Case Report

# Anaesthetic management of a child with congenital afibrinogenemia - A rare inherited coagulation disorder

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## ABSTRACT

Congenital afibrinogenemia is a very rare autosomal recessive disorder, results from mutation that affects plasma fibrinogen concentration. It is frequently associated with bleeding diathesis of varying severity. We describe the case of a 10-year-old child diagnosed of congenital afibrinogenemia who presented to hospital with subperiosteal haematoma and was posted for incision and drainage. Replacement therapy is the mainstay of treatment of bleeding episodes in this patient and plasma-derived fibrinogen concentrate is the agent of choice. Cryoprecipitate and fresh frozen plasma are alternative treatments. Appropriate amount of cryoprecipitate were transfused pre-operatively to the child. Individuals with congenital afibrinogenemia should be managed by a comprehensive bleeding disorder care team experienced in diagnosing and managing inherited bleeding disorders. Anaesthesiologist, surgeons and haematologist should work like a unit to manage the surgical emergencies.

**Key words:** Congenital afibrinogenemia, cryoprecipitate, fibrinogen

## INTRODUCTION

Congenital Afibrinogenemia or hypofibrinogenemia is an extremely rare autosomal recessive coagulation disorder with an estimated incidence of one to two cases per million births, mostly with consanguineous parents.[1,2] It leads to deficiency or lack of coagulation protein fibrinogen. These patients may be asymptomatic in their early infancy but some of them may present late with variable clinical events, ranging from moderate to minimal bleeding to cataclysmic haemorrhage.

## CASE REPORT

We report the case of a 10-year-old boy weighing 28 Kg, a diagnosed case of congenital afibrinogenemia who presented to hospital with swelling of mandible on right side. Congenital afibrinogenemia was diagnosed at the time of birth due to prolonged bleeding from the umbilical cord and was kept in neonatal intensive care unit (NICU). Laboratory examination revealed a plasma fibrinogen concentration of less than 50 mg/dl (normal range=150-450 mg/dl). The child gave history of easy bruisability, prolonged bleeding from pin prick sites that used to stop after applying sustained pressure for long time. The patient also sustained injury to left infraorbital and maxillary area two months back causing ecchymosis that needed hospitalisation and was treated with two units of fresh frozen plasma. The boy was born out of consanguineous marriage and elder sibling had similar bleeding problems with history of multiple blood transfusions several times.

At recent hospitalisation, the boy presented with throbbing pain and progressive swelling of right side of mandible for the past six days. No significant history of trauma or fever was noted. Boy was immunised with hepatitis A and hepatitis B vaccine. Laboratory examination revealed a plasma fibrinogen concentration of less than 50 mg/dl, haemoglobin (Hb)=13 mg/dl, platelet count=160000/cu.mm (clumps+), TLC (total leucocyte count)=14800/cu.mm, bleeding time=10 minutes 30 seconds, prothrombin time (PT) >120 seconds, activated partial thromboplastin time (aPTT) >120 seconds and thrombin time=22 seconds. The working diagnosis was subperiosteal haematoma. The boy was

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posted for incision and drainage of haematoma by oromaxillofacial surgeons.

In view of patient's deranged coagulation profile, it was planned to transfuse four units of cryoprecipitate overnight. A repeat coagulation profile done in the morning revealed bleeding time=3 minutes, clotting time=3 minutes, PT=22.2/14.8 seconds, international normalised ratio (INR)=1.68, aPTT=31.1/34.0 seconds, thrombin time=22 seconds and fibrinogen assay <50 mg/dl. Since the patient's fibrinogen assay was below than an acceptable level of 100 mg/dl, we decided to transfuse another two units of cryoprecipitate at 6 A.M. and the boy was taken up for surgery under general anaesthesia at 9:30 A.M. Parents were counselled about the involved risks in the surgery and its outcome. The boy was given a titrated dose of 1.5 mg intravenous midazolam through *in situ* intravenous (i.v) cannula in the preoperative room for anxiolysis. In the operating room, anaesthetic induction with increasing concentration of sevoflurane in oxygen was done. Neuromuscular blockade was achieved by i.v atracurium 15 mg. Trachea was intubated gently after confirming Train-of-Four (TOF) count of zero, oral cavity was inspected again for any evidence of bleeding. A pharyngeal pack was put around the laryngeal inlet to prevent aspiration. Needle aspiration of subperiosteal haematoma was done, collection up to 30 ml was drained and pressure dressing was done. At the end of the surgery, pharyngeal pack was removed and any bleeding points inside the oral cavity were inspected, residual neuromuscular blockade was reversed with 1.5 mg neostigmine and glycopyrrolate 0.3 mg and trachea was extubated after the boy was fully awake with functional gag and cough reflexes. Boy was shifted to postoperative ICU for further monitoring. The boy was closely followed-up for three days, postoperatively, in postoperative ICU and also in the ward. The repeat coagulation profile revealed PT=21.1/14.8 seconds, INR=1.50, aPTT=31.8/34.0 seconds, fibrinogen assay was still <50 mg/dl. Since there was no evidence of active bleed, no further cryoprecipitate was transfused.

## DISCUSSION

Congenital afibrinogenemia is a rare coagulopathy, exhibits autosomal recessive inheritance with a male to female ratio 1:1. Its estimated incidence is one to two cases per million births. A high rate of consanguinity has been reported.[1] The clinical severity of congenital afibrinogenemia varies considerably. The prolonged bleeding from umbilical cord is usually the first manifestation in 85% cases[1,2] but most are asymptomatic (60%).[1] Other symptoms include epistaxis, oral mucosal bleeding, gastrointestinal (GI) bleeding, menorrhagia and traumatic bleed. Afibrinogenemia has also been associated with poor wound healing, wound dehiscence, spontaneous abortion and rarely intracranial haemorrhage.[1-3] PT and aPTT are prolonged in afibrinogenemia and may be prolonged in hypofibrinogenemia and dysfibrinogenemia. The thrombin time is also prolonged but more sensitive than PT or aPTT for quantitative and qualitative defects in fibrinogen. In afibrinogenemia, fibrinogen concentrations are low usually less than 10 mg/dl and often undetectable in symptomatic individuals.[1] The fibrinogen levels are measured by modified clauss method in our hospital. By this method, minimum fibrinogen level measured is 80 mg/dl (AMAX Destiny plus™ machine). The boy is a member of haemophiliac society, but the genetic counselling was not done for him. Clinical bleeding due to afibrinogenemia is treated with fibrinogen to a level of more than 100 mg/dl to maintain haemostasis. Replacement therapy is the mainstay of treatment of bleeding episodes in these patients and plasma derived fibrinogen concentrate is the agent of choice. Human fibrinogen concentrate pasteurised (HFCP) is a sterile preservative free, lyophilised fibrinogen concentrate in a single use vial.[4] It is reconstituted in 50 ml sterile water. Each vial contains 900-1300 mg fibrinogen; 400-700 mg human albumin, 375-660 mg L-arginine, 200-350 mg of sodium chloride and 50-100 mg of sodium citrate.[4] Cryoprecipitate and fresh frozen plasma are alternative treatments that should be used only when fibrinogen concentrate is not available. Plasma-derived fibrinogen concentrates have the advantage of virus inactivation.[1,4] The usual starting dose for adults is one to two gram iv once daily (qd) and the paediatric dose is 30-100 mg/kg iv qd depending on the severity and site of bleeding.[1] The infusion rate should not exceed 5 ml/minute (100 mg/minute).[4]

Cryoprecipitate has been used as a source of fibrinogen due to the non availability of fibrinogen concentrate in our set up; each concentrate of cryoprecipitate contains 150-300 mg of fibrinogen.[5] One bag of cryoprecipitate is expected to raise the fibrinogen level by a minimum of 30 mg/dl with a half-life of three to six days.[5] To prevent excessive bleeding during surgical procedures, prophylactic treatment to raise fibrinogen levels to 100-150 mg/dl during the procedure is recommended.[5] Replacement should be continued

for 4-14 days following the surgery depending on the nature of the surgical procedure and time to complete healing. In our patient, after transfusion of four units of cryoprecipitate, the bleeding parameters improved except for fibrinogen assay and INR being 1.68; hence, two units of cryoprecipitate were transfused empirically on the morning before surgery. Post operatively, repeat coagulation revealed INR 1.5 but fibrinogen level was still less than 50 mg/dl. The reason being, fibrinogen concentrate in blood takes time of 18 to 36 hours to reach at its peak level after transfusion.

Genetic counselling and family studies should be part of a complete evaluation. Antifibrinolytics are useful along with fibrinogen replacement for mucosal bleeding, particularly oronasopharynx to decrease the frequency of rebleeding. Inhibition of local fibrinolysis allows maintenance of the clot and decreases the frequency of rebleeding. Aminocaproic acid inhibits fibrinolysis by blocking binding of plasmin to lysine residues on fibrin given in a dose of 30 g/day PO (per oral)/IV divided q3-6 hour, paediatric 50 mg/kg PO/IV three times a day (tid)/four times a day (qid), not to exceed 200 mg/kg/day. Tranexemic acid inhibits fibrinolysis by displacing plasminogen from fibrin administered in a dose of 25 mg/kg PO tid/qid or 10 mg/kg IV tid/qid in patients unable to take PO.[1] Individuals with afibrinogenemia should be followed up by a comprehensive bleeding disorder care team experienced in diagnosing and managing inherited bleeding disorders. Surgeons, haematologist and anaesthesiologist should work like a unit to manage these types of surgical emergencies. Individuals requiring plasma-derived coagulation factor concentrates should be immunised with the hepatitis A and hepatitis B vaccine. Patients should avoid aspirin and other drugs that affect platelet function.

## CONCLUSION

The patients with inherited disorder of coagulation like congenital afibrinogenemia should be followed up by a comprehensive bleeding disorder care team. Replacement therapy with plasma derived fibrinogen concentrate is the treatment of choice for symptomatic bleeding patients. Cryoprecipitate and fresh frozen plasma are alternative treatments that should be used only when fibrinogen concentrate is not available. The anaesthesiologist should work with surgeons and haematologists in unison to manage such patients who present for various surgical emergencies.

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