

## Shortness of breath in an HIV-infected patient

Saturday, 01 July 2006

A 36-year-old man was diagnosed to be infected with HIV in November 2000 and was started on azidothymidine/lamivudine /nevirapine in January 2001. He tolerated this treatment well for 20 months, achieving suppression of the viral load to undetectable levels and increase of his CD4 count to 1,506 cells/ml. Then, he began to complain of nausea, fatigue, dyspnea, and pain in the epigastrium. He did not take any other prescription or over the counter medications.

On admission, he was slightly tachypneic (20 breaths/min); physical examination was notable only for mild epigastric tenderness. Laboratory work-up showed mildly elevated transaminases (AST: 44 U/L, normal: 7-40, and ALT: 64 U/L, normal: 7-40), elevated triglycerides (268 mg/dL, normal: 50-150), cholesterol (317 mg/dL, normal: <190) and a lactate level of 13.1 mmol/L (normal: 0.6-2.4), with mild metabolic acidosis (pH: 7.34, HCO<sub>3</sub>: 18.3 mmol/L). Hepatitis serologies for hepatitis B and C viruses were negative. Antero-posterior and lateral chest X-rays were normal.

What was the cause of his hyperlactaemia?

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What was the cause of his hyperlactaemia?Diagnosis

An extensive investigation ruled out various pathologic conditions that could lead to hyperlactatemia. Empirical therapy consisted of discontinuation of the antiretrovirals and administration of L-carnitine and a multivitamin tablet containing thiamine and vitamin B6 (2,3). This was followed by marked clinical improvement and gradual decrease of lactate to 5 mmol/l, 3 weeks later. At this time, and due to a viral load rise, a decision was made to start treatment with nevirapine/saquinavir/ritonavir, (eliminating in this way the NRTIs azidothymidine and lamivudine), and continue the cofactors' supplementation. Six weeks later, symptoms recurred, accompanied by a lactate rise to 12.1 mmol/l. Finally, the antiretroviral regimen was changed to saquinavir/lopinavir-ritonavir and this was followed by normalization of the lactate level (despite discontinuation of the vitamins); this persists up to the last follow-up visit (December 2005). Figure 1 shows the progression of lactate level over time and its association with the therapeutic interventions.

### Teaching points

- Hyperlactatemia in HIV-infected patients treated with nucleoside-analogue reverse transcriptase inhibitors (NRTIs) is a well-known adverse reaction (1). However, inconclusive data exist regarding its association with the other two widely used classes of antiretrovirals, non-nucleoside reverse transcriptase inhibitors (NNRTIs) and protease inhibitors (PIs).
- Our report presents a well-documented case of hyperlactatemia associated with the use of the NNRTI nevirapine. In fact, determination of the Naranjo probability scale reveals a score of 9, indicating a "highly probable" adverse event (4).
- Of note, a recently published cohort study (5) revealed an association between the NNRTI efavirenz, but not nevirapine, and hyperlactatemia, while, in the past, a similar association was also shown with the protease inhibitor ritonavir. Even though we did not perform sophisticated biochemical analysis (e.g., determination of the enzymatic activity of the respiratory chain and documentation of mitochondrial DNA depletion), and we cannot exclude the possibility that the first episode of hyperlactatemia was related to the combination of NRTIs and the second episode related to the combination of PIs, we think it is more logical to pinpoint nevirapine as the culprit medication.
- We suggest that clinicians taking care of HIV-infected patients should be vigilant of the development of hyperlactatemia, even in non-NRTI-including regimens.

### Acknowledgements

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### References

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