

## Successful laparoscopic radical prostatectomy in a patient with factor XI deficiency

Mihály Murányi, Mátyás Benyó, Zoltán Kiss, Tibor Flaskó

### ABSTRACT

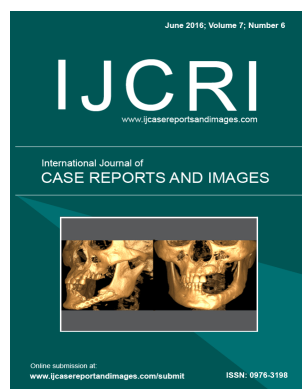
**Introduction:** Factor XI deficiency is a rare type of hemophilia. It is associated with profuse bleeding after traumas and surgical procedures. In a patient with factor XI deficiency, the serum coagulation factor level does not predict bleeding tendency appropriately. Operations in sites without fibrinolytic activity are less likely to be complicated by bleeding, while surgery in areas with fibrinolytic activity, like prostatectomy, increases the risk of bleeding. The optimal treatment should be determined by individual circumstances. Radical prostatectomy is a procedure when severe bleeding requiring transfusion can occur even without any bleeding disorder. At the same time radical prostatectomy carries a significant risk of potentially fatal thromboembolism. Thus keeping the balance between procoagulant and anticoagulant activity is the challenging part in cases of radical prostatectomy of factor XI deficiency.

**Case Report:** A 67-year-old patient is presented with organ confined intermediate-risk prostate cancer. Prolonged bleeding after tooth extraction and prostate biopsy indicated assessment of hemostatic system. Laboratory tests revealed factor XI deficiency. Successful laparoscopic extraperitoneal radical prostatectomy and bilateral pelvic lymphadenectomy was performed with low amount of blood loss. Recombinant activated coagulation factor VII was administered to prevent perioperative bleeding. The postoperative period was uneventful, no complications were observed.

**Conclusion:** Despite the high risk of hemorrhage, laparoscopic radical prostatectomy is a feasible procedure even in a patient with factor XI deficiency, providing that the patient receive adequate preparation and a meticulously performed operation carried out by an experienced surgeon.



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CASE REPORT

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**Introduction:** Factor XI deficiency is a rare type of hemophilia. It is associated with profuse bleeding after traumas and surgical procedures. In a patient with factor XI deficiency, the serum coagulation factor level does not predict bleeding tendency appropriately. Operations in sites without fibrinolytic activity are less likely to be complicated by bleeding, while surgery in areas with fibrinolytic activity, like prostatectomy, increases the risk of bleeding. The optimal treatment should be determined by individual circumstances. Radical prostatectomy is a procedure when severe bleeding requiring transfusion can occur even without any bleeding disorder. At the same time radical prostatectomy carries a significant risk of potentially fatal thromboembolism. Thus keeping the balance between procoagulant and anticoagulant activity is the challenging part in cases of radical prostatectomy of factor XI deficiency. **Case Report:** A 67-year-old patient is presented with organ confined intermediate-risk prostate cancer. Prolonged bleeding after tooth extraction

and prostate biopsy indicated assessment of hemostatic system. Laboratory tests revealed factor XI deficiency. Successful laparoscopic extraperitoneal radical prostatectomy and bilateral pelvic lymphadenectomy was performed with low amount of blood loss. Recombinant activated coagulation factor VII was administered to prevent perioperative bleeding. The postoperative period was uneventful, no complications were observed. **Conclusion:** Despite the high risk of hemorrhage, laparoscopic radical prostatectomy is a feasible procedure even in a patient with factor XI deficiency, providing that the patient receive adequate preparation and a meticulously performed operation carried out by an experienced surgeon.

**Keywords:** Factor XI deficiency, Hemophilia, Laparoscopy, Radical prostatectomy

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## INTRODUCTION

Factor XI deficiency is a rare type of hemophilia, which can associated with profuse bleeding after surgery.

It is also called hemophilia C, plasma thromboplastin antecedent (PTA) deficiency and Rosenthal syndrome. Rosenthal described first these autosomal hereditary blood coagulation disorder in 1953 [1]. Due to its autosomal inheritance it affects both men and women, unlike hemophilia A and B. It is rare worldwide, but considerably common in Ashkenazi Jews. Factor XI deficiency is less severe hemophilia than hemophilia A and B. Spontaneous bleeding is rare, but severe bleeding can occur after traumas and surgical procedures. In contrast to hemophilia A and B, the serum coagulation factor level does not predict bleeding tendency appropriately. Assessment of bleeding risk during upcoming surgical procedures is difficult in patients with no prior surgeries. Furthermore replacement therapy may be associated with risk of thrombosis [2, 3].

A 67-year-old patient is presented with factor XI deficiency and prostate cancer. Successful laparoscopic radical prostatectomy with lymphadenectomy was performed.

## CASE REPORT

The 67-year-old patient had a history of hypertension, diabetes mellitus and profuse bleeding after extraction of a tooth. Elevated (16 ng/ml) prostate specific antigen (PSA) level indicated transrectal ultrasound-guided prostate biopsy, which revealed Gleason score 4+3=7 prostate adenocarcinoma. Hematuria occurred and lasted for 10 days after the procedure. Hemostasis laboratory test revealed factor XI deficiency. The activity of factor XI was 15%. Activity of factor VII and VIII were in normal range, 123% and 157%, respectively. Thrombin time, prothrombin time, international normalized ratio, activated partial thromboplastin time, fibrinogen, platelet count and platelet function assay test were 15.4 sec, 8.0 sec, 0.98, 41.0 sec, 3.65 g/L, 187 Giga/L and 91 sec, respectively. Staging diagnostical tests suggested organ confined prostate cancer. Alternative therapeutical options (external beam radiation therapy, brachytherapy) were offered, but the patient insisted on radical prostatectomy applying laparoscopic approach. After hematological consultation laparoscopic extraperitoneal radical prostatectomy and bilateral pelvic lymphadenectomy was performed. The following attempts were done during the procedure to minimize bleeding: early ligation of Santorini's plexus; application of a multifunctional ultrasonic and bipolar instrument (Thunderbeat - Olympus, Japan) and polymer clips (Hem-o-lok - Teleflex, United States) for maximal vascular control (Figure 1). Furthermore recombinant activated coagulation factor VII (NovoSeven - Novo Nordisk, Bagsvaerd, Denmark) was administered during the procedure and the postoperative period in order to prevent excessive bleeding. First 3 mg dose of factor VII was given right before the operation, then 2 mg every two hours until 24 hours. On the next day the patient

received 2 mg factor VII every three hours, thereafter on the strength of clinical course. Altogether 63 mg coagulation factor VII was dosed. Full blood count, thrombin time, prothrombin time, activated partial thromboplastin time, fibrinogen and activity of factor VII were investigated for monitoring hematological status during the postoperative period. First tests were done on the morning of the first postoperative day before the administration of NovoSeven and thirty minutes after the injection, then every morning. Treatment with non-steroidal anti-inflammatory drugs was avoided during the perioperative period. Low molecular weight heparin administration (40 mg enoxaparin sodium [clexane]/day) was started one day prior to the surgical intervention and was continued for five weeks to prevent thromboembolism. Intraoperative and postoperative period was uneventful due to our efforts. Operation time was 140 minutes, estimated blood loss was 200 mL, thus transfusion was not indicated. The histology revealed pT3a, No Gleason score 4+3=7 prostate adenocarcinoma with negative surgical margins. Postoperative PSA level was under 0.2 ng/ml, eighteen months after the operation the patient had no biochemical or clinical relapse.

## DISCUSSION

The hemostatic system secures the constant blood flow and prevents bleeding from the vascular system. The imbalance between procoagulant and anticoagulant activity – caused by diseases, or medical interventions – will lead to thromboembolism or hemorrhage. The severity of the disease will determine the severity of the changes in the hemostatic system.

Factor XI deficiency is an autosomal hereditary blood coagulation disorder, which affects both men and women.

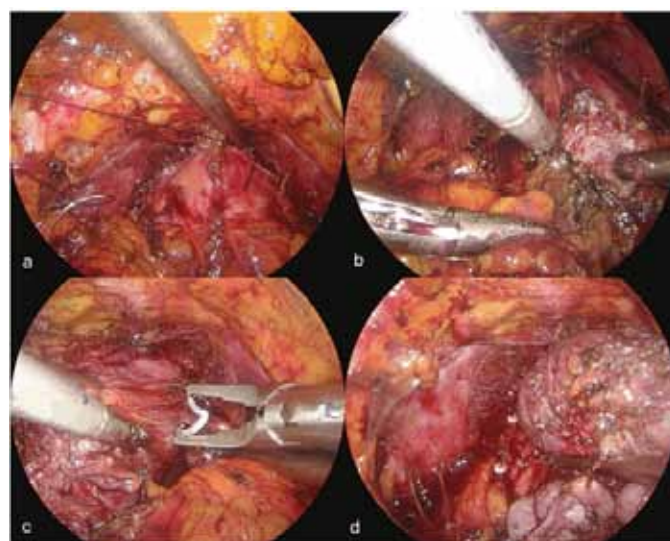


Figure 1: Essential steps to prevent bleeding: (a) Early ligation of Santorini's plexus, (b) Usage of an ultrasonic and bipolar instrument during dissection of the bladder neck, (c-d) Usage of polymer clips during the dissection of prostate pedicle.

Unlike hemophilia A and B, spontaneous bleeding is rare, but severe bleeding can occur after traumas and surgical procedures [2–3]. Bleeding tendency in factor XI deficiency do not correlate with the factor XI level, therefore the optimal treatment should be determined by the clinical course and individual circumstances [4–5]. A retrospective analysis of bleeding complications in patients with factor XI deficiency revealed that extent and severity of the surgery influences the risk of bleeding. Operations in sites without fibrinolytic activity, like orthopedic procedures and appendectomy, are less likely to be complicated by bleeding. While surgery in areas with fibrinolytic activity increases the risk of bleeding, like tonsillectomy, dental extraction and prostatectomy [6]. Potential treatment options are the fibrinolytic inhibitor tranexamic acid, the synthetic vasopressin analogue desmopressin, fresh frozen plasma, recombinant coagulation factor VII and coagulation factor XI concentrates. In certain cases with partial deficiency, only observation can be sufficient [7].

Radical prostatectomy is a procedure when severe bleeding requiring transfusion can occur even without any bleeding disorder. Prostate is well supplied with vessels and it locates close to the Santorini's venous plexus, which can result in significant blood loss during the procedure. In contrast with open procedure magnification and increased intra-abdominal pressure during laparoscopy can reduce blood loss performed by experienced laparoscopic surgeon. So experience in the field of laparoscopy has a key role to prevent any major complications as proven by a comparative study [8].

Venous thromboembolism is the most common cause of death after pelvic cancer surgery. Radical prostatectomy carries a significant risk (ranging 0.8–6.2%) of potentially fatal thromboembolism event as proven by a recent study [9]. Thus keeping the balance between procoagulant and anticoagulant activity is the challenging part in cases of radical prostatectomy of factor XI deficiency, hence thrombosis prophylaxis should be considered as well.

## CONCLUSION

In conclusion, despite the high risk of hemorrhage, laparoscopic radical prostatectomy is a feasible procedure even in a patient with factor XI deficiency, providing that the patient receive adequate preparation and a meticulously performed operation carried out by an experienced surgeon.

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## Author Contributions

Mihály Murányi – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Mátyás Benyó – Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Zoltán Kiss – Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Tibor Flaskó – Substantial contributions to conception and design, Revising it critically for important intellectual content, Final approval of the version to be published

## Guarantor

The corresponding author is the guarantor of submission.

## Conflict of Interest

Authors declare no conflict of interest.

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