AFIBRINOGENEMIA AND GANGRENE
A case report

E. GOUIDER 1, N. BEN SALAH 1, L. AISSAOUI 2, R. JEDDI 2, M. ZORGATI 3, W. EL BORG 1, R. HAFSIA 1

1- Biological Hematology department - Aziza Othmana Hospital - Tunis
2- Clinical Hematology department - Aziza Othmana Hospital – Tunis
3- Biochemistry department - Institut Pasteur de Tunis

INTRODUCTION
Congenital deficiency of fibrinogen was first described by Rabe and Salomon in 1920 (1). It is a rare bleeding disorder inherited as autosomal recessive traits. Its prevalence is about 1 in 1000,000 for the homozygous forms (2). Afibrinogenemia is usually responsible for hemorrhagic diathesis. We report a case of a woman with congenital afibrinogenemia who develop a gangrene of the 5th toe.

CASE HISTORY
Mrs HB, a 21-years old woman had suffered from recurring haemorrhages since early life. Her bleeding tendency manifested itself at birth, when she had umbilical cord bleed. Laboratory studies showed complete absence of fibrinogen by clotting test and pondered dosage. Her brother and sister have also afibrinogenemia. Her parents are cousin and have normal blood coagulation test. No molecular studies are available. Bleeding manifestations were dental bleed, nose bruise, ecchymosed, and menorrhagia. She required frequent transfusions, initially of cryoprecipitate but since 1999 of fibrinogen concentrates that became available in our country. In order to control her menorrhagia she was initially treated with combined oral contraceptives pills (microgynon®), but quickly stopped because of hypertension. She was explored in internal medicine department and no secondary cause was found to explain hypertension. She was treated with LOPRIL®.

In recent years, 3 g of fibrinogen was given every month in the beginning of menstrual bleeding. After one year, she felt pain in the 5th right toe. Exam showed blue colour of the toe that was cold. Glycaemia was normal and blood pressure correct. Capillaroscopy exam showed Raynaud's phenomenon. Inherited markers of thrombophilia were excluded. Surgical amputation of the toe was done because of necrosis.

One month later she showed the same symptom appeared in the 4th right toe. Anti aggregate treatment with low doses of aspirin combined to less 1g of fibrinogen (instead of 3g) was successful to stop pain finger and control menorrhagia.

DISCUSSION
Thrombotic event are uncommon in afibrinogenemia, whereas it is in dysfibrinogenemia. Some cases of thrombotic event are reported in the literature (3,4,5,6,7,8,9). The disorder itself was described in 1920, but its genetic molecular basis has only been characterized. Distinct from the inherited dysfibrinogenemias, in which biosynthesis of a structural abnormal fibrinogen molecule that exhibits altered functional properties is produced, congenital afibrinogenemia is a disease that results in the inability to synthesize any fibrinogen at all, where bleeding is the major clinical problem (10). Despite absence of plasma fibrinogen, thromboembolism may occur. The mechanisms are not well known. Prothrombotic conditions don’t seem to be the principle mechanism (2). Thrombogenicity of oral contraceptives, venous stasis were thought to be responsible of thrombosis (11). Platelets’ hyper aggregation may be one of the mechanisms of thrombosis: High amount of thrombin generation and lack of fibrin in afibrinogenemia induces raised thrombin levels in the circulation that stimulate platelets aggregation (12, 13, 14, 15). High level of circulating thrombin may be also responsible of vascular lesions by cytokine release, inducing myointimal proliferation (16, 17).
Occasional thrombosis events are rare event in afibrinogenemia, that almost occur after...
substitution (2). It has been shown that intravenous fibrin suspensions can cause vascular changes and thrombosis in the pulmonary and systemic circulation either as a result of the altered physical or chemical properties of fibrin-dried fibrinogen, or by the action of antifibrinogen antibodies on fibrinogen molecule (18). Thrombosis in afibrinogenemia seems to be paradox, since bleeding manifestations are the usual symptoms because of absence of a clotting factor. Mechanisms are not very clear. Because of it is seldom, international studies must be done to elucidate this phenomena.

REFERENCES