

# Factor V Leiden mutation: An added risk in single ventricle palliation

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## ABSTRACT

We present the case report of a child with Factor V Leiden mutation who underwent Fontan procedure. Thromboembolism is a widely recognized complication of the Fontan procedure and its modifications. Factor V Leiden mutation, being a hypercoagulable state, posed a higher risk for thromboembolism in this child. Appropriate measures taken before and after surgery prevented postoperative coagulopathy.

**Keywords:** Factor V Leiden mutation, Fontan, thromboembolism

## INTRODUCTION

Thromboembolism is a widely recognized complication of Fontan procedure and its modifications.<sup>[1-3]</sup> It is attributed to low flow state, stasis in the venous pathways, right-to-left shunts, blind cul-de-sacs, prosthetic material, atrial arrhythmias, and hypercoagulable state. We share our experience of dealing with factor V Leiden mutation (FVL), a prothrombotic state, in a patient undergoing Fontan surgery. Though coagulation abnormalities and thromboembolism in Fontan patients have been widely studied, Fontan procedure in a known case of FVL mutation has not been reported to our knowledge.

## CASE REPORT

A 12-year-old boy, born to nonconsanguineous parents, was diagnosed to have situs inversus, levocardia, and tricuspid valve atresia with severe pulmonary stenosis in his early infancy. He had undergone bidirectional Glenn procedure at 2 years of age. Later his father had recurrent superficial vein thrombosis and was diagnosed to have FVL mutation (by real-time polymerase chain reaction).

The child was subsequently screened and found to be heterozygous for FVL (by real-time polymerase chain reaction). But the boy did not have any history suggestive of thrombotic episodes. When a Fontan procedure was planned, haematologist opinion was obtained and he was screened for other prothrombotic conditions with protein C, protein S, prothrombin mutation, antithrombin III, anticardiolipin, and lupus anticoagulant studies. He was negative for all these tests. Diagnostic cardiac catheterization was done and the hemodynamics were found suitable for Fontan. The mean pulmonary artery pressure was 10 mm Hg. One collateral was embolized with a coil. Heparin was used in the routine dose (2500 units) during catheterization and there were no complications after the procedure. Subsequently he underwent extracardiac Fontan surgery using 18 mm PTFE graft without fenestration. The following strategies were followed to prevent thrombosis during the Fontan procedure. (1) Heparin infusion was started preoperatively and continued postoperatively for 2 days so as to maintain an APTT of 1.5–2 times the control. (2) Central venous catheter was removed early. (3) Warfarin was added on the first postoperative day. (4) He was ambulated early to prevent venous thrombosis. (5) Heparin infusion was changed to subcutaneous low molecular weight heparin at a dose of 0.1 mg/kg q12h and continued for 7 days postoperatively till his INR was consistently above 2.0. His postoperative recovery was uneventful with only two days of right pleural drainage. There were no thromboembolic events and the Fontan circuit was functioning well at the time of discharge. He was discharged on oral anticoagulants and was advised to maintain a higher INR of 2.0–2.5.

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## DISCUSSION

Factor V Leiden mutation is a point mutation in the factor V gene (chromosome 1 q23) at the nucleotide position 1691 with guanine substituting for adenine. FVL mutation causes activated protein C resistance, hence, leading to the hypercoagulable state. Heterozygous carriers have a five to seven fold increased risk of venous thromboembolism and homozygotes have a 25 to 50 fold increased risk.<sup>[4]</sup> Though the risk is considered to increase with age, there are several case reports of thrombosis in children and neonates heterozygous for FVL. Hagstrom and associates reviewed 85 children with documented thrombotic events and found that 14% were heterozygous for FVL mutation.<sup>[5]</sup> Simsic *et al.* reported a case of recurrent thrombosis of systemic to pulmonary artery shunt in a neonate heterozygous for FVL.<sup>[6]</sup>

Thromboembolic events in patients who have undergone Fontan operation have been reported to be as high as 20% to 33%.<sup>[1-3]</sup> Jahangiri *et al.* have studied the coagulation profile abnormalities in 20 children before and after Fontan. A significant increase was noted postoperatively in the concentration of factor VIII, factor X, and prothrombin fraction F1+2. A significant decrease in the levels of antithrombin III, protein C, and protein S was also found. They concluded that there is an increased tendency toward coagulation after Fontan procedure.<sup>[7,8]</sup> In the study done by Odegard *et al.*, coagulation factors were assayed in 36 infants with single-ventricle cardiac defects immediately before undergoing the bidirectional Glenn procedure. Concentrations of protein C, factors II, V, VII, IX, and X; plasminogen, fibrinogen, and antithrombin III were significantly lower in the pre-Glenn infants compared with the age-matched control subjects. They suggested that procoagulant and anticoagulant factor abnormalities occur early in the course of single-ventricle repair and precede the cavopulmonary connection.<sup>[9]</sup>

Ong and his colleagues studied the prevalence of FVL mutation in 200 patients with congenital heart disease. The prevalence of FVL was determined to be 4.5% in patients with CHD, which was not different from the population at large.<sup>[10]</sup> But there are no studies to define the prevalence of FVL mutation in patients with single ventricle physiology. Fontan procedure in a known case of FVL mutation has not yet been reported. There are no published data on the guidelines to be followed during a Fontan procedure in a hypercoagulable condition. In our case, we took all necessary precautions to prevent thrombosis in the perioperative and postoperative periods.

We would recommend to include FVL mutation assay in any patient awaiting Fontan surgery with the history of thrombotic tendency in the family. Appropriate measures as mentioned above during the perioperative period would prevent coagulopathy in such patients. Further studies on the prevalence of FVL in pre-Fontan patients would help to set guidelines on the management of such patients during Fontan surgery.

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