Angiostatin, a novel biomarker of lupus nephritis?

Tianfu Wu, PhD
Division of Rheumatic Diseases, UT Southwestern Medical Center at Dallas

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Antibody-based protein array exhibited a dramatic increase of urinary angiostatin in lupus nephritis

Healthy control

Lupus nephritis

What is Angiostatin?

Inhibition of Capillary Endothelial Cell Proliferation by Serum or Urine of Tumor Bearing Animals

O'Reilly & Folkman, Cell, 1994
Angiostatin has the ability to block tumor growth in vivo by inhibiting the formation of new tumor blood vessels (O'Reilly & Folkman, 1994).

Angiostatin plays a role in the inhibition of endothelial cell migration, proliferation and induction of apoptosis (Redlitz A et al, 1999).

Angiostatin, anything to do with lupus nephritis?

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Angiostatin is significantly elevated in the urine of SLE

SLE Patients: Female 86%, Age (mean) 35, Race AA/Hisp/Cauc, SLEDAI (median) 9.5, (5SLEDAI) (median) 4.0.
Healthy: Female 41%, Age (mean) 35, Race AA/Hisp/Cauc.

SLE:
- Mixture of Diabetic nephropathy (88%), ANCA (3%), Membranous nephropathy (10%), minimal change disease (10%), FSGS (10%).

Table

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<thead>
<tr>
<th>SLEDAI</th>
<th>0-2</th>
<th>≥4</th>
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<td>SLE vs HC, AUC=0.93</td>
<td>SLE vs CKD, AUC=0.58</td>
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ROC curve on urine angiostatin

SLE vs HC, AUC=0.93
Active vs HC, AUC=0.93
Correlation with disease severity

SLICC renal activity score was computed as described by Petri M (2008, A&R):
- proteinuria 0.5–1 g/day (3 points),
- proteinuria >1–3 g/day (5 points),
- proteinuria >3 g/day (11 points),
- urine red blood cell count >10/high-power field (3 points),
- and urine white blood cell count >10/high-power field (1 point).

Correlation with renal function:

eGFR and SLICC renal activity score

Serum angiostatin does not correlate with SLEDAI or renal SLEDAI

Urine angiostatin level is increasingly elevated with the deterioration of renal disease.

Angiostatin Expression in Human Kidney

Higher levels of angiostatin expression were found in the kidney of class III and class V patients, compared to healthy controls.

Serum is not the major source of the increased urine angiostatin in lupus nephritis

* Urine/serum samples were collected within 6 months of kidney biopsy.
Concurrent kidney biopsy/urine samples

Summary

- Urinary angiostatin is significantly increased in SLE compared to healthy controls. Within SLE, it is significantly increased in active SLE compared to inactive SLE.
- ROC curve confirmed that urinary angiostatin has the capacity to discriminate active SLE from healthy controls, more importantly, it can also discriminate active SLE from inactive SLE.
- Urinary angiostatin level positively correlates with SLEDAI, rSLEDAI and SLICC renal activity score, suggesting it may have predictive value for disease severity.
- Urinary angiostatin appears to be largely kidney-derived, rather than serum-derived.
- From a renal pathologist’s view, urinary angiostatin level positively correlates with renal chronicity Index, indicating it might be a chronicity marker.
- Collectively, urinary angiostatin might be a novel biomarker of lupus nephritis. Longitudinal studies are in progress.

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