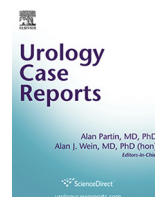




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## Inflammation and Infection

## Complete Penile Necrosis in a Patient With Heparin-induced Thrombocytopenia: A Case Report

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## ABSTRACT

Penile necrosis is a rare condition that has been mostly described in association with diabetes mellitus and end-stage renal disease. We report an unusual case of acute penile necrosis because of heparin-induced thrombocytopenia. A 75-year-old man presented with acute renal failure and experienced cardiac complications during the hospitalization. The patient was treated twice with intravenous heparin. He developed symptoms of penile necrosis 4 days after the reintroduction of heparin. At that moment, the platelet count dropped by 61%, and the analysis of heparin-pf4 antibodies was positive for heparin-induced thrombocytopenia. The patient underwent a total penectomy and a perineal urethrostomy.

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## Introduction

Penile necrosis is a rare but devastating condition. Its rarity is because of the excellent collateral circulation of the perineum and the lower abdomen. However, a number of penile necrosis cases have been described in association with diabetes, chronic renal failure, and warfarin use.<sup>1,2</sup> In this report, we describe an unusual case of penile necrosis presenting in a patient with a hypercoagulable state because of heparin-induced thrombocytopenia (HIT).

## Case presentation

A 75-year-old Caucasian man presented with asymptomatic acute renal failure on May 14, 2012. The patient reported a history of factor V Leiden, severe coronary atherosclerotic disease, and chronic renal failure because of a diabetic nephropathy. He had no history of thrombosis. At admission, his blood analysis showed elevated creatine kinase and a normal platelet count of  $225 \times 10^9/L$ . A computed tomographic scan revealed dilated ureters with hydronephrosis, so a Foley catheter was inserted to relieve the

obstruction. During the hospitalization, the patient developed cardiac issues. In this context, he was stented and treated with therapeutic intravenous heparin from May 17th to 22nd. Subsequently, the heparin was changed for prophylactic subcutaneous low molecular weight heparin (Fragmin). Owing to new cardiac deterioration while on Fragmin, the treatment was then reverted to therapeutic intravenous heparin on July 10th. Three to 4 days after the reintroduction of heparin, the patient complained of burning sensation to his urinary meatus, scrotal pain, and erythema of the glans. Physical examination revealed a purple, indurated, and necrotic penis painful on palpation (Fig. 1). The pain lasted only a few hours. The external genitals were swollen, but the penis was not engorged. New blood analyses were made, and the patient underwent penile aspiration. The platelet count reached a nadir of  $88 \times 10^9/L$  on July 15th. This represents a drop in platelet count of 61%. Heparin-pf4 antibodies were measured and showed a result of 107%. The penile blood gas analysis revealed a pH of 6.88, a pCO<sub>2</sub> of 149 mm Hg, and a HCO<sub>3</sub> of 33 mm Hg, which is compatible with severe acidosis of the penis. Doppler sonography of the penis showed absence of blood circulation in both the cavernous bodies and the spongiosus body. The heparin was then stopped and replaced by a direct thrombin inhibitor (Argatroban). The disease progressed over the next days. After discussion at that moment, the patient refused only palliative care. The patient underwent a total penectomy and a perineal urethrostomy. Unfortunately, the patient died 6 days after surgery secondary to cardiac and renal failure and possibly surgical complications. Pathology demonstrated extensive hemorrhagic necrosis of the penis (Fig. 2).

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**Figure 1.** Indurated and necrotic penis before surgery.



**Figure 2.** Penile specimen sent to pathology showing the necrotic glans.

## Discussion

In this case, HIT is the most likely cause of the acute penile necrosis. HIT is a common complication of pharmacologic heparin administration. The pathogenesis of HIT involves the formation of complexes between heparin and platelet factor.<sup>3,4</sup> Antibodies are generated against these complexes and cause a hypercoagulable state. HIT usually develops between 5 and 14 days after the beginning of heparin therapy. However, if the patient has already been exposed to heparin in the past, it can develop before 5 days. The diagnosis is made when the platelet count falls below 50% of the baseline value. The detection of heparin platelet factor 4 antibodies of  $>20\%$  also strongly suggests the diagnosis of HIT. The major complications are bleeding and thrombosis.

In the present report, all the blood analysis and the use of heparin strongly suggest the diagnostic of HIT. As described previously, the fall in the platelet count and the heparin platelet factor 4 antibodies were positive for HIT 5 days after the introduction of heparin. The patient had already been exposed to heparin at the beginning of the hospitalization. Early cessation of heparin and initiation of Argatroban was the appropriate medical management in our case. Other factors might have contributed to penile necrosis, such as low cardiac flow followed by cardiac failure and diabetic nephropathy. However, the severity of the penile necrosis and the chronology of the events are in favor of penile necrosis secondary to HIT.

To our knowledge, it is only the second case of penile necrosis secondary to HIT described in the literature. The first case described was that of a 56-year-old man with lung cancer.<sup>5</sup> He was admitted in the hospital for pulmonary thrombosis, for which a treatment of

heparin and Warfarine was initiated. Similar to our case, the patient complained of symptoms of penile necrosis 4 days after the beginning of heparin therapy. The diagnosis of HIT was made after a drop in platelet count of 69%. As illustrated by this case and our case, penile symptoms of HIT were present when thrombocytopenia was confirmed. The patient underwent a partial penectomy and died of complications 3 weeks later. The pathology demonstrated hemorrhagic necrosis with thrombi.

Factoring in all the previously mentioned, we believe that penile necrosis is an unusual complication of HIT. However, the pathology of penile necrosis because of HIT seems unclear. Despite thrombocytopenia, HIT is rarely described in association with bleeding.<sup>3</sup> In fact, thrombosis is more frequent. In our case, pathology demonstrated extensive hemorrhagic necrosis of the penis without thrombus. However, an hypothesis is that the patient could have developed venous thrombosis. The thrombus could have disappeared with the treatment of Argatroban and have caused hemorrhagic damages to the penis. There was no other explanation apart from the HIT to explain the extensive acute penile necrosis our patient has developed.

## Conclusion

This case demonstrates that the hypercoagulable state brought on by HIT is a cause of acute penile necrosis. Approximately 1%–5% of patients exposed to some form of heparin will develop a HIT.<sup>4</sup> Prompt diagnosis of HIT should be encouraged to avoid complications such as penile necrosis. Moreover, HIT should be researched when a diagnosis of penile necrosis is made to avoid thrombosis of other organs and deterioration of penile acute ischemia.

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