Hemophilia, Complications and Management: Series of 3 Cases with a Brief Review of Literature

Kamal Kant Sahu*, Subhash Chander Varma, Pankaj Malhotra, Gaurav Prakash, Alka Khadwal, T D Yadav, Jasmina Ahluwalia, Neelam Varma

Department of Internal Medicine, Postgraduate Institute of Medical, Education and Research, Chandigarh, India

Introduction

Hemophilic pseudo tumors are rare, but well known complication of severe hemophilia, which most frequently develop at the femur, tibia, pelvic bones [1]. A pseudotumor may occur spontaneously or following multiple bleeding episodes into closed space which can either be bone or soft tissue resulting in loculated collection with encapsulation. As swelling enlarges, increasing pressure may also lead to slow destruction of adjacent structures. Massive pseudo tumors are very rare in cases of mild/moderate Hemophilia. Here we would like to share our experience with three cases of hemophilia who presented with varied complications with brief description regarding management issues and review of literature.

Case Report 1

A 38 year old male diagnosed as congenital Hemophilia A since 1985 with history of multiple bleeding episodes and transusions with factor VIII concentrates presented with complaints of left sided limping and lump sensation over left lumbar area for 10 months, initially of the size of coconut that gradually enlarged to present massive size (Figures 1A and 1B) despite receiving multiple factor VIII concentrates. Examination and MRI abdomen (Figures 1C and 1D) suggested massive pseudotumor in entire left lumbar region predominantly involving the lateral and posterior aspect and extending from posterior costal margin above to till iliac crest inferiorly. Coagulation profile revealed a PTT of 58 seconds. Factor VIII activity was 7.5% with absent VIII inhibitors and HCV positivity. With a goal to raise factor VIII activity to 80% he was transfused accordingly with Factor VIII concentrates and excision of pseudotumor was done without intra/postoperative complications.

Case Report 2

A 19 year old male being symptomatic since the age of 2 years for recurrent episodes of epistaxis and bleeding into major joints predominantly of knee and elbow and being diagnosed as Hemophilia B with history of multiple transusions of fresh-frozen-plasma and factor IX concentrates in past. He now came for complaints of gradually increasing distension of right sided abdomen (Figures 2A and 2B). Lab investigations revealed a PTT prolongation of 30 seconds, normal liver levels and normal coagulation profile. MRI of hip joint, hence keeping this fact in mind hip replacement was kept for 1 year postoperatively. Postoperative day 1-3, dose given and therapeutic level (trough and peak level) of factor VIII.

<table>
<thead>
<tr>
<th>Postoperative day</th>
<th>Factor VIII dosage</th>
<th>Factor VIII level (Trough level)</th>
<th>Factor VIII level (Peak level)</th>
<th>Bleeding episodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAY1-3</td>
<td>40 IU/kg BD</td>
<td>60%</td>
<td>102%</td>
<td>No</td>
</tr>
<tr>
<td>DAY4-6</td>
<td>25 IU/kg BD</td>
<td>60%</td>
<td>101%</td>
<td>No</td>
</tr>
<tr>
<td>DAY6 onwards</td>
<td>15 IU/kg BD</td>
<td>40%</td>
<td>58%</td>
<td>No</td>
</tr>
</tbody>
</table>

Table 1: Postoperative day, dose given and therapeutic level (trough and peak level) of factor VIII.

*Corresponding author: Kamal Kant Sahu, Department of Internal Medicine, Postgraduate Institute of Medical, Education and Research, Chandigarh, India, E-mail: everlastingkamal@yahoo.com

Received November 19, 2013; Accepted December 26, 2013; Published December 28, 2013


Copyright: © 2013 Sahu KK, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Case Report 3

This 17-year-old male, diagnosed case of hemophilia B presented to orthopedic OPD with complaints of fall and subsequently pain over left thigh. He underwent X-ray (Figures 3A and 3B) and MRI of left thigh which showed fracture of left sided shaft of femur without hematoma formation. Baseline factor IX level were <1% with no detection of inhibitors. Hence he underwent fixation of pathological shaft fracture by closed interlock nailing with 38×11 cm nail respectively. Similar to above case, this patient was also given factor IX concentrates with similar factor IX levels being maintained thorough out the course of his hospital without intra or post-operative complications.

Discussion

Hemophilia is challenging in many ways. Hemophilia B symptoms are similar to those of hemophilia A, including numerous, large deep bruises and prolonged bleeding. Lifelong risk of bleeding, hematoma formation, joint contracture, risk of blood transfusion infections like HCV, HBV, HIV, financial issues, social and psychological brunt’s are few among the challenges which hemophilic patients go through on daily basis throughout their life especially in resource constraint settings. The degree of severity of clinical manifestations depends on factor level. The joints are the most frequent site of bleeding followed by the soft tissues and bones [2].

Pseudo tumors or blood cysts are rare but dangerous complications of hemophilia, occurring in 1-2% of patients with severe forms of the disease [2]. It is essentially a chronic, slowly expanding hematoma resulting from repetitive bleeding and is surrounded by thick fibrous capsule and most commonly develops in the femur, tibia and pelvic bones, while orbit, small bones of the hand, mandible, clavicle, spinal canal are less common site. The first description of hemophilic Pseudotumor was done by Starker in 1918 in a 14-year-old male child. Clinically bleeding symptoms criteria may confuse because patients with factor VIII or factor IX levels <1% occasionally have little or no spontaneous bleeding and appear to have clinically moderate or mild hemophilia. Further, the reverse is also true for patients with pro-coagulant activities of 1-5%, who may present with symptoms of clinically severe disease [3] (Table 2).

Treatment

Even though treatment of hemophilia has undergone rapid development in the past decade, at present hemophilic pseudotumor lacks standard management guidelines. Decisions based on individual cases are more appropriate rather than fixed guidelines and treatment options range from varied approaches with factors replacement, arterial embolization, localized radiation and surgical excision:

Conservative management

Simplest of all, but most challenging among the available is conservative approach which requires clotting factor replacement to keep an activity of 80%-100% during intra-operative period at least. For patient with inhibitors, recombinant factor VIIa or prothrombin complex concentrates can be used. However in general, operative removal of the entire mass is a reliable treatment because the pseudotumor likely will reform if it is not completely removed.

Surgical excision

Surgical excision of entire mass is a reliable method as it ensures complete removal if done properly and prevents the risk of recurrence. Surgical intervention in the person with hemophilia may be elective or emergency in nature. Whenever possible, the patient should be transferred to a Hemophilia Treatment Centre. Recommendations suggest to maintain trough levels of either VIII and IX factors in between 80-100% for major surgeries during 1st three days and 60-80% for next four days and latter of approximately 40-60% to sustain hemostatic status.

Arterial embolization

1st successful Trans catheter arterial embolization in a case of hemophilic pseudotumor was done by Pisco in 1990 [17]. After this, many case reports have been published till now sharing the experience of embolization of feeding vessels to pseudotumor [17-20]. Ethanol is a well-known sclerosing agent with curative potential. It exerts a direct toxic effect on the vascular wall, inducing significant thrombosis by denaturing blood proteins, dehydrating vascular endothelial cells, and...
Role of radiotherapy

Radiotherapy has come up with convincing data in terms of promising modality of treatment in cases where surgery is contraindicated, or resistant to conservative treatment. Kang et al. in 1999 reported successful treatment of hemophilic pseudotumor located in ulna with low dose radiation (total dose of 900 cGy in 6 fractions) [23]. Purskait et al. [4] reported a case of Hemophilia A with nasal bone pseudotumor with complaints of recurrent epistaxis which was refractory to conventional factor IX deficiency. Similar case report by Rijal et al. [13] have supported the role of radiotherapy in pseudo tumors. Similarly Ozbek et al. treated a 13-year-old hemophiliac boy who had a pseudotumor of the tibia with low-dose radiotherapy (600 cGy) successfully [24]. The exact mechanism of hemophilic pseudotumor to respond to radiotherapy is not known. However different opinion suggests that radiation results in:

(a) Endarteritis in an acute bleeding hematoma [25]
(b) Direct injury of small vessels causing fibrosis and healing [26]
(c) Stimulation of fibroblasts resulting in fibrosis [23].

There has been considerable variation in the literature in radiotherapy dose. As low as 600 cGy to as high as 2350 cGy, with or without factor replacement, have shown good response with complete resolution of lesions. However most of the data available in literature regarding use of radiotherapy primarily in the treatment of pseudo tumors were those in which the hematomas are located intrasosseously or within close compartment like orbit and in cases were patients had presence of anti-hemophilic factor antibodies. And hence in all these such above mentioned conditions, it will be risky to operate upon surgically and better to opt localized radiotherapy, however in our 1st two cases we did not primarily considered radiotherapy due to massive size of pseudotumor with lack of convincing data for role of radiotherapy in such bulky hematomas and absence of inhibitors making surgical excision safe and one time procedure without risk of any unwanted radiation exposure. Even though, no standard radiation dose and fractionation schedule exists in the management of hemophilic pseudo tumors, radiation therapy should be tried in cases especially where lesions are located in the bone with growth potential and with presence of anti-hemophilic factor antibodies and with significant surgical risks [23].

Conclusion

Above mentioned series of three cases suggest that hemophiliac individuals are at potential risk of recurrent internal bleed leading to massive pseudo tumors which are although rare in mild/moderate hemophilia A but can occur to such severity so as to cause extensive bone destruction and adequate replacement therapy in the perioperative period is necessary to achieve safe surgical removal. Similarly orthopedic procedures which seem to be simple in normal individuals may be challenging and complicated in case of hemophilacs and needs excellency in surgical skills and adequate support in terms of availability of factor concentrates to ensure hemostasis during intra as well as post-operative period.

Acknowledgement

Dr. Kamal Kant Sahu-Wrote the paper; Dr. Gaurav Prakash-Assisted in manuscript and discussion; Dr. Akash Khadwal-Assisted in manuscript and discussion; Dr. Pankaj Malhotra-Designed the work; Dr. Subhash Chander Varma-Designed the work; Dr. T.D Yadav-Performed the surgery of intra-abdominal pseudo tumors; Dr. Sandeep Patel-Performed closed interlock nailing for fixing fracture of shaft of femur; Dr. Jasminia Khutwalia-Performed mixing studies to assess factor VIII and IX levels and detection of inhibitors; Dr. Neelam Varma-Performed mixing studies to assess factor VIII and IX levels and detection of inhibitors.

Table 2: Few recent publications of pseudotumor involving various regions and therapy.

<table>
<thead>
<tr>
<th>Author (year of publication)</th>
<th>Hemophilia type</th>
<th>Location of pseudotumor</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present case 2 (2013)</td>
<td>Hemophilia B</td>
<td>Intra-abdominal parietal mass</td>
<td>Factor IX replacement Surgical excision</td>
</tr>
<tr>
<td>Present case 3 (2013)</td>
<td>Hemophilia B</td>
<td>Shaft fracture femur (left)</td>
<td>Factor IX replacement and intramedullary closed interlock nailing</td>
</tr>
<tr>
<td>Pruzansky et al. (2012) [8]</td>
<td>Hemophilia A</td>
<td>Distal radius</td>
<td>Excision</td>
</tr>
<tr>
<td>Thordason et al. (2011) [9]</td>
<td>Hemophilia A</td>
<td>Mandible</td>
<td>Curettage of lesion</td>
</tr>
<tr>
<td>Mittal et al. (2011) [10]</td>
<td>Hemophilia B</td>
<td>Proximal tibia</td>
<td>Excision</td>
</tr>
<tr>
<td>Cox et al. (2011) [12]</td>
<td>Hemophilia B</td>
<td>Mandible</td>
<td>Excision</td>
</tr>
<tr>
<td>Liu et al. (2011) [14]</td>
<td>Hemophilia A and HIV</td>
<td>Right Hip joint</td>
<td>Hip joint amputation</td>
</tr>
<tr>
<td>Kumar et al. (2011) [15]</td>
<td>Pelvic pseudotumor and pseudo aneurysm</td>
<td>Factor IX replacement (ineffective) Coil embolization followed by surgical extirpation of the lesion 24 hours later.</td>
<td></td>
</tr>
<tr>
<td>Garcia-Perez et al. (2010) [16]</td>
<td>Hemophilia A</td>
<td>Intraabdominal pseudotumor</td>
<td>Factor VIII replacement Surgical excision</td>
</tr>
</tbody>
</table>

References


