HCD. Histiocytic Disorders
NIHR BioResource – Rare Diseases study project

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V1 04/07/2019

Summary

Histiocytic Disorders are characterised by excessive accumulation or activation of tissue-resident white blood cells known as ‘histiocytes’. Histiocytes are present in nearly all tissues and ultimately come from the bone marrow or blood-forming organs. In health they perform critical functions maintaining the health of tissues. In a histiocytic disorder, accumulation of activated histiocytes can have severe consequences leading to tissue damage and organ failure.

Two major types of histiocytosis are known. The first type includes diseases such as Langerhans Cell Histiocytosis (LCH), Juvenile Xanthogranuloma (JXG), Erdheim Chester Disease (ECD), and Rosai Dorfman Disease (RDD). In these conditions, histiocytes are abnormally programmed by genetic mutations, causing them to accumulate and attract other immune cells to form inflammatory masses, destructive lesions or fibrous scar tissue.
The second type of histiocytic disorder is known as Haemophagocytic Lymphohistiocytosis (HLH). HLH is characterised by the presence of super-activated histiocytes that cause body-wide inflammation and prevent the production of blood cells by the bone marrow. In children HLH usually only occurs when there is an inherited genetic defect, often in the genes required to make immune responses to viruses. In adults, HLH can be triggered by infections or cancer and the role of genetic factors is less well understood.

In addition to these two main types, there are many rare and poorly characterised disorders in which histiocytosis is observed. These may also have a genetic cause that is no yet known.

The NIHR BioResource will enable much more rapid progress in understanding the genetic basis, prevalence and health impact of Histiocytic Disorders. This is vital for making rapid and accurate diagnosis, using personalised medicine approaches, and defining the healthcare resources required to care for patients effectively.

**Recruitment Criteria**

**Inclusion**

1) **Neoplastic Histiocytosis**
Children or adults with a diagnosis of histiocytosis including Langerhans Cell Histiocytosis (LCH), Juvenile Xanthogranuloma (JXG), Erdheim Chester Disease (ECD), Rosai Dorfman Disease (RDD) and any other histiocytic disorder of groups L, C, R and M, as defined by Emile et al. 2016.

2) **Haemophagocytic Lympho-Histiocytosis**
   a) Children meeting the diagnostic criteria for HLH according to Histiocyte Society guidelines described by Henter et al. 2007 based upon the presence of 5/8 of:
      * fever
      * splenomegaly
      * cytopenias
      * hypertriglyceridaemia or hypo-fibrinogenaemia
      * haemophagocytosis
      * hyperferritinaemia
      * elevated soluble CD25
      * absent NK activity
b) Adults meeting the diagnostic criteria for HLH according to Histiocyte Society guidelines (above) or alternatively, exceeding an H Score of 169 as defined by Fardet et al. 2014\(^3\) based upon weighted scores of:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>degree</th>
<th>H</th>
<th>degree</th>
<th>H</th>
<th>degree</th>
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<tbody>
<tr>
<td>Immunosuppressed</td>
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<td>0</td>
<td>yes</td>
<td>18</td>
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<tr>
<td>Temperature (°C)</td>
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<td>38.4-39.4</td>
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<td>&gt;39.4</td>
<td>49</td>
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<tr>
<td>Organomegaly</td>
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<td>0</td>
<td>hep or spleen</td>
<td>23</td>
<td>both</td>
<td>38</td>
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<tr>
<td>No. of cytopenias</td>
<td>1 lineage</td>
<td>0</td>
<td>2 lineages</td>
<td>24</td>
<td>3 lineages</td>
<td>34</td>
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<tr>
<td>Ferritin (ng/ml)</td>
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<td>2000-6000</td>
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<td>&gt;6000</td>
<td>50</td>
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<td>Triglyceride (mmoles/L)</td>
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<td>&gt;4</td>
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<td>AST (IU/L)</td>
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<td>≥30</td>
<td>19</td>
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<td>Hemophagocytosis</td>
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<td>35</td>
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</tr>
</tbody>
</table>

3) Rare, poorly characterised disorders with histiocytic pathology

Including but not limited to:
- Orofacial granulomatosis
- Giant cell granuloma
- Blau’s syndrome
- Granulomatous angiitis
- Granuloma annulare
- Actinic granuloma
- Granulomatous Rosacea

References