Editorial

Von Willebrand disease - an under diagnosed entity

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von Willebrand factor (VWF) is a central component of haemostasis serving both as a carrier of factor VIII and as an adhesive link between platelets and the injured blood vessel wall.[1] Defects in VWF, therefore, may cause bleeding by impairing both platelets adhesion and blood clotting. Von Willebrand disease (VWD) has been defined as an inherited bleeding disorder caused by a quantitative or qualitative defect of VWF secondary to a mutation in VWF gene located on chromosome 12.[2] VWD has been classified into three different types: type 1 and 3 refers to a partial and complete deficiency of VWF respectively, while type 2 includes the qualitative abnormalities of VWF structure and / or function. Type 2 VWD is further subdivided into subtype A, B, M and N.

VWD is the most common inherited bleeding disorder with western literature showing a prevalence of 0.7 to 1.6 per cent in their population.[3] Type 1 VWD is the commonest (70 - 80%) and inherited as an autosomal dominant trait.[4] Although not many studies are available on the prevalence of VWD in Pakistan, some of the tertiary care centers and institutions have reported a prevalence of 3.18-7.74 per cent among the cases with hereditary bleeding disorders.[5] VWD therefore remains an under diagnosed or misdiagnosed entity in Pakistan. Furthermore, the prevalence of different subtypes is also not known.

Patients with VWD may present at any age because of wide range in severity of symptoms and some patients may have no apparent bleeding history. Type 1 and 2 VWD commonly presents as a mild to moderate bleeding disorder of platelet dysfunction i.e. bruising, epistaxis, gum bleeding, menorrhagia, and prolonged bleeding after haemostatic challenge e.g. after circumcision, tooth extraction or other surgical intervention. Type 3 VWD is serious in nature and can present with cephalhaematomas in newborns, soft tissue bleeding, haemarthrosis etc. resembling that of patients with haemophilia.[6]

Laboratory testing in VWD vary from center to center and largely depends on the availability of specific diagnostic tests. Platelet count and peripheral blood film examination along with coagulation screen are usually carried out as initial first line tests.[7] Platelet aggregation studies are also sometimes important to exclude functional disorders. Specific laboratory tests including VWF antigen, F VIII activity and ristocetin cofactor assay are carried out in patients with suspected VWD on initial screening test. Additional tests that aid in classifying the type of VWF once a diagnosis is established include a VWF multimer analysis and ristocetin induced platelet aggregation (RIPA).[8]

Laboratory findings are variable but the typical diagnostic pattern is a combination of prolonged bleeding time, normal platelet count and prothrombin time, prolonged partial thromboplastin time, decreased factor VIII activity, decreased plasma VWF concentration and a parallel reduction in its functional activity (ristocetin cofactor assay).[9] Great care must be exercised when interpreting these laboratory results and diagnosis should not be made on the basis of an individual test alone and these tests should be interpreted in conjunction with other screening and specific diagnostic tests. Due to the lack of specific testing, a significant number of patients with VWD are likely to be misdiagnosed as haemophilia based on the results of factor VIII levels. There are also reports where VWD is being misdiagnosed as Bernard Soulier syndrome when platelet aggregation is viewed in isolation and type 2B VWD being misdiagnosed as immune-mediated thrombocytopenia.[10] It is also important to remember that the screening tests may turn out to be normal in patients with mild VWD, and there are various other factors which affect the VWF level e.g. pregnancy, adrenergic stimulation, hormone replacement therapy, inflammatory process, age and ABO blood group.[11,12] Therefore, repeat testing is usually necessary if the diagnosis of VWD is to be established.

Notwithstanding the growing recognition of this disease, there is still a marked under diagnosis of this entity, as it has a wide range of clinical presentation and large variability in laboratory values. Therefore, the need to confirm or exclude VWD as the cause of bleeding disorder involves a strong clinical suspicion, comprehensive clinical evaluation, with a judicious use and interpretation of various screening tests. These can be followed by more specific diagnostic tests which could include repeated laboratory testing.

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