

# Cleft Lip and Palate Surgery in a Hemophilia A Patient

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## Abstract

Hemophilia A is the most common congenital bleeding disorder. It is a sex-linked disease caused by the deficiency of clotting factor VIII. Being an X-linked disorder, it occurs in males. Approximately, 250 cases of female hemophilia have been reported in the literature. The severity of hemorrhagic episodes correlates directly with the plasma FVIII concentration; mild being 5–40% of normal, moderate being 1–5% of normal, and <1% of normal is considered severe. Globally, the prevalence of cleft lip is 0.3/1000 live births. An unoperated cleft lip patient can have speech disorders, feeding difficulty, and can have psychosocial problems. The deficient coagulation factor needs to be administered perioperatively to ensure proper hemostasis and wound healing. Hemophilia is not an absolute contraindication for any reconstructive procedure.

**Key words:** Cleft lip, Haemophilia A, Factor VIII

Hemophilia A is the most common congenital bleeding disorder. It is a sex-linked disease caused by the deficiency of clotting factor VIII. It affects F8 and F9 genes located at the Xq28 and Xq27 loci of the X chromosome, which are responsible for the formation of blood coagulation factors VIII and IX. Any change leads to coagulation disorders such as Hemophilia A, Hemophilia B, and von Willebrand disease.<sup>[1]</sup> Being an X-linked disorder, it occurs in males. Approximately 250 cases of female hemophilia have been reported in the literature.<sup>[2]</sup> Females also require the same dose and frequency of factor transfusions for the treatment.<sup>[3]</sup> The severity of hemorrhagic episodes correlates directly with the plasma FVIII concentration; mild being 5–40% of normal, moderate being 1–5% of normal, and <1% of normal is considered severe.<sup>[4]</sup> In mild hemophilia, bleeding occurs following trauma or surgery, whereas spontaneous bleeding can occur in severe hemophilia.

Globally, the prevalence of cleft lip is 0.3/1000 live births.<sup>[5]</sup> An unoperated cleft lip patient can have speech

disorders, feeding difficulties, and psychosocial problems. The bleeding risk during the surgery of a hemophiliac and the unavailability of proper medical guidance in rural areas can affect timely surgical interventions.

Here is a case of a 4-year-old female patient with hemophilia A (Figure 1). The patient is born with an isolated left-sided incomplete cleft lip. The patient had a history of falls at 8 months, and uncontrolled bleeding from the cleft margin led to further investigation. The patient underwent a hemostatic profile workup.

Here, the parameters noted were hemoglobin level, platelet count, bleeding time, prothrombin time, thrombin time, activated partial thromboplastin time, factor level assay, inhibitors, mixing studies, von Willebrand factor (VWF) antigen level, clot retraction in 1<sup>st</sup> h, platelet function aggregation PF-3 release, and plasma fibrinogen level.

The patient was diagnosed to have Hemophilia A (2% factor level).

An elective cleft lip repair surgery was planned after obtaining anesthesia clearance and coordinating with the hematology department. A short-acting factor VIII (optivate) was transfused perioperatively. It contains human coagulation factor VIII and human VWF concentrate that is stored in 2–25°. It comes in powder form with sterile water to dissolve it forming 100 IU/mL of solution. The

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**Figure 1: (a) Pre-operative image of a Hemophilia A patient with isolated cleft lip. (b) Post-operative image**

amount of factors to be given is decided according to the body weight of the patient and the severity of the condition.

- 100% of factor VIII correction was done one before the surgery
- 100% of factor VIII was injected 12 hourly post-surgery for 3 consecutive days
- 60% of factor VIII was injected 12 hourly for the next 4 days
- 40% of factor VIII was injected 12 hourly for the next 7 days.

Factor recovery level is checked on the 2<sup>nd</sup> and the 7<sup>th</sup> day 1 h post-factor infusion.

Factor trough level is checked on the 2<sup>nd</sup> and the 7<sup>th</sup> day before factor infusion.

Inhibitor screening was done on day 5.

The patient underwent Randall–Tennison lip repair. The perioperative period was uneventful.

The mainstay of treatment in patients with Hemophilia A is FVIII replacement using purified factor concentrates. Hussein *et al.* suggested anti-hemophilia globulin treatment to be continued for 14 days till the mucoperiosteal wound healed in the cleft palate.<sup>[6]</sup> The emergence of alloantibodies (inhibitors) diminishes the efficacy of factor replacements. Hence, new therapies are being developed.

In recent studies, bi-specific monoclonal antibody emicizumab is used for long-term prophylaxis in patients with severe hemophilia A. Emicizumab is a humanized recombinant bispecific antibody with specificity for activated factor IX and factor X.<sup>[7]</sup> It mimics the activity of FVIII *in vivo* and thus enables the generation of activated FX (FXa), which is required for the conversion of prothrombin to thrombin. Emicizumab binding affinity for FIXa and FX is

11-fold lower than that of FVIIIa, thereby reducing the risk of non-localized coagulation, although it has thrombotic risk.<sup>[8]</sup> Emicizumab is administered subcutaneously and has a longer half-life of approximately 28 days; it can be used regardless of the presence of FVIII inhibitors.<sup>[9]</sup>

Hemophilia is a hereditary disorder, and hence, gene therapy strategies can be utilized. Gene therapy targeting hemophilia involves the intravenous administration of the F8 transgene within a viral capsid of adeno-associated viral (AAV) vectors.<sup>[10]</sup> Patients cannot be treated with multiple doses as AAV-neutralizing antibodies can develop following the administration of AAV-based gene therapy.<sup>[11]</sup>

The deficient coagulation factor needs to be administered preoperatively and postoperatively to ensure proper hemostasis and wound healing. Hemostasis must be achieved intraoperatively by proper usage of sutures and electrocautery. Hemophilia is not an absolute contraindication for any plastic and reconstructive procedure. With a multidisciplinary approach, no child needs to face the stigma of a facial cleft.

## REFERENCES

1. McVey JH, Rallapalli PM, Kembal-Cook G, Kembal-Cook G, Hampshire DJ, Giansily-Blaizot M, *et al.* The European Association for haemophilia and allied disorders (EAHAD) coagulation factor variant databases: Important resources for haemostasis clinicians and researchers. *Haemophilia* 2020;26:306-13.
2. Miller CH, Bean CJ. Genetic causes of haemophilia in women and girls. *Haemophilia* 2021;27:e164-79.
3. Miller CH, Soucie JM, Byams VR, Payne AB, Sidonio RF Jr., Buckner TW, Bean CJ. Women and girls with haemophilia receiving care at specialized haemophilia treatment centres in the United States. *Haemophilia* 2021;27:1037-44.
4. Peyvandi F, Garagiola I, Young G. The past and future of haemophilia: Diagnosis, treatments, and its complications. *Lancet* 2016;388:187-97.
5. Salari N, Darvishi N, Heydari M, Bokae S, Darvishi F, Mohammadi M. Global prevalence of cleft palate, cleft lip and cleft palate and lip: A comprehensive systematic review and meta-analysis. *J Stomatol Oral Maxillofac Surg* 2022;123:110-20.
6. Hussein MA, Matthews JM, Weber AB. The management of a complete cleft of the lip and palate in a baby with severe classical haemophilia. *Br J Plastic Surg* 1966;19:220-5.
7. Shima M, Hanabusa H, Taki M, Matsushita T, Sato T, Fukutake K, *et al.* Factor VIII-mimetic function of humanized bispecific antibody in hemophilia A. *N Engl J Med* 2016;374:2044-53.
8. Lenting PJ, Denis CV, Christophe OD. Emicizumab, a bispecific antibody recognizing coagulation factors IX and X: How does it actually compare to factor VIII? *Blood* 2017;130:2463-8.
9. Oldenburg J, Mahlangu JN, Kim B, Schmitt C, Callaghan MU, Young G, *et al.* Emicizumab prophylaxis in hemophilia A with inhibitors. *N Engl J Med* 2017;377:809-18.
10. Duan D. Systemic delivery of adeno-associated viral vectors. *Curr Opin Virol* 2016;21:16-25.
11. Ohmori T. Advances in gene therapy for hemophilia: Basis, current status, and future perspectives. *Int J Hematol* 2020;111:31-41.

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