

## Pediatric cardiac surgery under cardiopulmonary bypass in factor VII deficiency

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We present a case of an atrial septal defect repair under cardiopulmonary bypass in a child with factor VII deficiency. A four-year-old girl, with the diagnosis of secundum atrial septal defect, was referred to surgery. Coagulation tests showed an international normalized ratio of 2.4. Further investigations revealed deficiency of factor VII with 42% activity. Fifteen minutes before the induction of anesthesia, 20 µg/kg dose of recombinant factor VIIa concentrate was administrated. The atrial septal defect repair was performed uneventfully. Factor VII activity markedly improved to 174%, and international normalized ratio declined to 1.1 within 1.5 hours after the substitution therapy. In our case, under a low-dose substitution therapy with recombinant factor VIIa concentrate, atrial septal defect repair under cardiopulmonary bypass was performed safely in a child with moderate congenital factor VII deficiency.

**Key words:** cardiac surgery, atrial septal defect, factor VII deficiency.

Congenital factor VII (FVII) deficiency is a rare hemorrhagic disorder with an incidence of approximately 1 in every 500,000 live births<sup>1</sup>. In pediatric cardiac surgery under cardiopulmonary bypass (CPB), the risk of preoperative and postoperative bleeding is increased whereas FVII deficiency might aggravate the drainage<sup>2</sup>. Pediatric cardiac surgery in the presence of FVII deficiency is extremely rare, with the literature showing only two reports to date<sup>3,4</sup>.

We describe here a successful atrial septal defect (ASD) repair under CPB in a child with FVII deficiency.

### Case Report

In a four-year-old girl, weighing 13 kg, echocardiography established the diagnosis of secundum ASD with diameter of 35 mm and  $Q_p/Q_s$  ratio of 1.8/1. When the diameter of the ASD was considered, surgical closure of the ASD was planned rather than transcatheter device closure. Preoperative routine coagulation tests showed that the prothrombin time (PT) was abnormally prolonged to 26.5 seconds (laboratory normal range: 11.0 to 13.5 seconds) and international normalized ratio (INR) was

2.4 (laboratory normal range: 1.0 to 1.3), whereas the activated partial thromboplastin time was normal. There was neither personal nor familial previous history of bleeding disorder. Further investigations revealed a mild but significant deficiency of FVII with 42% activity (laboratory normal range: 60% to 150%). Other factor levels, complete blood count, blood biochemistry parameters, and other laboratory tests were within the normal range. Informed consent was obtained from the parents of the child.

Fifteen minutes before the induction of anesthesia, 20 µg/kg dose of recombinant factor VIIa concentrate (rFVIIa) (NovoSeven, Novo Nordisk A/S, Bagsvaerd, Denmark) was administrated by intravenous bolus injection. The operation was performed through a median sternotomy on normothermic total CPB with standard heparin (3 mg/kg) dosage. The right atrium was entered and the secundum ASD was repaired with a Dacron patch. The patient was weaned from CPB and the activated clotting time was returned to 114 seconds after protamine. Hemorrhage was controlled uneventfully. X-clamp time was 27 minutes and

CPB time was 35 minutes. One mediastinal drain was inserted. The operation lasted 85 minutes in total. Postoperatively, 100 ml of whole packed blood was transfused in the intensive care unit.

Factor VII activity markedly improved to 174%, PT improved to 12 seconds and INR declined to 1.1 within 1.5 hours after the substitution therapy. Three hours later, FVII activity was 166%, PT was 15.5 seconds and INR rose to 1.3. Postoperative mediastinal drainage was 190 ml and 240 ml at 12 hours and 24

hours, respectively. The drain was removed at postoperative 46 hours with a total of 340 ml drainage. FVII levels decreased to 94% on the first postoperative day, 70% on the second day and 54% on the third day. PT levels were 17, 18.5 and 19 seconds, respectively, and INR levels were 1.3, 1.5 and 1.7, respectively, on the first, second and third postoperative days. FVII activity, PT, INR levels, and clinical status did not warrant further substitution therapy (Table I). On postoperative day 7, the child was discharged without any bleeding or thrombotic complications.

Table I. Coagulation Tests Before and After the Substitution Therapy

|  | Factor VII activity (%) | PT (seconds) | INR |
|--|-------------------------|--------------|-----|
| Preoperative levels                      | 42                      | 26.5         | 2.4 |
| 1.5 hours after the substitution therapy | 174                     | 12           | 1.1 |
| 3 hours after the substitution therapy   | 166                     | 15.5         | 1.3 |
| Postoperative day 1                      | 94                      | 17           | 1.3 |
| Postoperative day 2                      | 70                      | 18.5         | 1.5 |
| Postoperative day 3                      | 54                      | 19           | 1.7 |

PT: Prothrombin time. INR: International normalized ratio.

## Discussion

Among all the coagulation factors, FVII has the shortest half-life (3-4 hours)<sup>5</sup>. Therefore, in FVII deficiency, multiple doses of fresh frozen plasma, pooled factor and prothrombin complex concentrates or plasma-derived FVII concentrates may be needed for bleed management after surgery<sup>6,7</sup>. This may lead to an unwanted increase in levels of other factors, induce activation of blood coagulation, and increase risk of thrombotic complications, infection and volume overload<sup>8-10</sup>. To avoid thrombotic complications, viral transmission and volume overload, which are very important issues in a child undergoing cardiac surgery, rFVIIa is the preferred substitution therapy in FVII deficiency<sup>11</sup>. Although rFVIIa is a common treatment in hemorrhagic complications, there is only one case in which rFVIIa was used as

substitution therapy in pediatric cardiac surgery with FVII deficiency.

Ferster et al.<sup>3</sup> reported the first successful pediatric cardiac surgery with CPB in a two-year-old child with FVII deficiency. The child underwent surgical repair of ASD uneventfully with the use of FVII concentrate for substitution therapy. In the late 1980's, the recombinant form of activated FVII was developed that provided only the missing factor. It is a highly concentrated preparation and is devoid of other human proteins or viruses<sup>12</sup>. Tokunaga et al.<sup>4</sup> reported a successful pediatric cardiac surgery with CPB in an infant with FVII deficiency at the age of 60 days. This is the only infantile case reported. The repair of the right ventricular outflow tract and right modified Blalock-Taussig shunt were performed uneventfully with the use of rFVIIa.

We report a case of ASD repair in a patient with congenital FVII deficiency in whom rFVIIa was used successfully for substitution therapy. The patient had a FVII activity level of 42% and no history of bleeding disorders. Although it was not a severe FVII deficiency, the child had an INR level of 2.4 and she had to undergo ASD repair under CPB; therefore, we decided to use substitution therapy with low dose 20 U/kg rFVIIa concentrate. Preoperative one bolus dose was sufficient to achieve normal hemostasis in the per- and postoperative period.

In conclusion, in our case, under a low-dose substitution therapy with rFVIIa concentrate, ASD repair under CPB was performed safely in a child with moderate congenital FVII deficiency.

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