Inadvertent surgeries for patients with haemophilia - Emergent need for creating awareness

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Abstract

Introduction: Majority of patients with hemophilia (PwH) has musculoskeletal (MSK) abnormalities and a large proportion of surgeries done in PwH are for MSK related complications. Often PwH have their initial presentation to orthopedicians with joint swelling even prior to bleeding from any other sites. Yet, haemophilia is an under-recognized entity among orthopedicians.

Materials & Methods: This is a retrospective analysis of institutional haemophilia registry data of patients who has been operated for different MSK related abnormalities with special focus on those patients inadvertently operated by orthopedic surgeons without a prior diagnosis of haemophilia. Pre-operative evaluation and circumstances which led to the predicament of those patients were reviewed. All patients subsequently underwent a full coagulation work up including factor assay and inhibitor screen on suspecting a bleeding diathesis.

Results: Out of a total 212 patients in the registry, 32 (15%) patients required surgical intervention and 16 (50%) of them were for MSK complications. Eleven (69%) patients underwent elective procedures with prior work up and five 5 (31%) patients underwent orthopaedic procedures inadvertently without a prior diagnosis of haemophilia. All the 5 patients (Haemophilia A-3 and Haemophilia B-2) achieved haemostasis with replacement therapy with varied surgical outcomes.

Conclusions: Hemophilic arthropathy must be considered as a differential diagnosis in mono-articular arthritis. Careful elicitation of history and appropriate preoperative screening with prothrombin time (PT) and activated partial thromboplastin time (aPTT) is the antecedent to make a definitive diagnosis in a patient with suspected increased risk of bleeding.

Keywords: Haemophilia, Inadvertent Surgeries, Awareness.

Introduction

Hemophilia A and B are single gene disorders occurring due to a mutation in coagulation factor VIII gene (hemophilia A) and coagulation factor IX gene (hemophilia B) located on the X chromosome. This results in deficient synthesis of coagulation factor VIII or IX and clinically manifests with hemorrhagic tendencies in patients.[1]

Hemophilia A represents 80-85% of the total hemophilia population and affects males on the maternal side.[2] As per the 2014 global survey, India has the highest number (17470) of PwH.[3] The estimated number of PwH in India should be approximately 1,20,000. However the number of diagnosed patients is less than 15%. This reflects the low awareness, poor diagnostic facilities and limited data registry.[4]

Hemophilia services in India are still in their infancy, and increased awareness among healthcare providers as well as expansion of treatment facilities is the need of the hour. Most patients are diagnosed after much delay with severe hemophilia detected at 11–15 years of age.[5] A previous study from Punjab showed that the median age of first bleed in hemophilia was 18 months in hemophilia A and 15 months for hemophilia B with a lag period in diagnosis at 48 months and 60 months respectively after the onset of first bleed. Approximately 80% of PwH in the study had musculoskeletal abnormalities and many of them would require orthopaedic interventions.[6] As per the World Bank data, an estimated 62.4% of Indians seek medical care through out-of--pocket (OOP) expenses.[7] Indian families suffer catastrophic expenses on haemophilia treatment alone and hence only a fraction would undergo definitive procedures.[8] Logistics of doing surgery in PwH involves close interaction with the surgeon, haemophilia expert and the laboratory personnel with regard to factor infusion, optimizing the factor levels and frequent assays to ascertain the target levels. Often lack of awareness and limited facilities lead to inadvertent interventions which lead to life threatening bleeding events. In this paper, we describe a case series of PwH who underwent orthopedic procedures/surgeries without a prior diagnosis of hemophilia.

Materials & Methods

This is a retrospective analysis of institutional registry data between July 2008 and June 2017. The study population was patients who had been operated for MSK related complications. Special focus was made to detail on the patients operated inadvertently by orthopaedic surgeons without a prior diagnosis of haemophilia. Eligibility criteria of patients were those who have been operated for various indications and post operatively diagnosed to have haemophilia due to bleeding consequences. Pre-operative evaluation among the patients was reviewed and all patients underwent a

full coagulation work up including factor assay and inhibitor screen on suspecting a bleeding diathesis. Pre-operative events which prompted the surgery and reasons were noted based on the notes the patients carried with them and post-operative complications, clinical characteristics and long term consequences were recorded. The natural course of PwH undergoing surgery without a prior diagnosis is being described as per the recommended draft characteristics of a case series.[9]

Results

A total of 212 PwH are registered at our institution (Haemophilia A=176 (83%) and Haemophilia B=36 (17%). Of these, 32 (15%) patients required surgical interventions for various indications. Sixteen (50%) interventions were for musculoskeletal complications performed by orthopaedic surgeons. Eleven (69%) patients underwent elective procedures with prior coagulation work up with inhibitor screen and factor assays and five 5 (31%) patients underwent orthopedic procedures without a prior diagnosis of haemophilia and was referred to our center [Haemophilia A =3 (mild, moderate and severe one each) Haemophilia B=2 (severe)]. The median age of these 5 patients was 21 years (range 15-37 years). (Table:1, 2)

Table: 1 Indications of inadvertent surgery and Interventions for PwH

Patient	Age	Type and severity of hemophilia	Indication of procedure/surgery	Time delay for diagnosis (days)diagnosis of hemophilia	Intervention following
1	15	A, Moderate	Osteosarcoma	10	Factor support only
2	37	A, Mild	Crush Injury	14	Factor support only
3	37	B, Severe	Osteoarthritis	2	Factor support only
4	17	A, Severe	Septic arthritis	10	Re-exploration, skin grafting, factor support
5	21	B, Severe	Tuberculous arthritis	14	Re-exploration, factor support

Table 2: Planned musculoskeletal surgical indications for orthopaedic interventions in PwH

Indication of procedure/surgery	Number
Above knee amputation: Pseudotumor of femur	1
Shoulder arthrodesis: Instability and bleed	1
Pelvic exploration: Pelvic pseudotumor	2
Hip disarticulation: Pseudotumor of knee	1
Corrective osteotomy of femur and tendoachilis lengthening: Distal femur malunion	1
Implant removal: Previous fracture femur, implant in situ	1
Enucleation and curettage: Pseudotumor of thumb	1
Total Knee Replacement: Osteoarthritis	3

Two patients were diagnosed after above knee amputation (one for suspected osteosarcoma and one for post traumatic crush injury).One patient underwent arthrotomy for suspected septic arthritis and one patient underwent arthroscopy and biopsy for suspected tuberculous arthritis. One patient underwent total knee replacement for osteoarthritis. **(Table: 1)**

A detailed evaluation showed that 4 patients had history of prolonged bleeding following trauma and three of them also had spontaneous swelling of multiple joints in the past. Only the patient with moderate hemophilia A with road traffic accident did not have prior bleeding or any hemostatic challenge in the past. There was no family history of bleeding diathesis in all five patients.

None of the patients had pre-operative Prothrombin time (PT) or activated partial thromboplastin time (aPTT) testing. In 2 patients, clotting time had been done pre-operatively which was normal. The median time to make a definitive diagnosis of hemophilia post operatively was 10 days (range: 2-14 days).

Four patients had received fresh frozen plasma (FFP) and packed red transfusions prior to hematology consultation and hence accurate severity classification

of hemophilia was delayed. All the 5 patients were inhibitor negative. Three patients were managed only with factor support and the other 2 patients in addition required re-exploration with one of them also requiring skin grafting along with prolonged antibiotic support due to secondary infection. **(Table 1).**

Patient 1 underwent an elective above knee (AK) amputation for osteosarcoma while patient 2 was taken up as emergency cases for road traffic accident. Both of them were later rehabilitated with prosthesis. Patient 3 who underwent TKR recovered with minimal residual deformity. Although re-exploration and interval skin grafting were successful in patient 4, he continued to have joint deformity. The patient who underwent re-exploration and secondary suturing has recovered well and chronic effects of the initial injury need to be followed up.

Discussion

The purpose of this case series is to highlight the need for improving the awareness regarding hemophilia among orthopedicians who frequently encounter mono or polyarticular arthritis in clinical practice. The differential diagnosis of a mono arthritic joint includes septic arthritis, reactive arthritis, hematological malignancies, juvenile arthritis, tuberculosis, sarcoidosis and spontaneous or traumatic hemarthrosis. It may be difficult at times to differentiate joint changes resulting from infective/inflammatory conditions from those seen secondary to bleeding diathesis.[10]

A careful history is paramount in requesting for appropriate preoperative laboratory testing. In our series, the patients did not recognize the prior swelling of the joints as joint bleed and the orthopedicians also failed to suspect a bleeding disorder prior to surgery. Patients may not identify spontaneous joint swelling as a bleed and attribute it to injury or an inflammatory reaction. All the patients presented without a family history of bleeding and one thirds of all cases with hemophilia occur spontaneously with sporadic mutations and no family history.[2]

Lack of awareness and poor availability of diagnostic facilities have led to many iliopsoas and intra-abdominal bleeds being misdiagnosed as acute appendicitis by general surgeons. Similarly, many spontaneous intracranial bleeds in children are evaluated only after the surgery due to recurrence of bleed.[11,12] Hence many patients may have had mortality or life threatening haemorrhage without even a diagnosis of haemophilia.

Doing baseline coagulation screening including PT and aPTT is important in this group of patients especially in the absence of accurate bleeding history or prior haemostatic challenge. Prolonged aPTT, if found pre-operatively would then prompt a correction study and subsequent factor assay to demonstrate deficiency of FVIII or FIX. Whole blood clotting time (CT) is a poor screening test with a sensitivity of only 11.1% and even the CT test by capillary method is highly unreliable.[13,14] In two of our patients, clotting time was normal although they had prolonged APTT.

Current guidelines for preoperative coagulation screening recommend testing only if history and examination suggests an increased bleeding risk. Ideally a bleeding assessment tool (BAT) needs to be applied to each patient preoperatively which is based on a standardized bleeding questionnaire.[15] If there is a suspicion of increased bleeding risk or if the BAT is not applied, the recommended screening tests of coagulation are PT, aPTT and platelet count. Additional tests should be ordered only if any of above is abnormal. There is no data supporting the use of preoperative bleeding time and clotting time as predictors of excessive surgical bleeding.[16,17]

The delay in making the diagnosis of hemophilia even after substantial post-operative bleeding occurs due to the general assumption that the deranged coagulation profile may be due to disseminated intravascular coagulation (DIC). Patients are given fresh frozen plasma which further poses diagnostic challenges as the FFP given interferes with accurate estimation of the factor assay and initiation of appropriate clotting factor concentrate (CFC) treatment. Three of our patients got their factor assays performed in a private laboratory outside the hospital premises who reported mixed (multiple) clotting factor deficiencies, possibly due to sample deterioration during transport. Ideally screening coagulation tests and factor assays have to be performed within 4 hours of collection of sample or adequately processed and transported before testing. In case standardization of the same is suspect, it may be prudent to send the patient to a referral laboratory for onsite sampling and testing.

Hemophilia can also present with chronic arthropathy mimicking osteoarthritis and patient 3 should have elicited a suspicion to evaluate the cause of arthritis in a young man prior to embarking on total knee replacement. Timely diagnosis of hemophilia also enables screening of family members for carrier status for prevention of hemophilia.[18]

Ours is a single center data of patients who have been referred to a tertiary hospital where coagulation work up and supportive care is available. The magnitude of the problem may be even more considering that many of the patients may succumb to bleeding before even reaching a referral center.

With many PwH having musculoskeletal symptoms, it is important that the orthopedicians should consider hemophilia as a differential diagnosis before attempting invasive procedures or surgery in patients with such problems.

This data suggests, approximately 50% of the surgeries are for PwH are done for MSK related problems and 1/3rd of them are being done inadvertently without a prior diagnosis of haemophilia. Hence it is important to integrate hemophilia care in the

existing healthcare system in a more elaborate way. It is also vital to emphasize coagulation disorders in the MBBS curriculum and during post graduate training.[19] Orthopedicians play an important role in providing comprehensive hemophilia care and it is important to expose post graduate students to hemophilia management.

Conclusion

Hemophilic arthropathy must be considered as a differential diagnosis in mono-articular arthritis and necessary coagulation screening tests should be done before deciding to perform invasive procedures or surgeries.

References

1. Kemball-Cook, G. and Gomez, K. Molecular Basis of Hemophilia A. In: Lee, CA, Berntrop E, Hoots WK. 2nd edition. 2010. Wiley-Blackwell, Oxford, UK.
2. Srivastava A, Brewer AK, Mauser-Bunschoten EP, Key NS, Kitchen S, Llinas A, et al. Guidelines for the management of hemophilia. Haemophilia. 2013;19:e1-47.
3. World Federation of Hemophilia. Report on the Annual Global Survey 2014.October 2015 WFH website. http://www1.wfh.org/publications/files/pdf-1627.pdf Accessed 27 October 2016.
4. Chandy M, Khanduri U, Dennison D. Developing hemophilia services in India. Southeast Asian J Trop Med Public Health. 1993;24 Suppl 1:66-8.
5. Kar A, Potnis-Lele M. Descriptive epidemiology of haemophilia in Maharashtra, India. Haemophilia. 2001;7:561-7.
6. Joseph MJ, Kakkar N, Mathew A, Philip CC, Ramandeep K, Jasprit S. Demographics and estimated prevalence of Haemophilia: The gap is wide. Experience from Punjab, India, a developing country. East Asian Haemophilia Forum, Nara, Japan. 1-A3, 2015.
7. Out-of-pocket health expenditure (% of total expenditure on health). World Health Organization Global Health Expenditure database. Available from http://data.worldbank.org/indicator/SH.XPD.OOPC.TO.ZS?end=2014&locations=IN&start=1995&view=chart [Accessed July 20, 2017]
8. Dharmarajan S, Phadnis S, Gund P, Kar A. Out-of-pocket and catastrophic expenditure on treatment of haemophilia by Indian families. Haemophilia. 2014;20:382-7.
9. Carey TS, Boden SD. A critical guide to case series reports. Spine (Phila Pa 1976). 2003;28:1631-4.
10. Prabhu AS, Balan S. Approach to a child with monoarthritis. Indian J Pediatr. 2010 Sep;77(9):997-1004
11. Ghosh K, Shetty S, Sahu D. Haemophilia care in India: innovations and integrations by various chapters of Haemophilia Federation of India (HFI). Haemophilia. 2010;16:61-5.
12. Phadke S. Hemophilia care in India: a review and experience from a tertiary care centre in Uttar Pradesh. Indian Journal of Hematology and Blood Transfusion. 2011;27:121-6.
13. Gokhale S. Preoperative bleeding time and clotting time tests: Useful or wasteful Med J Armed Forces India. 2002l;58:285.
14. Kinra P, Tewari V, Raman RT. Role of bleeding time and clotting time in preoperative hemostasis evaluation. Ind J Aerospace Med. 2009;53:56-61.
15. Rodeghiero F, Tosetto A, Abshire T, Arnold DM, Coller B, James P, et al. ISTH/SSC bleeding assessment tool: a standardized questionnaire and a proposal for a new bleeding score for inherited bleeding disorders. J Thromb Haemost. 2010;8:2063-5.
16. Thiruvenkatarajan V, Pruett A, Adhikary SD. Coagulation testing in the perioperative period. Indian J Anaesth. 2014;58:565-72.
17. Chee YL, Crawford JC, Watson HG, Greaves M. Guidelines on the assessment of bleeding risk prior to surgery or invasive procedures. British J Haematol. 2008;140:496-504.
18. MacLean PE, Fijnvandraat K, Beijlevelt M, Peters M. The impact of unaware carriership on the clinical presentation of haemophilia. Haemophilia. 2004;10:560-4.
19. Chuansumrit A. Treatment of haemophilia in the developing countries. Haemophilia. 2003;9:387-90.