British Paediatric Orphan Lung Diseases (BPOLD)

Idiopathic Pulmonary Haemosiderosis - Dr Stephen Cunningham

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Definition

Idiopathic Pulmonary Haemosiderosis is a condition of periodic, variable microvascular alveolar bleeding. Long term damage to the lung tissue may lead to death from progressive pulmonary fibrosis.
Children are affected more than adults, with a peak age of 1 to 7 years. Some series now report 86% 5 year survival on treatment; significantly better than early reports. Incidence is reported as 0.24 – 1.0 per million children per year.

Causes

Idiopathic Pulmonary Haemosiderosis is a diagnosis of exclusion. Secondary causes of pulmonary haemosiderosis include Goodpasture's syndrome, Heiner's syndrome, environmental moulds, autoimmune disease, pulmonary veno-occlusive disease, intercurrent pneumonia.
Idiopathic pulmonary haemosiderosis can recur in transplanted lungs, and 25% of long-term survivors proceed to autoimmune disease, raising the possibility of genetic/autoimmune aetiology.

Clinical Presentations

Diffuse alveolar haemorrhage presents with anaemia (often microcytic) and during the acute phase with the effects of blood irritation of the airways (cough, bronchospasm, tachypnoea, crepitations, desaturation). Iron deficiency anaemia resistant to treatment may be the main presentation (with apparent lack of respiratory symptoms). Haemoptysis may not be present in children. Long term growth failure may be seen.

Investigations

Children presenting with an acute pulmonary bleed will have a reduced haemoglobin and widespread bilateral infiltrates on chest x-ray. Bronchoalveolar lavage contains haemosiderin loaded macrophages for 3 – 14 days following an acute bleed. Lung biopsy (not usually indicated) identifies defects of the alveolar capillary basement membrane and endothelial cells.
Secondary causes of pulmonary haemosiderosis need to be excluded. A diagnostic exclusion checklist should be made. Click HERE to see a suitable diagnostic checklist.

Treatment

Supportive therapies are required for acute bleeding episodes (blood transfusion, iron and folate supplementation, oxygen therapy etc).
Children with acute bleeding episodes are treated with corticosteroids, most commonly Prednisolone (2mg/kg/day). Observational studies imply that such treatment is able to abbreviate acute episodes. The role of prophylactic immunosuppressives are less clear. Although there is some evidence for long term benefit with Azathioprine or

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Hydroxychloroquine, there are no randomised controlled trials of therapies in the acute or chronic management of idiopathic pulmonary haemosiderosis.

Useful references:

1. Idiopathic Pulmonary Haemosiderosis Revisited.	**Ioachimescu OC, Sieber S, Kotch A**	**Eur Resp J 2004;24:162-170**
2. Pulmonary hemorrhage/hemoptysis in children	**Godfrey S.**	**Pediatr Pulmonol 2004.37:476-484**
3. Hemosiderosis	**McCoy KS.**	**In; Pediatric Respiratory Medicine, Taussig & Landau Eds; Mosby, St Louis. 1999. 835 – 841.**

Potential Research Questions:

- Incidence and Prevalence in UK with agreed diagnostic exclusion criteria
- Treatments
  - Response to therapy during acute episodes (oral prednisolone 2mg/kg vs methylprednisolone pulse) (RR, HR, delta Hb, retics)
  - Survival and poor prognostic factors at 5 years following onset
  - Role of chronic therapy (treat acute episodes prednisolone only, prednisolong + azathioprine, prednisolone + hydroxychlorquine).
- Histology and vessel stability: No significant studies for c30 years.
  - Serum and BAL vascular (VEGF 185) and basement membrane (MMP's/TIMPs) markers during acute and quiescent phases (+/- Angiopoietins, PDGF, ?HIF). ELISA.
  - Retrospective lung tissue examination for vascular markers associated with break in capillary basement membrange (VEGF, ang 1 and 2, endothelin etc) ?obtain lung tissue. In situ hybridisation studies.