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CASE REPORT

Acquired and Isolated Deficiencies in Factor VII

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SUMMARY

Background: **Acquired and isolated deficiencies in FVII are exceptional. They have mainly been reported during states of severe sepsis by the presence of proteases destroying the factor or neoplastic pathologies by the presence of an inhibitor. Consequently, very few cases have been published.**
Methods and Results: **We report two cases of isolated and acquired deficiency of factor VII due to the presence of inhibitors which were related to bacterial sepsis in the first patient and to squamous cell carcinoma in the second patient, diagnosed in the Hematology Laboratory of the CHU Ibn Rochd.**
Conclusions: **Factor VII deficiency is a rare and poorly described deficiency that can be acquired or constitutional. The search for anti-factor VII antibodies by diluted thromboplastin time should be requested depending on the clinical context.**
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KEYWORDS

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INTRODUCTION

Acquired deficiencies in factor VII are exceptional; they are most often secondary to neoplasia or severe sepsis and are then linked to the presence of an inhibitor [1]. Factor VII deficiency can be acquired or constitutional. The constitutional deficiency in FVII is a rare deficiency, it affects 1/500,000 and is transmitted according to an autosomal recessive mode [2,3]. However, very few cases of acquired deficit have been published.
We report two cases of isolated and acquired factor VII deficiency diagnosed in the hematology laboratory of the CHU Ibn Rochd.

CASE PRESENTATION

Case 1: This is a 39-year-old patient with a history of chronic asthma admitted for tumor of the maxillary sinus with extension to the orbital area and to the base of the skull. As part of the preoperative assessment, a he-

mostasis assessment was performed showing an isolated decrease in prothrombin time (PT) to 62% (normal value: 70% to 140%) and a normal activated partial thromboplastin time (APTT). The dosage of factor VII activity objectified a rate which is low at 33% (normal value 70% to 140%). Due to the clinical context, the diagnosis of acquired factor VII deficiency was made. A search for inhibitors by the diluted thromboplastin time was carried out and came back positive; however, the titration was not carried out. The patient was put on corticosteroid therapy by his attending physician at a dose of 2 mg/kg/day for 10 days. A control hemostasis assessment was redone showing a correction of his prothrombin time, then a biopsy of the tumor was performed. The anatomopathological study of the tumor mass was in favor of a verrucous squamous cell carcinoma.

Case 2: This is a 50-year-old patient hospitalized in the hematology department for acute myeloblastic leukemia with non-hyperleukocytic granular maturation, initially with an intermediate prognosis (karyotype: 48,XY +8, +11). The initial hemostasis assessment was normal. The patient is treated with the national AML protocol (cytarabine 100 mg*2/day for 10 days, daunorubicin 50 mg/m² on D2, D4, D6). On D8 of induction, the patient presented a fever with a blood culture objectifying a pseudomonas aeruginosa sensitive to B-lactams. Despite appropriate antibiotic therapy, the patient remained febrile. Aspergillus antigenemia came back positive and the patient was put on Voriconazole (200 mg x 2/d). The hemostasis assessments carried out during this phase showed an aggravation of the decrease in PT, which went from a normal rate to a rate of 34% (normal value 70% to 140%) with a TCA still normal.
The dosage of factor activities was normal except for factor VII which was at 35.7% (normal value 70% to 140%). The PT did not correct after adding control plasma, the diagnosis of factor VII deficiency secondary to the presence of inhibitor was made. Diluted thromboplastin time was positive at 2.5 (negative < 1.2), and inhibitor titer was positive at 3 Bethesda units.

DISCUSSION

Acquired factor VII deficiency is a rare condition. There are very few published cases of acquired and isolated FVII deficiencies, although several authors suggest that this is an underestimated deficiency [4,5].
We distinguish two types of discovery circumstances; in the context of a pre-anesthetic assessment or medical pathologies, the FVII assay is carried out in front of a low PT associated with a normal APTT; the most reported pathologies are neoplastic and infectious diseases [5-8]. During trauma, it is the absence of correction of PT by fresh frozen plasma (FFP) that is suggestive [9]. In our two patients, the FVII deficiency was acquired secondary to neoplasia in the first patient and severe sepsis in the second.
Several explanations have been put forward on the pathophysiology of this acquired deficit, it is most often linked to the presence of a FVII inhibitor with a normal TCA on the hemostasis assessment and a low TP not corrected by the addition of witness plasma [1]. Other physiopathological hypotheses have been suggested during sepsis. The decrease in FVII could be due to enzymatic degradation by proteases released by neutrophils or due to isolated consumption of FVII by excessive exposure to tissue factor released by endothelial cells [5].
The evolution of the FVII inhibitor most often follows the underlying pathology, it can regress after treatment and reappear in the event of a relapse [1].
We used the dilute thromboplastin test (DTT) in our two patients to highlight the presence of an inhibitor, the DTT explores active circulating anticoagulants on the extrinsic pathway of coagulation. It makes it possible to sensitize the prothrombin time with a very dilute thromboplastin (usually to 1/500) in order to increase its sensitivity and to simulate physiological conditions. The sensitivity of the test depends on the thromboplastin and the dilutions used; the test is very sensitive to the presence of circulating anticoagulants.
The technique is based on the dilution of the thromboplastin by calcium to 1/500 and, subsequently, the measurement of the patient's quick time (QT) and the control QT. We determine the patient/control ratio with an alarm threshold of 1.2. Thus, if > 1.2 he testifies on the presence of ACC on the other hand if < 1.2 he testifies on the absence of ACC.
However, for some authors, the absence of a global (circulating anticoagulant) or specific (autoantibodies) inhibitor during the study of *in vitro* plasmas would not exclude the presence of a small quantity of inhibitor that is rapidly fixed to FVII and, therefore, not detectable [9].
The therapeutic management of acquired or constitutional factor deficiency is based on the administration of specific replacement therapy using coagulation factor concentrates. But in the presence of an inhibitor, the treatment is mainly etiological and/or by immunosuppressant [1,6]. Recombinant FVIIa has been used in patients with isolated and acquired FVII deficiency, particularly in the presence of autoantibodies [10].

CONCLUSION

Factor VII deficiency is a rare and poorly described deficiency that can be acquired or constitutional. The search for anti-factor VII antibodies by diluted thromboplastin time should be requested depending on the clinical context.

Declaration of Interest:
The authors declare that they have no conflicts of interest.

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