Open Access Case Report

Head Injury in a Male Reveals Mild Haemophilia

***Sundas Ali*[1]**
***Huma Abdul Shakoor*[2]**
***Samina Tufail Amanat*[3]**
***Sana Syed*[4]**
***Masooma Raza*[5]**

[1]*Pakistan Institute of Medical Sciences (PIMS), Islamabad, Pakistan*
[2]*Atomic Energy Cancer Hospital, NORI, Islamabad*
[3,4,5]*PAEC General Hospital, Islamabad*

Address for Correspondence
Dr Sundas Ali
sundasali243@gmail.com

Abstract

Mild hemophilia A is a coagulation disorder which may remain undiagnosed and become noticeable late in life after some traumatic event. We describe a case report of a 39 year old male who presented with headache and vomiting after having a minor head injury. Detailed investigation revealed a diagnosis of mild hemophilia-A

Key words: Mild hemophilia A, head trauma, factor VIII, APTT

Case Report

A 39 years old male, resident of Rawalpindi, presented in the emergency department of P.A.E.C General Hospital, Islamabad, Pakistan with complaints of altered level of consciousness and drooping of left eyelid 12 hours before presenting to hospital. According to the patient, he was alright a week before, when he started to develop gradual headache of mild to moderate intensity. This headache was associated with intermittent vomiting. Vomiting was non-projectile, contents depended upon what patient had taken in diet and there was no history of haematemesis. There was no history of unconsciousness, fits, drugs intake or significant trauma.

Upon further probing, patient gave history of minor trauma when he accidently hit his head against public transport van. Systemic inquiry was insignificant. Past history was also unremarkable as patient gave no history of easy bruisability or spontaneous bleeds. Moreover, there was no history of bleeding disorders in family. Past medical and surgical history was unremarkable. General physical examination revealed young male conscious with ptosis of left eyelid, slightly confused but obeying verbal commands. His vitals were stable with B.P of 120/80mmHg, respiratory rate of 15/min and pulse of 80/min. C.N.S examination revealed intact motor with no evidence of muscle wasting. Sensory system was also normal bilaterally. All the reflexes were normal. On examination there was exotropia of left eye with restricted eye movement and partial ptosis. On evaluation of autonomic system, pupil of left side was found dilated with absent accommodation. Right eye was normal. Other cranial nerves were intact. Fundoscopic examination of both the eyes was normal. Rest of systemic examination was unremarkable. Patient was admitted for work up of complete 3rd Nerve palsy and to rule out sub-dural hematoma. His complete blood picture, liver function tests, renal function tests and blood sugar levels were normal. Coagulation studies showed APTT prolongation to 51 seconds (control 30 sec.). PT was normal. No further evaluation was carried out. His M.R.I revealed a significant sub-dural haematoma in left fronto-parietal region causing significant mass effect upon ipsilateral hemisphere, brain stem & ipsilateral ventricle with subfalcine herniation. Surgical intervention was planned by surgical department under cover of single dose of 4 units of fresh frozen plasma. Craniotomy was done and a large haematoma was evacuated. Post surgically patient remained well except that he developed slight re-bleed which resolved conservatively during 1 week stay at hospital. There was complete recovery of ophthalmic symptoms. On follow up there was consistent prolongation of APTT. Patient was therefore referred to Haematology Department for further workup. Preliminary mixing study showed correction, suggestive of factor deficiency. For this, Factor VIII, IX and Von Willebrand antigen levels were performed which showed mild deficiency of factor VIII 36% (normal 50-150%), normal levels of F-IX (98%), and von Willebrand antigen (105%). All the tests were performed on fully automated coagulation analyser CA-550. Diagnosis of mild Haemophilia A was made. However genetic study of patient could not be performed due to non-availability in our set up. Patient is still in follow up with us with no repeat bleeding episode since initial event. However,

patient did develop one episode of epilepsy. EEG and MRI were normal. He has been advised anti-epileptic medication by medical team.

Discussion

The general prevalence of hemophilia is estimated to be 1 in 10,000 individuals. [1] However, the proportion of individuals with mild hemophilia within the population fluctuates across countries and may vary over time within a specific country. This variability is influenced by factors such as the accessibility of diagnostic resources and the level of awareness about hemophilia among healthcare providers. Approximately half of all hemophilia patients are classified as having severe disease, while 10% have moderate disease, and 40% exhibit mild disease.[2] Despite this distribution, the mild form of hemophilia A has historically received less attention compared to its severe counterpart.

Mild hemophilia stands out distinctly from severe hemophilia A, showing notable differences both in phenotype and genotype[3] Mutations associated with mild hemophilia A encompass over 200 small deletions or missense mutations. However, the molecular mechanisms underlying mild hemophilia A are not completely elucidated.[4]

Mild hemophilia often goes undiagnosed, particularly in resource-limited regions, as its manifestations are less pronounced compared to severe hemophilia. However, serious clinical complications may prompt recognition because spontaneous hemorrhages are infrequent in individuals with mild hemophilia A, unlike those with moderate to severe forms. Diagnosis of mild hemophilia typically arises during detailed family history, following one or more bleeding episodes, or as a consequence of investigations initiated by bleeding complications post-surgery, or after tooth extraction or trauma.[2] In this patient there was no significant family history of increased bleeding tendency. Moreover he never underwent any major surgical procedures or had any significant trauma. It was only when post operatively patient showed mild re bleed and continuous prolongation of APTT on his follow up visits that he was further investigated. But still suspicion of hereditary bleeding disorder was not suspected, as in these patients classical joint bleed is not seen. People with mild haemophilia (PWMH) encounter intermittent bleeding episodes and often face delays in receiving timely diagnosis, suitable treatment, and medical attention.

Individuals with mild hemophilia typically do not receive equivalent levels of medical attention compared to those with severe forms. While this discrepancy may be warranted to some extent, it has occasionally led to significant neglect A retrospective-prospective registry was initiated within the Italian Association of Hemophilia Centers network to document all intracranial hemorrhages (ICHs) in individuals with hemophilia spanning from 2009 to 2019, detailing their clinical presentations, treatment modalities, and resulting outcomes. Results revealed a total of forty-six recorded ICH cases from thirteen participating centers. Among these cases, fifteen occurred in children (with ten being under the age of two), while thirty-one were observed in adults, with 45.2% of them diagnosed with mild hemophilia.[6] Fortunately in our patient there was no significant bleed during craniotomy for clot evacuation although he only received one dose of FFPs (4units) and oral Tranexamic acid 500mg TDS for five days.

Inhibitors can also manifest in individuals with mild hemophilia, typically following intensive exposure to factor concentrates. The epidemiological, pathogenic, clinical, and therapeutic characteristics of inhibitors in mild/moderate hemophilia A patients differ from those observed in individuals with severe hemophilia A. The cumulative incidence of inhibitors in patients with mild hemophilia A has been documented to range from 3 to 13% by the age of 33 in certain populations. Both type I and type II reaction-kinetic inhibitors have been reported in patients with mild hemophilia A, although type II inhibitors appear to be more prevalent compared to those in patients with severe hemophilia A, where type I inhibitors are more commonly encountered. [7,8] However inhibitor screen in our patient didn't reveal presence of inhibitors most probably as patient did not have any exposure to factor VIII concentrate.

Conclusion

Mild hemophilia is a neglected diagnosis which can be improved by the multidisciplinary approach.

References

1. Shah MA, Azeem R, Riaz H. Frequency of hemophilia A and severity of the disease at presentation. *NJMS*. 2017;2(1):46-9.

2. Berntorp E, Fischer K, Hart DP, Mancuso ME, Stephensen D, Shapiro AD. Haemophilia. *Nat Rev Dis Primers*. 2021;7(1):45-51. doi:10.1038/s41572-021-00278-x
3. Khan MT, Taj AS. Genotype-phenotype heterogeneity in haemophilia. *Hemophilia-Recent Advances*. 2019 Apr 10.
4. Pezeshkpoor B, Oldenburg J, Pavlova A. Insights into the molecular genetic of hemophilia A and hemophilia B: the relevance of genetic testing in routine clinical practice. *Hämostaseologie*. 2022;42(6):390-9. doi:10.1055/a-1945-9429
5. Daffunchio C, Landro ME, Galatro G, Neme D, Cambiaggi G, Moretti N, et al. How mild is mild haemophilia?. *Haemophilia*. 2023;29(2):530-7. doi:10.1111/hae.14750
6. Zanon E, Pasca S, Demartis F, Tagliaferri A, Santoro C, Cantori I, et al. Intracranial haemorrhage in haemophilia patients is still an open issue: the final results of the Italian EMO.REC registry. *J Clin Med*. 2022;11(7):1969. doi:10.3390/jcm11071969
7. Witmer C, Young G. Factor VIII inhibitors in hemophilia A: rationale and latest evidence. *Ther Adv Hematol*. 2013;4(1):59-72. doi:10.1177/2040620712464509
8. Makris M, Oldenburg J, Mauser-Bunschoten EP, Peerlinck K, Castaman G, Fijnvandraat K; Subcommittee on Factor VIII, Factor IX and Rare Bleeding Disorders. The definition, diagnosis and management of mild hemophilia A: communication from the SSC of the ISTH. *J Thromb Haemost*. 2018;16(12):2530-3. doi:10.1111/jth.14315