Parahaemophilia: A Rare Case Report

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Abstract:
Parahaemophilia or Owren’s disease is a rare haemorrhagic disorder occurs due to congenital and frequently familial deficiency of Factor V. It is characterized by epistaxis, bruising, mucosal bleeding, soft tissue bleeding and haemarthrosis. We report a case of 6 year old female patient with overlapping features with other haemorrhagic disorder. With the complaints of recurrent episodic per rectal bleeding, patient was evaluated at different hospitals in Chattagram and was diagnosed as a case of Haemophilia B and treated accordingly. As her condition was not improved expectedly, she was referred to Armed Forces Institute of Pathology (AFIP) for further evaluation. The lab tests showed prolongation of prothrombin time (PT) and activated partial thromboplastin time (APTT), with normal bleeding time (BT) and thrombin time (TT). Coagulation factors assay revealed a significant decrease of factor V, 1% of normal range. Other coagulation factors are normal. She was treated with FFP and recovered four weeks after treatment.

Key word: Autosomal Recessive Disorder, FFP-Fresh Frozen Plasma, Parahaemophilia, RICD-Rare InheritedCoagulation Disorder.

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Introduction:
Parahaemophilia isa rareinherited coagulation disorder (RICD) which affects both sexes. Factor V deficiency was first described in a Norwegian patient in 1943 and reported by Dr. Paul Owren in 1947. The hereditary Factor V deficiency is very rare, and probably fewer than 500 patient’s affected worldwide have been reported since its discovery in 1943. Prevalence of homozygous forms is estimated at 1/1,000,000. Bleeding diathesis and the concentration of plasma factor V in patients with factor V deficiency was not as well related as plasma factor level. Miletich at el. Have proposed that platelet factor V level as much better correlated with bleeding symptoms. Congenital Factor V deficiency is caused by mutations in the F5 gene (1q23) controlling the production of plasma Factor V. Transmission is autosomal recessive.

Congenital Factor V deficiency can manifest at any age, with the most severe forms manifesting early in life. Common clinical signs include epistaxis, bruising, mucosal bleeding, soft tissue bleeding and haemarthrosis. Excessive and prolonged bleeding during or following surgery, delivery or trauma are frequent. Women may present with menorrhagia. In severe forms of the disease, there can be a risk of intracranial, pulmonary or gastrointestinal bleedings. The severity of the bleeding manifestations correlates with the Factor V levels.

We are reporting a case of 6 year old female patient with features overlapping with other haemorrhagic disorders. This paper aimed at bringing awareness to health professionals of this rare congenital disorder in Bangladeshi population.

Case report:
A 6 year old young girl of consanguineous parents presented on 21 January 2020 with recurrent episodes of per rectal bleeding.
Prioritizing procedures in oral medicine (OM) and as the negative impact of COVID-19 infection on oral medicine and periodontology practice examination and appropriate procedures, such as an increased risk of severe complications, avoiding face-to-face contact in PD cases are crucial. Oral manifestations, such as mucous membrane coagulation disorder. If not investigated thoroughly, concentrates may be helpful. Prognosis is good with cases of severe bleeding, the addition of platelet concentrates can be prolonged in severe cases.  

References:

Table 1: Investigations details of reported case

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<th>Date</th>
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<th>Result</th>
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Fig-1: Photograph of the ecchymosis on patient’s lower limbs.

Laboratory findings of complete blood count (CBC) and peripheral blood film (PBF) revealed microcytic hypochromic anaemia, possibly iron deficiency anaemia.

Fig-2: Peripheral Blood Film (40X)

Her relevant lab reports have been tabulated in table-1
On the basis of history, clinical examinations and laboratory investigations— a diagnosis of Para-ahaemophilia was made. Patient was treated with FFP and haematinics. Two weeks later, follow up physical examination and investigations showed disappearance of ecchymosis, stoppage of per rectal bleeding and epistaxis with factor V level increasing up to 20% of normal range. She completely recovered after 04 weeks having factor V level 30% and has been followed up at the out patient department. Family screening of other family members revealed no coagulation abnormality. Due to non-availability, mutation study was not performed.

**Discussion:**

In 1943, Owren described a female patient who had a bleeding diathesis attributable to the lack of single blood clotting factor, namely factor V or labile factor. Owren designated the disease “parahaemophilia,” to emphasize the clinical similarity to hemophilia. At that time, only four coagulation factors were considered: fibrinogen, calcium, prothrombin, thrombokinase. After owren reported parahemophilia, it was soon found that labile factor and factor V were one and same factor.1,3

The coagulation factors that function as enzymatically active serine protease activators, factor VIII and factor V, are cofactors in the coagulation cascade. Activated factor V is a cofactor in the conversion of prothrombin to thrombin by factor Xa in an action that are phospholipid and calcium dependent. The activator complex formed by factor Xa, activated factor V, phospholipid and calcium was called the prothrombinase complex. Activation of factor V by thrombin is achieved through a series of proteolytic cleavages. Activated factor V was inactivated by activated protein C in a surface dependent reaction that requires calcium ion and protein S.6

Our patient presented with history and features which overlapped with the features of Haemophilia B and Von Willebrand Disease. These overlapping features posed a diagnostic dilemma. Parahaemophilia is a milder disorder than other congenital haemorrhagic disorder. Even though patient may develop
complications, like anaemia. If not timely diagnosed; it would have been fatal.

Factor V is labile coagulation factor which appears to be necessary both for the production of fully potent intrinsic thromboplastin and for the rapid conversion of prothrombin to thrombin in the presence of tissue thromboplastin. Thus, the patients with Factor V deficiency manifest impaired thromboplastin generation and prolongation of prothrombin time. Diagnosis is based on prolonged prothrombin (PT) and activated partial thromboplastin times (APTT) and on low plasma Factor V levels. Bleeding time (BT) can be prolonged in severe cases. Differential diagnoses include vWD, Haemophilia (homozygous type), inhibitors to coagulation factor, and very rarely combined deficiency of factor V and factor VIII.

The level of Factor V activity in the patients’ plasma is usually <5% of that in normal plasma. Most bleeding episodes in patients with factor V deficiency can be treated with sufficient fresh frozen plasma to raise the plasma factor V level to 30%. Fresh frozen plasma (FFP) is the only treatment as Factor V concentrates are not available. In acute cases of severe bleeding, the addition of platelet concentrates may be helpful. Prognosis is good with early diagnosis and adequate treatment.

Conclusion:

This is the first reported case on Parahaemophilia in Bangladesh. Parahaemophilia is a very rare inherited coagulation disorder. If not investigated thoroughly, patients can be misdiagnosed. Screening test and associated coagulation factor assay should be done for proper diagnosis. Although factor V deficiency is a milder disorder than Haemophilia A/B, patients with factor V deficiency may sometimes require replacement therapy. With proper treatment, prognosis is good. If untreated, it can be fatal.

References:

5. Miletich JP, Majerus DW, Majerus PW. Patients with congenital factor V deficiency have decreased factor Xa binding sites on their platelets. J Clin Invest 1978;62:824-831. https://doi.org/10.1172/JCI109194, PMid:701480; PMCID:PMC371834