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Case Report

Flap cover in a patient with severe haemophilia type A

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ABSTRACT

Haemophilia A is a rare haematological disorder due to deficiency of Factor VIII, causing an abnormal coagulation response to injury. In severe haemophilia A, Factor VIII level is <1%, often manifesting with spontaneous bleeding into joints. Judicious use of recombinant Factor VIII therapy to maintain adequate levels in the intraoperative, immediate and late post-operative periods, together with adjuvant pro-coagulants, can ensure a safe outcome following surgery. We describe the successful management of one such patient suffering from Marjolin's ulcer of the right gluteal region, who needed wide local excision followed by flap cover. A protocol for management of such patients is also suggested. This is the first such case report from the Indian subcontinent, with only a few such published reports from the West.

KEY WORDS

Factor VIII; flap cover; haemophilia

INTRODUCTION

The incidence of haemophilia is estimated to be around 1 in 5000 newborn males, with over 400,000 people living with this disorder worldwide.[1] Further, an estimated 1300 children are born with haemophilia every year in India, now home to about 50,000 severe haemophiliacs.[1]

Severity of the bleeding diathesis directly correlates with the levels of Factor VIII[2] [Table 1]. This inherited severe bleeding tendency makes any surgical procedure risky and this risk is increased with flap surgery where adequate haemostasis is critical.

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CASE REPORT

The patient in this case is a 38-year-old gentleman, diagnosed with haemophilia type A soon after birth, and having been on follow-up at this institution since then. He also suffered from post-poliomyelitis residual paralysis from the hip downwards, together with hiatus hernia and a conservatively managed left neck of femur fracture. The scars of tuberculosis abscess drainage in the right gluteal region (operated in 2002) had now given rise to biopsy-proven Marjolin's ulcer, with surrounding induration.

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Table 1: Relationship of bleeding severity to clotting factor level]

Severity	*Clotting factor VIII level*	*Bleeding episodes*
Mild	5-40 IU/dL (0.05-0.40 IU/mL) or 5%-40% of normal	Severe bleeding with major trauma or surgery. Spontaneous bleeding is rare
Moderate	1-5 IU/dL (0.01-0.05 IU/mL) or 1%-5% of normal	Occasional spontaneous bleeding and prolonged bleeding with minor trauma or surgery
Severe	<1 IU/dL (<0.01 IU/mL) or <1% of normal	Spontaneous bleeding into joints or muscles

After wide local excision, the defect's dimensions would be 14 cm × 12 cm cranio-caudal in the right gluteal region, and bone deep, close to the anal verge. Our first plan for cover was free tissue transfer using a parascapular flap, with inferior gluteal artery thigh flap as our second option. Possible need for a diversion colostomy was also discussed [Figure 1].

Haematological investigations revealed Factor VIII assay level – 0.2% (severe type A) with no inhibitors, and rest of coagulation cascade being normal. The haematologist advised Factor VIII replacement therapy combined with tranexamic acid. Following a detailed literature search,[3-6] administration of Factor VIII to achieve a target of 100% Factor VIII levels on the day of surgery and the first post-operative day, followed by 50% levels for the next 2 weeks, was decided upon.

A test injection of 1000 IU of Factor VIII was found to provide a trough level of 25% at the end of 8 hours, in our patient weighing 58 kg.

Therefore, a loading dose of 4000 IU (1000 IU × 4 as 25% × 4 = 100%) was decided upon, with a plan for 1000 IU every 8 hours to maintain the same levels in the post-operative period.

Following day, he was given an induction dose of 4000 IU immediately before surgery. Following wide local excision of the tumour and 'frozen section' confirmation of negative margins, he underwent right gluteal inferiorly based rotation flap using the sliding rotation-transposition template method[7] to cover the resulting defect [Figure 2].

The maintenance dose of 1000 IU was repeated 3 hours after induction. Prior to closure, 250 IU of Factor VIII was sprinkled over the wound [Figure 3]. Intravenous (IV) tranexamic acid was given during the procedure as a 2 g infusion and repeated every 8th hourly subsequently. Factor VIII levels were assayed and found to be 75% on post-operative day 1. Factor VIII was continued at 1000 IU q8hourly until post-operative day 3 [Figure 4].

Figure 1: Pre-operative view of patient's right buttock showing Marjolin's ulcer with planned area of resection. Note that the patient has posteriorly subluxed hip joints

From post-operative day 3, Factor VIII administration was tapered to 750 IU/day for the 1st week, and then to 500 IU daily for the 2nd week, with 8th hourly infusion of tranexamic acid continued throughout the first 2 weeks. A repeat assay revealed Factor VIII level to be 25% during the 1st week.

On 15th post-operative day, a fresh bolus of 3000 IU was given and his sutures were removed. He had an uneventful post-operative period [Figure 5].

On long-term follow-up of over a year, his flap has remained healthy.

DISCUSSION

Recombinant Factor VIII requirements in haemophilia[5] can be estimated using the following formula:

Factor VIII (in IU) = Body weight in kg × % desired increase in Factor VIII level × 0.5

Their half-life is 8–12 hours. Their pharmacokinetics can be assessed with a single dose of 1000 IU, and checking Factor VIII assay at the end of 8 hours, to further help refine Factor VIII replacement therapy.

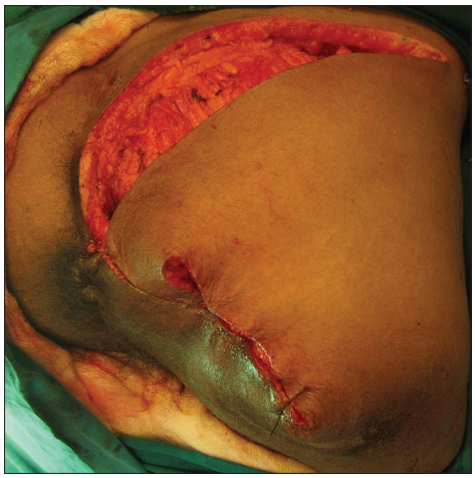

Figure 2: Intraoperative view: followingwide local resection of lesion with partial cover with gluteal rotation flap

Figure 3: Before completion, 250 IU of Factor VIII was sprayed over the wound edges and closed over a suction drain

Figure 4: Vials of recombinant Factor VIII used in operation theatre

Figure 5: One month after surgery

We calculated our required dosage by assessing the Factor VIII levels after a single test dose of 1000 IU, at 8 hours after injection. As Factor VIII level was 25%, we realised that 4 × 1000 IU, or 4000 IU, would be required to attain a level of 100% for the first 8 h. In consultation with our haematologist, we decided that a dose of 1000 IU should help maintain that level when given every 8 hours, for the first 2 days. IV tranexamic acid (2 g) was given every 8th hourly in addition. We were happy to see that, with this regimen, our flap surgery went ahead well with good haemostasis and minimal blood loss. The suction drain was removed on the 4th post-operative day.

From 3rd post-operative day, we found that the administration of 750 IU per day for the 1st week, and 500 IU per day during the 2nd week, was adequate to ensure no late post-operative bleeding complications occurred. The Factor VIII levels during this time were around 25%. This is in contrast to Western literature, which advices to maintain levels at 50% till completion of 2 weeks' post-procedure. The decision to try a lower maintenance schedule of Factor VIII was motivated, principally, by the high cost and limited availability of recombinant Factor VIII vials, with an estimated cost of around Rs. 11,000 per 500 IU vial (from BAXTER©).[8-10] Given that the surgical procedure and early post-operative period were uneventful, we were encouraged to try this lower dosage schedule and were glad that it proved adequate. The Factor VIII levels were assayed at periodic intervals to help guide this management.

Tranexamic acid works by inhibiting plasminogen activation, thus preventing degradation of fibrin cross-linkages. With a half-life of 2 hours, it is excreted by the kidneys, and its anti-fibrinolytic effects last up to 8 hours. Its uses are expanding; apart from patients with

bleeding disorders, it has shown promise in reducing mortality in bleeding trauma patients.[11]

Despite a number of previous administrations of Factor VIII, thankfully, our patient did not develop antibodies to it (Factor VIII antibody level = 0), else management would have been even more challenging.[12,13]

The protocol we wish to use in such patients hereafter is as follows:

a. Loading dose at induction calculated to keep Factor VIII levels at 100% on the day of surgery
b. Maintenance doses at periodic intervals to keep Factor VIII levels at 50% up to 3rd post-operative day, and thereafter at 25% up to suture removal
c. Adjuvant pro-coagulant: IV tranexamic acid (10 mg/kg body weight every 8th hourly) until suture removal.

CONCLUSION

Familiarity with, and judicious use of, Factor VIII therapy, together with adjuvant pro-coagulants, can make major surgical procedures in severe haemophiliacs safe and effective. Although such encounters are, fortunately, rare, knowledge of Factor VIII therapeutic potential, together with adjuvants, can help us save the day.

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Conflicts of interest

There are no conflicts of interest.

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