

## Congenital Afibrinogenemia; a Rare Disorder with Unusual Clinical Manifestations

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**Afibrinogenemia**, sometimes called congenital afibrinogenemia, is a rare, genetically inherited blood disorder in which the blood does not clot normally, due to the lack of fibrinogen (plasma levels <10 mg/dL), a blood protein necessary for coagulation (or coagulation factor I), which is needed for the blood to clot [1,2]. Afibrinogenemia is thought to be transmitted as an autosomal recessive gene located on chromosome 4 (q26-q28) [3], meaning that two unaffected parents can have a child with the disorder.

Clinical manifestations range from minimal bleeding to serious hemorrhage. Affected individuals may have severe and uncontrollable bleeding episodes, particularly during infancy and childhood and is presented in the form of bleeding from different parts of the body [4]. The first symptom usually seen is hemorrhage from the umbilical cord that is hard to stop [1]. Other symptoms include the following: nasal bleeding that is difficult to stop, bleeding in the mucus membranes, bleeding in the joints, bruising easily, gastrointestinal bleeding, prolonged menstruation in women, CNS hemorrhaging and abortion.

A missense or nonsense mutation in the genes that code for the fibrinogen protein are affected. So that this disease is characterized by the complete absence or extremely reduced levels of fibrinogen. Hypofibrinogenemia (partial deficiency of fibrinogen) is a milder disorder. This defect in fibrinogen synthesis can result from mutations in one or another of the fibrinogen genes, which provides instructions for making one part (subunit) of the fibrinogen protein, including alpha (*FGA*), beta (*FGB*) or gamma (*FGG*). Afibrinogenemia happens in the homozygous state while hypofibrinogenemia in heterozygotes [3]. This results in the absence of fibrin, so blood clots cannot form, leading to the excessive bleeding seen in people with afibrinogenemia and because the genetically based, there is no way to prevent the disease. And so, persons can get genetic testing done to see if they are a carrier of the trait, and if so, may choose to complete genetic counseling to better understand the disorder.

When a problem of fibrinogen is suspected, the following tests can be ordered, in which coagulation tests which depend on clot formation, such as clotting time, prothrombin time (PT), partial thromboplastin time (PTT), and thrombin time, may be prolonged and abnormalities of platelet function such as bleeding time, adhesion and aggregation usually exist. Blood fibrinogen levels of less than 0.1 g/L and prolonged bleeding test times are indicators of an individual having afibrinogenemia [1] and in the absence of consumptive coagulopathy, an unmeasurable fibrinogen level is diagnostic of the condition.

Cryoprecipitate or FFP is used as the most common treatments to help with bleeding episodes.

Based on theories, the aim levels for the treatment of bleeding, range from 30-50 mg/dL [5] to 100 mg/dL [6] and a hemostatic level can be prepared via therapy with 100 mg/ kg of fibrinogen.

Although some studies do not recommend prophylactic treatment with regular infusions of cryoprecipitate, but because of lethal bleeding due to lack of *fibrinogen* prophylaxis is recommended.

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