electron microscopy, and flow cytometry.[1] Also, the number of unsatisfactory smears of 8.8% is within the reported range in the literature.[2] The problem of false positivity, a worrisome aspect of FNAC is not reported in this study, as none of the smears with reactive hyperplasia were interpreted as tuberculous, lymphoma, or metastatic carcinoma. Our results in this series reported high rates of false negative in tuberculous lymphadenitis (55%), which is significantly higher than reported in the literature.[5] These were interpreted as reactive hyperplasia. This may be explained by the fact that tuberculous lymphadenitis frequently displays changes that are compatible with nonspecific reactive hyperplasia. Sometimes only a few epithelioid cells are found in small groups or as single cells, or the histiocytes may have the typical appearance of epithelioid cells. The pattern then approaches that of non-specific reactive lymphadenitis with prominent histiocytes. This may be the case particularly in toxoplasma lymphadenitis, and in early stages of sarcoidosis. Also, patients with necrotizing or pyogenic tuberculous lymphadenitis may not necessarily exhibit a picture of TB lymphadenitis, and could easily mimic other forms of necrotizing lymphadenitis (atypical mycobacteriosis, cat scratch disease, lymphogranuloma venereum, and so forth), and more seriously tumor necrosis.[6] It is therefore essentially required that a clinically suspected case is submitted also for bacteriological and culture study examination to improve the diagnostic accuracy. The constitutional symptoms of fever, night sweating, and weight loss were found in a third of patients with reactive hyperplasia, and in almost 40% of patients with tuberculous lymphadenitis and lymphoma. This finding suggests that clinical evaluation alone is not sufficient in differentiating the different causes of peripheral lymphadenopathy. Based on high specificity and low sensitivity of our results, we recommend surgical excision of the lymph nodes if the FNAC reported reactive hyperplasia. Although the routine use of ancillary studies such as flow cytometry, immunocytochemistry, in situ hybridization, and polymerase chain reaction may improve the diagnostic accuracy of FNAC, excisional biopsy, and immunohistochemical stains sometimes are required for subtyping of lymphoma. In contrast, if the FNAC showed tuberculous lymphadenitis, appropriate drugs therapy could be instituted and the patients spared unnecessary surgery. Ziehl-Neelsen stain and tuberculous culture are indicated, but a negative result does not exclude the diagnosis of tuberculosis.[4] If FNAC revealed metastatic carcinoma, a careful search is made to identify the primary tumor.

In conclusion, FNAC therefore proves to be a useful (screening) procedure by selecting out those patients who would require further assessment including surgical biopsy. However, due to its limitations, it does not totally replace surgical biopsy in the investigation of peripheral lymphadenopathy.

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A life-sustaining single dose of recombinant activated factor VII for an Egyptian patient with hemorrhagic crisis

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Bleeding is a well-known complication of anticoagulant treatment. The annual incidence of major hemorrhages with, for example, vitamin K antagonists has been reported to vary between 2-7%. This incidence is 2-3-fold higher for minor bleeds.[1] For a one-week course of intravenous heparin therapy, the major bleeding rate is approximately 1–3%.[1] When such a serious bleeding episode occurs, the use of a specific antidote is an option. There are 3 main types

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of antidotes for the most frequently used anticoagulant drugs: protamine sulfate, vitamin K1, and plasma products containing coagulation factors. Protamine can be given to reverse the action of unfractionated heparin;[2] it is given intravenously and acts immediately. Although protamine can be used to reverse the action of low molecular weight fractions of heparin (LMWH), it has been reported that only half of the antifactor Xa activity is neutralized by protamine. However, the effect of protamine on the thrombin clotting time and the activated partial thromboplastin time (APTT) is complete. It is unclear what the influence of protamine on clinical bleeding during LMWH treatment is.[2] Plasma, or concentrates derived from it, can be given intravenously to counteract the effects of vitamin K1 antagonists by the infusion of functioning coagulation factors. Examples are 'fresh frozen' plasma and concentrates of vitamin K-dependent coagulation factors, which both act immediately. Vitamin K1 given as Konakion, phytomenadione or phytonadione can be used to reverse the action of warfarin and its derivatives, and can be given orally or intravenously. In comparison with protamine, vitamin K1 works slowly since it facilitates synthesis of the affected coagulation factors, some of which may take days before their concentration is normal again. The use of vitamin K1 is more reliable and rapid than simply withholding the vitamin K antagonists.[3] Recombinant activated factor (F) VII is used mainly for the treatment of hemophilia patients with inhibitors. Its unique mechanism of action, activation of FX by forming a complex with tissue factor (TF) at the site of active bleeding, has laid the basis for the treatment of various coagulopathies and severe bleeding episodes. This report demonstrates the beneficial effect of recombinant factor VIIa (rFVIIa) in controlling life-threatening bleeding in a patient with mitral valve replacement.

A 30-year-old male was admitted to the National Liver Institute (NLI), Minufiya University with persistent hematemesis, and hemoptysis with melena 6 hours before admission. The bleeding was precipitated by a large dose of non-steroidal anti-inflammatory drugs (NSAID) as oral diclofenac for his right arm fracture in an accident. He was using both warfarin and digitalis due to a mitral valve replacement 5 years ago. On admission, the blood pressure was 100/60, pulse 170, and temperature 38°C. The abdomen showed no localized or generalized tenderness, no splenomegaly, and the liver was not palpable. The electrocardiogram (ECG) showed rapid arterial fibrillation (AF), heart rate was 190/min. The laboratory investigations were found normal except the hemoglobin and prothrombin indices (**Table 1**). The chest x-ray showed cardiomegaly with shadow of the replaced mitral valve, and the lung showed a picture suggestive of broncho-pneumonia. The abdominal ultrasound showed the liver of normal size with periportal fibrosis, normal sized spleen (10 cm) and no ascites. The first treatment included intravenous vitamin K, omeprazole, 2 packs of red blood cells (RBCs), and 4 units of fresh-frozen plasma. Moreover, he received digoxin 0.25 ug, amiodarone HCl 200 mg/day, and cefotaxime one gm/6 hours. After extensive blood product support failed to control hemorrhage, he was transferred to the intensive care unit (ICU) and received a single dose of activated factor VIIa (90 ug/kg) in combination with amiodarone and digitalis. Commercially available rFVIIa, (Novo-Seven, Novo Nordisk, Denmark) was used. After administration, the bleeding settled dramatically and eventually ceased. Six hours later, the heart rate reached 90/min. One day later, an obvious recovery was obtained and the international normalized ratio (INR) value shifted to 2.2. Upper gastrointestinal endoscopy revealed non-bleeding multiple gastric and duodenal erosions. After improvement of his general condition, he was discharged with his medications to control the broncho-pneumonia and gastrointestinal tract erosions.

Life-threatening bleeding occurs when an acute hemorrhage is massive and uncontrollable with the patient receiving numerous transfusions in a short period. Massive loss of blood can also lead to a clotting impairment of the remaining blood. There are many underlying causes of clinically significant blood loss including trauma, surgery, and postpartum hemorrhages. Recombinant activated factor VII (Novoseven; Novo Nordisk A/S, Bagsvaerd, Denmark) has been recommended as a therapy of last resort to

Table 1 - Laboratory data obtained for the patient with bleeding.

Test	Patient	Reference range
Hemoglobin (gm/dl)	8	12-16
Platelets (μ x 10^3)	409	150-450
Creatinine (mg/dl)	1.1	up to 1.4
Total bilirubin (mg/dl)	1.2	up to 1
Direct bilirubin (mg/dl)	0.4	up to 0.25
Total protein (gm/dl)	6.5	6-8.5
Serum albumin (gm/dl)	3.7	3.5-5
Aspartate aminotransferase (U/I)	29	up to 45
Alanine aminotransferase (U/I)	27	up to 40
Alkaline phosphatase (U/I)	60	21-92
Gamma glutamyl-transferase (U/I)	34	up to 49
International normalized ratio	7	0.8-1.2
Activated partial thromboplastin time	32	24-40
Fibrin degradation product (μg/ml)	5	<10

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attain hemostasis in difficult clinical situations. The successful administration of recombinant activated factor VII has been reported in patients with severe trauma and those undergoing cardiac and abdominal surgery, in which the drug represents an effective and well-tolerated treatment for serious bleeding episodes during both surgery and postoperatively. The results of standard coagulation tests in our patient were remarkable, with abnormal prothrombin time but normal platelet count. Thus, a factor VII deficiency was included as a cause of bleeding. Factor VII deficiency should be suspected if only the prothrombin time is prolonged while other tests such as activated partial prothrombin time, thrombin time, and platelet count are normal.[4] Continuous bleeding led to a decrease in prothrombin time and platelet counts, although prothrombin complex concentrates, and fresh-frozen plasma were substituted. Changes in the hemostatic system are known to occur in patients who have experienced heavy blood loss and have received multiple blood transfusions. Those patients can experience impaired thrombin generation, which results in a less stabilized fibrin hemostatic plug that is very sensitive to fibrinolytic activity. Exogenous recombinant activated factor VII induces thrombin generation due to saturation of all tissue factor sites with activated factor VII at the site of injury, and it generates thrombin on the activated platelet surface. Thus, the thrombin-generating effect of recombinant activated factor VII was shown to be tissue factor-dependent (activation of factors IX and X by a complex of activated factor VII and tissue factor) and tissue factor-independent (by activation of factor X on activated platelets). Furthermore, at a lower platelet count, the initial activation was demonstrated to be enhanced after the addition of recombinant activated factor VII in a concentration-dependent manner, indicating that this clotting factor may compensate for a lower platelet count with regard to thrombin generation.[5] By exploiting the binding capacity of activated factor VII to platelets, recombinant activated factor VII is able to increase the capability of the hemostatic system, which is not achieved by administration of fresh-frozen plasma and prothrombin complex concentrates alone.

In conclusion, this report demonstrates the beneficial effect of recombinant factor VIIa (rFVIIa) in controlling life-threatening hematemesis and hemoptysis in a patient treated for long time with anticoagulants due to mitral valve replacement. Therefore, treatment of hemorrhage with rFVIIa reduces mortality, and improves outcomes in those cases. This makes recombinant activated factor VII useful as an additional hemostatic agent in very difficult bleeding situations after failure of conventional measures to achieve hemostasis.

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