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Additional information on aplastic anaemia

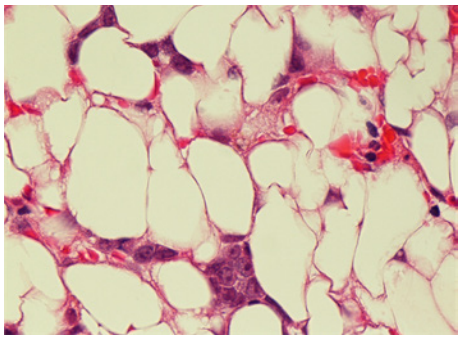
Epidemiology

Aplastic anaemia is a *heterogeneous*, rare disorder. The major features are *pancytopenia* with a *hypocellular* bone marrow with no abnormal infiltrates or bone marrow fibrosis. Pathogenesis seems to be through immune mediated destruction of haematopoietic stem cells. 70-80% of cases are *idiopathic* and some are due to inherited bone marrow failure syndromes (a group of rare genetic blood disorders). Although most cases are idiopathic, a careful history may reveal possible causes such as certain drugs, occupational exposure, or post-hepatitis aplastic anaemia. A multidisciplinary team approach to diagnosis is recommended.

In Europe the incidence of aplastic anaemia is approximately two cases per million per year, but higher in East Asia.[1,2] There is a bimodal age distribution with peaks at 10-25 years and over 60-years of age.[2,3] The incidence is equal between men and women although some data shows a male preponderance in East Asia and India.[1,2]

Diagnosis

In most circumstances aplastic anaemia is a diagnosis of exclusion, based upon the presence of peripheral blood pancytopenia, reticulocytopenia, molecular and/or genetic abnormalities and hypocellular bone marrow, and results of flow cytometry.[1,4] Blood cells that are present in the peripheral blood generally appear normal.[1,2] Bone marrow trephine will be hypocellular and contain increased numbers of fat cells with no significant dysplasia, blasts, fibrosis or other abnormal infiltrates.[1,5]



Bone marrow trephine of a patient with severe aplastic anaemia. Slide shows fat cells (white areas) and very few normal haematopoietic cells.

Risk stratification

The severity of aplastic anaemia is based upon bone marrow examination and peripheral blood count results.[4] The severity can vary from moderate pancytopenia to severe and life-threatening anaemia, haemorrhage and infection.[2-4]

Classification	Criteria
Non-severe/moderate	Bone marrow is hypocellular but the criteria for severe aplastic anaemia is not met and two of the following blood counts are detected: • Hb <100 g/L • Platelets 20-50 x 10^9/L • Absolute neutrophil count 0.5-1.5 x 10^9/L
Severe	Hypocellular bone marrow <25%, or 25-30% with <30% residual haematopoietic cells, and two or more of the following peripheral blood counts: • Absolute neutrophil count <0.5 x 10^9/L • Platelet count <20 x 10^9/L • Absolute reticulocyte count <20 x 10^9/L
Very severe	Meets severe criteria and absolute neutrophil count <0.2 x 10^9/L

Treatment

Treatment options vary depending upon patient age and disease severity with the severe form of the disease invariably requiring treatment. The non-severe, non-transfusion-dependent may be monitored for progression of cytopenias and development of abnormal cells.[1]

Treatment options include supportive therapy, immunosuppressive therapy (IST), potential for thrombopoietin analogues, anabolic steroids in combination with IST, monoclonal antibodies and haematopoietic stem cell transplant (HSCT).

Supportive care remains a vital part of treatment for patients with aplastic anaemia and includes red cell and platelet transfusions and prevention/treatment of infection.[2,4] Successful treatment with immunosuppressive therapy or HSCT has meant that many patients now avoid the need for long term transfusion.

Patient Outcomes

Patient age is a strong predictor of outcome, particularly survival, with 70-85% of adults between the age of 30 to 50 years having good outcomes following matched sibling donor HSCT.[6,7] Immunosuppressive therapy has a reasonable response in 60-80% of patients, and a functional cure is achieved in 50% of patients using this strategy. In patients treated with immunosuppressive therapy 10-15% develop myelodysplastic syndrome or acute leukaemia, and 10-25% may develop haemolytic *paroxysmal nocturnal haemoglobinuria*.[2]

Glossary terms

Heterogeneous	Conditions that have several etiologies eg hepatitis or diabetes.
Pancytopenia	Deficiency in all three types of blood cells - red cells, white cells and platelets.
Hypocellular	Contains less than the normal number of cells.
Idiopathic	Spontaneous and of unknown cause.
Paroxysmal nocturnal haemoglobinuria (PHN)	A rare acquired blood disorder characterised by haemolysis (destruction of red cells), thrombosis and impaired production of blood cells in the bone marrow. Abnormally increased haemolysis leads to haemoglobinuria (excess haemoglobin in the urine) leading to red coloured urine. It is more commonly noticed in the morning when urine is more concentrated.

References

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