POLICY POL87/2

Thrombasthenia

This Policy replaces
POL/MED/CM/005/01 & POL87/1

Copy Number

Effective **04/11/09**

Summary of Significant Changes

Change of author and contact for further information details

PURPOSE

This clinical policy is intended to provide information on the diagnosis, laboratory investigation and clinical management of glycoprotein specific antibodies occurring in patients with hereditary platelet glycoprotein deficiency for medical and scientific staff within the National Blood Service.

Applicable Documents

Coller BS (1994). Inherited disorders of platelet function. In: *Thrombosis and Haemostasis*. (ed. Bloom, A.L., Forbes, C.D., Thomas, D.P., et al) 3rd Ed, 723-739, Churchill Livingston, Oxford.

George JN, Caen JP, Nurden AT (1990). Glanzmann's thrombasthenia: the spectrum of clinical disease. *Blood* 75, 1383 - 1395.

POLICY

GLANZMANN'S THROMBASTHENIA (GT) AND BERNARD SOULIER SYNDROME (BSS)

Background

Glanzmann's thrombasthenia (GT) and Bernard Soulier Syndrome (BSS) are rare autosomal recessive, homozygous or compound heterozygous bleeding disorders. Often there is consanguinity.

In GT the bleeding disorder is characterized by defective platelet aggregation in response to multiple physiological agonists such as ADP, thrombin and collagen but normal aggregation in response to ristocetin. Patients with GT have a spectrum of qualitative and/or quantitative defects in the $\alpha_{IIb}\beta_3$ integrin or platelet glycoprotein (GP)IIb/IIIa (CD41/61) complex. The platelet count of these patients is usually normal. The patient is at risk of forming GPIIb/IIIa isoantibodies after transfusion or during pregnancy. These antibodies can severely complicate future platelet transfusion therapy.

In BSS, the bleeding disorder is characterized by defective platelet aggregation in response to ristocetin, but normal aggregation is seen with agonists such as ADP, thrombin, collagen etc. The platelet count of these patients is generally reduced, the mean platelet volume is significantly increased (sized as neutrophils), but it is not unlikely that the overall platelet mass is near normal. In BSS there is a spectrum of qualitative and/or quantitative defects in the Von Willebrand factor receptor or the GPIbα/Ibβ/IX/V complex (CD42) complex. The patient is at risk of forming

GPIbα/Ibβ/IX/V isoantibodies after transfusion or during pregnancy. These antibodies can severely complicate future platelet transfusion therapy.

Clinical Features
Clinical features depend on the type of genetic defect underlying the particular case. Recurrent and life-threatening bleeding episodes are common in severe disease. Ecchymoses and petechiae may be noticed at or soon after birth. Excessive bleeding following minor surgery such as circumcision and tooth extraction provides a warning and severe epistaxis is a feature. In puberty, menorrhagia is a universal manifestation among females. Gastrointestinal blood loss has been reported in some patients.

Surgical procedures may lead to excessive blood loss unless prophylactic platelet transfusions are administered together with other procoagulant therapies.

Transfusion Support
Platelet transfusion therapy is the treatment of choice in arresting significant bleeding in patients with GT or BSS, although many modalities of adjunctive therapy should be considered (e.g. prophylactic treatment with DDAVP or in case of severe bleeding, Tranexamic Acid and recombinant Factor VIIa (rFVIIa)). It has been shown in relatively small numbers of GT patients that rFVIIa concentrates may be useful in less than 50% of cases. Some would advocate that rFVIIa is selectively used in patients with refractory or matched donor platelets. If there is a need for transfusion support for GT or BSS patients every effort must be taken to prevent allo- and iso-immunization which may both lead to platelet refractoriness. However, a delay in the selection of ideal blood product should not compromise the need for an urgent life-saving transfusion.

Platelets
ABO and D identical, HLA class I matched platelets should be selected. In GT, HPA-1 and -3 genotyping is of no significance as the chance of HPA-1 or -3 alloantibody formation is very small when compared with the risk of isoantibody formation. The same is true of HPA2 alloimmunisation in BSS.

Red cells
The need for red cell transfusion is generally less, compared to platelet requirements. However, during surgical procedures or when there is severe and prolonged bleeding, it may be necessary to correct the anaemia by red cell transfusion. ABO and D compatible units should be selected.

Screening for platelet antibodies
We advise to screen for platelet antibodies (specific ones and HLA class I antibodies) after each transfusion episode and in the 18-20th week of pregnancy. It is important to remain informed about the patient's antibody status. If GPIIb/IIIa or GPIb/IX isoantibodies are formed, high dose intravenous immunoglobulin G (ivIgG) should be considered when platelet transfusions are required.

Registration with regional haemophilia centre
Any patient with a genetically determined bleeding disorder should be registered on the national database at the Oxford regional haemophilia centre. It is also advised by the DoH to seek advice from the regional haemophilia centre on the care plan of such patients.

Further information
For further information please do not hesitate to contact

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