	60	U/L	(4 - 40)
LD	832	2058	U/L	(135 - 225)
Haemoglobin	130	135	g/L	(130-170)
White cell count	13.7	21.6	$x10^9$/L	(4.0 - 11.0)
Platelet count	273	412	$x10^9$/L	(150 - 400)
Prothrombin time	12	22	sec	(10 - 14)
APTT	29	29	sec	(28 - 38)
Fibrinogen	5.0	-	g/L	(1.5 - 4.0)
D-Dimer	582	564	μg/L	(<296)

Figure 1. Serum electrolytes, liver function tests and haematology tests performed on admission (day 1) and on day ten.

Diagnosis: Elevated serum lactate dehydrogenase, urate and D-Dimer and unilateral lower lip paraesthesia (numb chin syndrome) due to lymphoma recurrence

The high lactate dehydrogenase and urate level in the absence of other cell injury markers are highly suggestive of lymphoma recurrence.[1] In addition, unilateral lower lip paraesthesia (numb chin syndrome) has been described as a pathognomonic sign of B cell lymphoma.[2,3,4] His ascites was drained and a Papanicalou smear of the cloudy fluid was made, which demonstrated a high-grade B cell lymphoma consistent with Burkitt's or Burkitt's-like lymphoma. The bone marrow aspirate and trephine performed at the same time showed no abnormality, but flow cytometry and leucocyte surface markers showed a monoclonal B cell population confirming the diagnosis of a Burkitt's-like lymphoma.

Lactate dehydrogenase (LD) is a cytoplasmic enzyme that reversibly catalyses the reduction of pyruvate to lactate using NADH as a co-enzyme. It is a tetramer made up of the combination of one or two types of the subunits M and H, and the resulting iso-enzymes are found in differing proportions in all tissues. Due to its ubiquitous nature, the serum concentration of LD is raised in many disorders including myocardial infarction, muscle injury, gut, kidney and liver diseases, lung disease, haemolytic anaemias, pernicious anaemia, atypical infections and malignancies.[1] It has been described as the ESR of clinical enzymology. It is artefactually raised in haemolysed plasma.

A very high serum LD activity of more than fifteen times the upper limit of normal is observed in acute leukaemias and lymphomas, mainly due to the isoenzymes LD_2 and LD_3.[5] An LD iso-enzyme assay is not often used for diagnostic purposes, as it has largely been made redundant by other tests. A recent systematic review commented that LD assays have only been found to be relevant in the diagnosis and monitoring of haemolytic anaemia, ovarian dysgerminoma, testicular germ cell tumour and prognostication and monitoring of the disease progress in Hodgkin's and non-Hodgkin's lymphoma.[1]

Despite its lack of specificity, serum LD continues to be reported as relevant to the diagnosis and prognosis of many processes. For example, it is recommended that a high serum LD can be used to suggest systemic infections such as PCP, histoplasmosis and disseminated toxoplasmosis in HIV/AIDS. In clinical practice, however, early effective surveillance and PCR has rendered the relevance of LD largely obsolete.[6]

Similarly, a raised D-dimer is a sensitive but non-specific marker of a number of conditions, including thromboembolic disease, disseminated intravascular coagulation, sepsis, aortic dissection and malignancy, particularly haematological malignancy.[7] Its clinical value in thromboembolism lies in its negative predictive value, where a negative test in the setting of low to moderate clinical suspicion of thromboembolic disease effectively rules the diagnosis 'out'.

Uric acid is the end product of purine metabolism, formed from xanthine by xanthine oxidase, the majority of which is actively secreted by the proximal tubules of the kidneys. Despite this, the plasma urate does not tend to rise until the glomerular filtration rate falls to less than 20 mL/min, and will often plateau at a level of approximately 0.6 mmol/L, with levels above this indicative of a cause other than renal failure.[5] Plasma levels will be higher in males, old age, obesity, pregnancy, fasting and in high meat and alcohol intakes, but significant hyperuricaemia is usually caused by overproduction. Primary overproduction may be idiopathic or due to inherited metabolic disease, while secondary overproduction is seen in diseases where there is a high turnover of nucleo-proteins (e.g. myeloproliferative diseases, myeloma, haematological malignancies, psoriasis, cytotoxic therapy and pre-eclampsia).

The past history of haematological malignancy was highly relevant, given the natural history of such diseases and the high relapse rate even after 'cure' or clinical remission. Non-Hodgkin's lymphomas (unlike Hodgkin's disease) may present or recur with minimal systemic symptoms and be difficult to diagnose particularly if no abdominal mass is noted. In some centers serum LD is still used for the detection of residual disease or recurrence, although in many it has largely been replaced by more specific and sensitive methods, such as flow cytometry and PCR.[8] While the unilateral lower lip numbness was an interesting hint, the combination of the abnormalities (e.g. very high LD, urate, and D-Dimer) suggested the diagnosis of lymphoma recurrence, which was subsequently confirmed by microscopy of the ascitic fluid.

P. GARRETT
Intensive Care Unit, Nambour Hospital, Sunshine Coast, NEW SOUTH WALES

REFERENCES

1. Huijgen HJ, Sanders GT, Koster RW, Vreeken J, Bossuyt PM. The clinical value of lactate dehydrogenase in serum: a quantitative review. Eur J Clin Chem Clin Biochem 1997;35:569-579.
2. Burt RK, Sharfman WH, Karp BI, Wilson WH. Mental neuropathy (numb chin syndrome). A harbinger of tumor progression or relapse. Cancer 1992;70:877-881.

3. Fenaux P, Lai JL, Miaux O, Zandecki M, Jouet JP, Bauters F. Burkitt cell acute leukaemia (L(sub 3) ALL) in adults: a report of 18 cases. Br J Haematol 1989;71:371-376.
4. Lossos A, Siegal T. Numb chin syndrome in cancer patients: etiology, response to treatment, and prognostic significance. Neurology 1992;42:1181-1184.
5. Walmsley RN, White GH. A guide to Diagnostic Clinical Chemistry 3rd edition Blackwell Scientific Publications 1994.
6. Silverman BA, Rubenstein A. Serum lactate dehydrogenase in adults and children with aquired immune deficiency syndrome (AIDS) and AIDS-related complex. Am J Med 1985;78:728-736.
7. Blomberg ME, Cappello M. Cancer and blood coagulation: molecular aspects. Cancer J Sci Am 1999;5:132-138.
8. Cowan RA, Jones M, Harris M, et al. Prognostic factors in high and intermediate grade non-Hodgkin's lymphoma. Br J Cancer 1989;59:276-282.