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CASE REPORT ON VON WILLEBRAND'S DISEASE

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Abstract:

Von Willebrand's disease (vWD) arises from abnormalities in von Willebrand factor (vWF), an adhesive glycoprotein uniquely involved in key aspects of both primary and secondary hemostasis. The current classification distinguishes disorders arising from partial (type 1) or complete (type 3) deficiencies and from qualitative defects (type 2). Type 2 vWD is further divided into four subtypes (A, B, N, and M), reflecting distinct classes of functional abnormalities. Mis-sense mutations account for most of type 2 vWD, whereas major disruptions in the vWF gene produce type 3 variants. The molecular basis of type 1 vWD is largely undefined. The laboratory diagnosis of vWD and its several variants is made on the basis of immunologic and functional studies of vWF, factor VIII levels, and specialized electrophoretic analysis (multimer gels). The mainstay of therapy for most patients with vWD in desmopressin, a pharmacologic agent that stimulates the release of endogenous pools of vWF. Cryoprecipitate and selected factor VIII concentrates are useful sources of exogenous vWF for the treatment of patients unresponsive to this desmopressin .

Index Terms - von Willebrand disease, Willebrand factor, glycoprotein, hemostasis, Mis-sense mutations, gene, factor-VIII, desmopressin, bleeding disorder**.**

Introduction:-

Von Willebrand's disease is an inherited bleeding disorder characterized by defective platelet adhesion and aggregation. The disorder was first described in 1926 by Erik von Willebrand, who recognized that it differed from hemophilia and named it "**hereditary pseudo hemophilia**"[1]. On the basis of population studies, the prevalence of von Willebrand's disease is 0.6 to 1.3%. Although the autosomal inheritance pattern would suggest an equal distribution of male patients and female patients, the disease is diagnosed in more females because of female-specific hemostatic challenges. Not all persons with low von Willebrand factor levels have clinically relevant bleeding symptoms[2] . Von Willebrand's disease is subdivided into types 1, 2, and 3. Type 1, which accounts for 70 to 80% of cases, is characterized by a quantitative deficiency of von Willebrand factor. Type 2, accounting for approximately 20% of cases, is caused by dysfunctional von Willebrand factor, resulting in a normal or reduced von Willebrand factor antigen concentration but a large reduction in von Willebrand factor function. Type 2 is further subdivided on the basis of specific phenotypic characteristics. Type 3 von Willebrand's disease is rare (accounting for <5% of cases), is the most severe form, and is caused by the absence of circulating von Willebrand factor[1]. The diagnosis of von Willebrand's disease is based on a personal history of bleeding, a family history of bleeding, or both, in combination with laboratory tests showing abnormalities in von Willebrand factor, factor VIII, or both. The assessment of the bleeding phenotype starts with a detailed history of all bleeding symptoms in the patient and family members. The rating of the severity of bleeding symptoms in von Willebrand's disease has received considerable

attention in recent years. Numerical scoring systems based on structured questionnaires, usually referred to as bleeding-assessment tools, have been developed and endorsed by the ISTH[3]. Treatment of von Willebrand's disease is based on normalizing von Willebrand factor and factor VIII levels in case of bleeding or before an intervention. This can be achieved by increasing the endogenous factor levels with the use of desmopressin or by infusing exogenous coagulation factors in the form of a high-purity von Willebrand factor concentrate or a low-purity factor VIII–von Willebrand factor concentrate. Additional treatments Fibrinolysis inhibitors, such as tranexamic acid and aminocaproic acid, are important as additional treatment of mucocutaneous bleeding. They can also be used to reduce bleeding and especially to prevent rebleeding in patients undergoing surgical or dental interventions, although evidence from randomized trials is lacking[4].

CASE REPORT:

A 27-year female patient wasadmitted to the hospital on 27/11/23 experiencing chief complaints of blood in sputum, loss of appetite, dark colored stools & pallor skin since 10 days. History of easy fatigue & generalized weakness was noted for past 3 months.

Patient was apparently normal and presented with blood in sputum, dark colored stools & pallor skin, easy fatigue, loss of appetite & generalized weakness. Patient had a history of blood transfusion 1 month back. Family and social history are insignificant. Patient's laboratory findings included hemoglobin of 2.1, bleeding time of 1 hour, Clotting time of 5 minutes, Total proteins :3.9, Total bilirubin: 0.27, Sr.creatinine : 0.55. Finally diagnosed as von Willebrand's disease with bleeding manifestations and severe anemia. The patient was prescribed with following medications Inj. Tranexamic acid 500mg IV BD, Inj. Iron sucrose 200mg in 100ml NS IV OD, Tab. Vitamin C 500mg PO OD, Tab. Iron Folic Acid 100+5mg PO OD, Inj. Pantoprazole 40mg IV BD, Syp. Sucralfate 10ml PO TID, Alternate days factor VIII 1500u transfusion and the treatment follow up by 9 days of therapy. After the treatment patient symptoms have reduced (Hemoglobin :3.6).

DISCUSSION:

In overall study, it was observed that Von Willebrand factor (VWF) is a large multimeric glycoprotein crucial for primary hemostasis and for coagulation. It is synthesized as a monomeric protein, secreted into plasma and their size is regulated by a specific cleaving-protease named ADAMTS13 (a disintegrin and metalloproteinase with thrombospondin type 1 repeats, member 13). VWF is synthesized by endothelial cells and megakaryocytes. The gene coding for VWF (VWF) has been cloned and located at chromosome 12p13.2. It is a large gene of approximately 178 kilobases and containing 52 exons. VWD is a complex genetic disorder in which three subtypes have been described. The simplified classification of VWD proposed Sadler is still in common use. type 1 accounts for 70% of cases and is the mildest form of the disease. Type 1 cases are caused bya partial deficiency of VWF. Type 2 cases are more difficult to diagnose due to the qualitative nature of the defect. These defects range from absence of certain protein multimers for binding during hemostasis to improper binding and decreased affinity. This Type 2 sub-group accounts for approximately 20-30% of cases. Qualitative VWD type 2 is further divided into four variants: 2A, 2B, 2N and 2M, based on the characteristics of the dysfunctional vWF. The type of mutation affecting the vWF locus forms the basis for classification of most type 2 VWD variants. Fortunately, the most severe form, Type 3, is rare. It accounts for 5% of cases overall.[5]

However, in some Swedish communities with prevalent disease, 1/ 200,000 people may have the severe form. The diagnosis of VWD is based on clinical and biological information. When patients present with mucocutaneous bleeding symptoms suggestive of a primary haemostatic disorder, a quantitative or qualitative abnormality of VWF is a possible cause or contributory factor. During the initial assessment it is important to remember that bleeding histories can be subjective and the disease characteristics can take time to evolve. A medical health history is important to help determine if other relatives have been diagnosed with a bleeding disorder or have experienced symptoms. For haemostatic activity, the relevant characteristics of these concentrates are the multimeric composition of the VWF and the amount of FVIII contained per unit of VWF. A VWF:RCo/VWF: Ag ratio close to 1 is desirable because it indicates the VWF has normal multimeric structure and adhesive function, but the appropriate amount of FVIII is debatable and will vary according to the circumstance.[5]

It's recommended for treatment of acute bleeding or emergency surgery, a VWF-FVIII concentrate or a combination of high purity FVIII and high purity VWF concentrates should be used. Treatment of acute bleeding episodes in VWD such as epistaxes, gum bleeding and menorrhagia. Post-traumatic bleeding can also occur and type 3 patients can develop spontaneous joint or muscle bleeding. When any of these are frequent, self-administration of desmopressin and tranexamic acid can be helpful. If the patient is non-desmopressin responsive, then acute treatment transfusion and secondary prophylaxis using concentrates should be considered. When bleeding persists despite apparently normal plasma levels of VWF activity, platelet transfusion may be helpful. Platelet transfusion is also the treatment of choice in platelet-type VWD pseudo (PT-VWD) and may be supplemented by FVIII-VWF concentrate. Because most cases of VWD are relatively mild and patients do not suffer from serious spontaneous bleeding, prophylaxis is rarely indicated. Exceptions include patients with type 3 disease plus haemarthroses, severe epistaxis, women with menorrhagia and those with VWD in conjunction with an on-going risk factor for bleeding, such as angiodysplasia.[6]

CONCLUSION:

Von Willebrand's disease (VWD) is the commonest inherited bleeding disorder. However, despite an increasing understanding of the pathophysiology of VWD, the diagnosis of VWD is frequently difficult because of uncertainty regarding the relationship between laboratory assays and function in vivo. The aim of this work is to show that von willebrand disease can be the cause of serious life-threatening hemorrhage and given its prevalence and presenting symptoms, VWD should always be considered in the assessment of children suspected of non-accidental injury, the risk for increased bleeding should be kept in mind when elective and medical procedures are undertaken in this hemostasis disorder.

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