Serum lactate dehydrogenase as early marker of posterior reversible encephalopathy syndrome: keep your eyes open

Posterior reversible encephalopathy syndrome (PRES) is associated with many clinical conditions including pre-eclampsia/eclampsia. So far, this association has been explained mainly in terms of blood pressure variation, failure of cerebral vasculature autoregulatory mechanism and brain oedema12. However, it is well known the main mechanism in pre-eclampsia is the endothelial activation and injury with systemic consequences, i.e. vasoconstriction, unstable blood pressure and abnormal response to vasopressors3.

L-lactate dehydrogenase (LDH) is an intracellular enzyme that converts lactic acid to pyruvic acid, elevated levels indicating cellular death or damage4. LDH isoenzymes are present in many body tissues such as brain, kidney, liver, lung, myocardium, spleen, erythrocytes, leucocytes and platelets5. Tissue levels of these isoenzymes are about 500 fold higher than those normally found in serum; leakage of the enzymes from a damaged tissue can increase the serum LDH levels5. Endothelial injuries or irregularities of the endothelial walls lead to a disruption or a morphological disturbance of red blood cells and to an increased release of LDH into the serum65. Moreover in eclampsia, overwhelming inflammatory response, placental-maternal immune reaction and anti-endothelial cell antibodies are responsible for the endothelial activation/injury, resulting in platelet adhesion/degranulation, haemolysis and LDH elevation, protein/fluid leakage and systemic oedema2.

Schwartz et al first reported the correlation between increased LDH levels and risk of PRES in individuals with pre-eclampsia/eclampsia. Indeed, in some cases, increased LDH value was the only abnormal laboratory parameter before the onset of symptoms6. Demirtas et al also reported raised LDH levels in pre-eclamptic/eclamptic patients with abnormal magnetic resonance imaging findings suggestive of PRES7. Finally, Finocchi et al showed abnormally high LDH levels in eclamptic subjects who developed PRES, even before the onset of the symptoms8.

We reviewed the clinical charts of the obstetric patients with PRES admitted at our intensive care unit during a period of 12 months. Analysis of the data (Table 1) revealed overall increased LDH levels (995.6±440.6 IU/l; n.v.227 to 450 IU/l) at presentation, including patients with normal

<table>
<thead>
<tr>
<th>Pt.</th>
<th>Age</th>
<th>Headache</th>
<th>Seizures</th>
<th>Impaired consciousness</th>
<th>Visual abnormalities</th>
<th>BP at presentation, mmHg</th>
<th>Distribution of MRI abnormalities</th>
<th>Brain oedema severity*</th>
<th>LDH level**</th>
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<tr>
<td>1</td>
<td>29</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<td>O, P, F, T</td>
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<td>1842</td>
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<tr>
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<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
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<tr>
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<td>22</td>
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<td>+</td>
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</tr>
</tbody>
</table>

* According to Liman et al9. ** Days before onset of PRES. LDH normal values: 227 to 450 IU/l. BP=blood pressure, MRI=magnetic resonance imaging, LDH=L-lactate dehydrogenase.
blood pressure values. Although we failed to find a clear association between LDH values and severity of brain oedema, all subjects showed abnormally high LDH levels already three (628.6±95.8 IU/l) or two (660.16±118.3 IU/l) days before the onset of PRES. Notably, the peak of LDH increase did not necessarily correspond to the symptoms presentation. In fact LDH increase already even some days before PRES would further support the role of asymptomatic or subclinical endothelial dysfunction/injury as the primum movens in both hypertensive and normotensive patients. The endothelial damage probably impairs the mechanism of vasorelaxation, which depends on normal endothelium function and that is responsible for a zone of vasoconstriction/vasodilatation also in the cerebral capillary bed, thus resulting in a blood-brain barrier breakdown10. The next step of this breakdown mechanism is the extravasation of fluid in resulting in vasogenic brain oedema. The pathogenetic mechanisms of PRES remain controversial. Opposing theories are the hypertension/hyperperfusion and vasoconstriction/hypoperfusion3. We believe that behind these two opposing theories there is a common denominator, i.e. endothelial damage that can explain both hypotheses.

M. Vargas
G. Servillo
P. Striano

Naples and Genoa, Italy

References