Kawasaki Disease: Time for Change

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The first cases of mucocutaneous lymph node syndrome (MLNS) were reported by Dr Tomisaku Kawasaki in 1967. His surname was later assigned to this new disease entity, and I was fortunate to meet him at the 100th Annual Conference of the German Paediatric Association in Berlin in 2004 [1]. According to our current understanding Kawasaki disease (KD) is a systemic autoimmune vasculitis which occurs in genetically susceptible people following an acute infection. Outside Japan KD has a low incidence and is notoriously difficult to diagnose because of its similarity to common infective childhood illnesses and a lack of specific and sensitive laboratory tests. The case report of KD by Bangert et al. [2] illustrates these difficulties aptly and calls for prompt diagnosis and treatment of this condition to avoid serious cardiovascular complications.

During the last few years significant progress has been made with the development of specific genome and proteome based blood and urine tests for KD by Ling et al. [3]. Designed a diagnostic algorithm that helps clinicians to differentiate between KD and other causes of persistent fever. It combines routine laboratory parameters with microarray gene analysis of peripheral blood cells and urine peptidome analysis. Using cell-type specific significance analysis (csSAM) these authors identified 87 genes that were down-regulated in KD patients. They also found 139 candidate urinary proteins through multidimensional protein identification technology (MUDPIT). They further compared a KD cohort (n = 30) with a cohort of other febrile conditions (n = 30) and performed matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS). Thirteen urine peptides, mainly collagens, were present in significantly higher concentrations in the KD patients.

Recently, a research group at Harvard Medical School [4] achieved a breakthrough in the development of KD-specific biomarkers. They analyzed over 2000 urine proteins in 53 KD patients and 54 febrile controls with high-accuracy mass spectrometry. Nearly 200 peptides were abundant in the KD group including those associated with endothelial and myocardial cell damage, and with immune regulation. The enzyme meprin A, also called endopeptidase-2 (EC 3.4.24.18), and the muscle protein filamin C, also called actin-binding-like protein, were evaluated further. Their concentrations were significantly elevated in urine and serum of KD patients compared with the non-KD controls. In addition, meprin A was highly expressed in coronary artery lesions of a mouse model suggesting a role in the pathophysiology of KD (Table 1).

Table 1. Potential Biomarkers for Kawasaki Disease

<table>
<thead>
<tr>
<th>Protein</th>
<th>Gene</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Titin (CMD1G)</td>
<td>TTN</td>
<td>Striated muscle contraction</td>
</tr>
<tr>
<td>Filamin C (ABP-L)</td>
<td>FLNC</td>
<td>Actin-cross-linking protein</td>
</tr>
<tr>
<td>Deleted in malignant brain tumors 1 protein (hensin)</td>
<td>DMBTI</td>
<td>Tumor suppressor gene, role in immune defense system</td>
</tr>
<tr>
<td>Meprin A (PPHA)</td>
<td>MEP1A, MEP1B</td>
<td>Peptide hydrolase</td>
</tr>
<tr>
<td>Collagens (glycoproteins)</td>
<td>Several different genes</td>
<td>Part of connective tissue</td>
</tr>
</tbody>
</table>

It is hoped that high-sensitivity enzyme-linked immunosorbent assays (ELISAs) for these two KD-specific proteins will soon become routinely available. This would raise awareness for Kawasaki disease among health professionals and enable pediatricians to diagnose and treat this potentially life-threatening vasculitis as early as possible.

CONFLICT OF INTEREST

The author confirm that this article content has no conflicts of interest.

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REFERENCES


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