POLICY POL/MED/CM/008/01

Investigation of Autoimmune Thrombocytopenia

Summary of Significant Changes
N/A

Policy
To provide a national approach to the laboratory investigation and management of patients with ITP.

Applicable Documents


Investigation of Autoimmune Thrombocytopenia

1 - Definition
Idiopathic thrombocytopenic purpura (ITP) is frequently mediated by an autoimmune process characterised by persistent thrombocytopenia (platelet count <150 x 10^9L) due to autoantibody binding to platelet antigen causing the premature destruction by the reticuloendothelial system. If an autoimmune process is identified the condition should be properly described as autoimmune thrombocytopenia (AITP).

2 - Background
The literature shows that the investigation and management of patients with thrombocytopenia vary widely and is not evidence-based due to a lack of clinical trials and quality research. The diagnosis of ITP remains one of exclusion. There is a BCSH Guideline for the investigation and management of ITP in adults, children and in pregnancy published in British Journal of Haematology, 120, 574-596 Additional information is also available in the NBS user guide 2003 Diagnostic and Cellular Therapy Service.

3 - Objectives of the Guidelines
To provide a national approach to the laboratory investigation and management of patients with ITP.

4 - Indication for testing
Investigation for platelet autoantibodies is only recommended in certain categories of thrombocytopenic patients with:
- The combination of bone marrow failure associated with possible immune-mediated thrombocytopenia
- ITP refractory to first and second line treatment
- drug-dependent immune thrombocytopenia
- miscellaneous disorders (rare) e.g. monoclonal gammaglobulinopathies, acquired thrombasthenia.

4.1 Bone marrow failure and immune-mediated thrombocytopenia
In some patients with thrombocytopenia due to inadequate thrombocytopoiesis, antibody-mediated platelet destruction may compound the thrombocytopenia, e.g. patients with proliferative disorders such as MDS, CLL or bone marrow transplant recipients. Reactive megakaryocytopoiesis is a diagnostic cornerstone of ITP but is not diagnostic if platelet autoimmunity is present in addition to bone marrow infiltration/failure. A PAIg test and determination of autoantibody specificity may be of use.

4.2 ITP patients refractory to first or second line treatment
For ITP patients for whom second or third line treatment is considered, a PAIg test and determination of antibody specificity may be indicated.

4.3 Drug-dependent immune thrombocytopenia (DDITP)
Many drugs are associated with thrombocytopenia. For some drugs there is firm evidence that the thrombocytopenia is antibody mediated. We recommend testing for DDITP for the following drugs:
- Heparin; antibiotics; quinine and quinidine; gold salts.

4.4 Monoclonal gammaglobulinopathies
Patients with a paraprotein band in their serum (MGUS, myeloma, secretory lymphoma) and a profound and unexplained thrombocytopenia should be investigated to determine whether the paraprotein is has an anti-platelet specificity. Although rare, reactivity of
paraproteins with platelets and thrombocytopenia has been reported and is the platelet homologue of cold haemagglutinin disease.

4.5 Acquired thrombasthenia
In cases with severe thrombocytopenia, a diagnosis of ITP is likely to be made. However, when the platelet count recovers during therapy a discrepancy between bleeding tendency and platelet count may be apparent. In such cases, platelet aggregation studies may be consistent with Glanzmann’s thrombasthenia, Bernard Soulier syndrome or a collagen receptor deficiency of the acquired type. PAIg and autoantibody specificity investigations are important in these rare cases to confirm the true pathophysiology.

5 - Specialised laboratory assays in the diagnosis of ITP

5.1 Assays for anti-platelet antibodies
The direct platelet immunofluorescence test (PIFT) is used to investigate referred samples for the presence of platelet-associated immunoglobulin IgG and IgM (PAIg); indirect testing is of little value in the investigation of suspected ITP because the sensitivity and specificity is even lower than for direct testing.

5.2 Increased levels of platelet-associated IgG (PAIgG) can be detected in most patients with ITP, but the results are not sufficiently sensitive or specific (patients with non-immune thrombocytopenias, e.g. septicaemia, frequently have positive results) to justify the routine use of these assays in patients with suspected ITP.

5.3 The absence of elevated PAIg does not exclude ITP.

5.4 In special cases, if further investigation is warranted, direct MAIPA will be performed only after consultation with the head of laboratory.

5.5 Sample required, see NBS User Guide 2003 Diagnostic and Cellular Therapy Service

6 - Investigation of ITP in childhood
Anti-platelet antibody testing does not assist in the diagnosis of ITP in childhood.

7 - Investigation of ITP in pregnancy

7.1 As in the non-pregnant patient, the diagnosis is largely one of exclusion as there is no confirmatory laboratory test.

7.2 As with non-pregnant adults and paediatric ITP, platelet-associated IgG is of no diagnostic value. Despite recent innovative methodologies, measurement of serum platelet autoantibodies are not clearly diagnostic of ITP in individual patients and do not predict the likelihood of neonatal thrombocytopenia.

8 - There is no indication for performing platelet-associated immunoglobulin tests out of hours