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CASE REPORT

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Acquired haemophilia A treated with recombinant factor VIIa by an infusion pump and midline catheter

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Summary

Acquired haemophilia A is an autoimmune bleeding disorder treated with immunosuppression and bypassing agents such as recombinant factor VIIa (rFVIIa). The half time of rFVIIa is short, which requires frequent bolus injections in order to maintain hemostasis. Providing a continuous pump infusion instead of bolus injections could not only be more time and cost-efficient but also safer by maintaining a constant level of the bypassing agent.

rFVIIa is administered intravenously usually through a peripheral venous catheter. In patients with prolonged intravenous treatment or difficult-to-access peripheral vasculature, midline long peripheral intravenous catheters are an interesting alternative. They have favourable dwell times and failure rates while maintaining the same risk of infection as other peripherally inserted central catheters. This technique has the potential to reduce the costs as well as risk to the patients.

Herein, we report a case of a patient with AHA, who was treated with rFVIIa by an infusion pump and midline catheter.

Keywords: acquired haemophilia A; infusion pump; recombinant factor VIIa; midline catheter

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Introduction

Acquired haemophilia A (AHA) is a bleeding disorder caused by an autoimmune reaction between the autoantibodies (inhibitors) and factor VIII (FVIII). It occurs mainly in elderly patients with comorbidities as well as women around their pregnancy, often causing severe and prolonged bleeding [1, 2].

Acquired haemophilia A is a rare but severe bleeding disorder. There is no strict relationship between the activity of FVIII in plasma and the severity of hemorrhagic diathesis. The treatment of choice is the use of bypassing agents such as recombinant factor VIIa (rFVIIa), activated prothrombin complex concentrate (aPCC) or a relatively new treatment option — recombinant porcine factor VIII (rpFVIII) along with immunosuppressants

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such as prednisone, cyclophosphamide or rituximab [3].

The half time of bypassing agents, such as rFVIIa, is short (2.8 h in vivo for rFVIIa), which requires frequent bolus injections in order to maintain hemostasis [4]. There are studies discussing the use of infusion pump instead of bolus injections in AHA patients [4–6]. Providing a continuous pump infusion for patients with AHA could not only be more time-efficient but also safer by maintaining a constant level of the bypassing agent [4–6].

rFVIIa is administered intravenously usually through a peripheral venous catheter. When the patient requires prolonged intravenous treatment or the placement of a peripheral venous cathether is impossible, midline long peripheral venous catheters (MC) can be a good alternative [7]. They can be inserted at the patient's bedside, require no radiological verification and their bleeding safety profile does not differ from other venous catheters [8].

Herein, we report patient with AHA, who was treated with rFVIIa by an infusion pump and midline catheter.

Case report

A 74-year-old Caucasian female was admitted to the General Haematology Inpatient Clinic due to ecchymoses of the upper and lower limbs, which had been occurring for several days. Prior to admission, patient was hospitalized due to sepsis and referred from county hospital with suspicion of AHA.

The patient had a history of Escherichia coli septic infection, pneumonia, urinary tract infection, chronic kidney disease, hypertension, chronic heart failure, atherosclerosis, bronchial asthma, hypothyroidism, depression, extrapyramidal symptoms and folic acid deficiency.

On admission, patient in average overall condition with extensive subcutaneous ecchymoses on the upper and lower limbs as well as lateral sides of thorax (Fig. 1–3). Laboratory studies revealed prolonged activated partial thromboplastin time (aPTT) of 104.9 s (normal range 25.4–36.9 s). There were no signs of thrombocytopenia, international normalized ratio (INR) and thrombin time (TT) were within the range. The level of factor VIII was less than 1% and inhibitor titer against human factor VIII was 4.9 j.B/ml (norm < 0.5 j.B/ml).

Patient was diagnosed with AHA and the following treatment was implemented: bypassing agent — recombinant human coagulation factor VIIa — eptacog alfa (0.09 mg/kg intravenously (iv) in infusion pump with bolus intervals of 3 hours) and eradication of inhibitor — prednisone (1 mg/kg per day). Due to the fact that the placement of a peripheral venous cathether was not possible, a midline long peripheral venous catheter was placed.

Figure 1. Extensive ecchymosis of the left upper limb

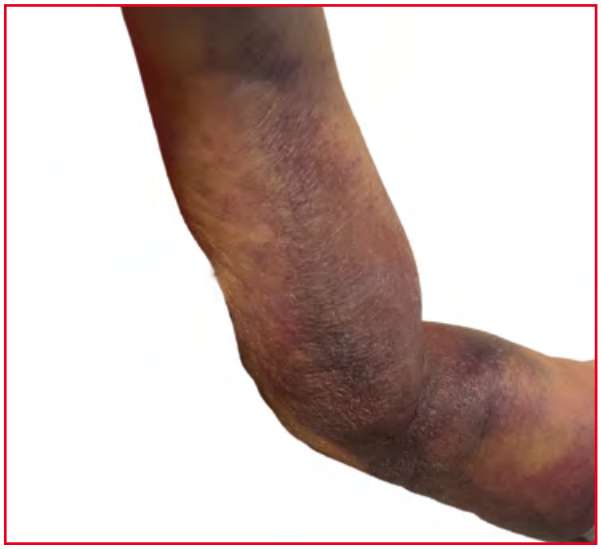

Figure 2. Extensive ecchymosis of the right upper limb

The frequency of rFVIIa administration was being progressively prolonged to respectively 4 h and 6 h bolus intervals and ultimately the treatment was switched from infusion pump to bolus injections. Hemostatic treatment was then changed to porcine factor, and due to the intensification of anemia and increased demand for factor VIII, Anti-

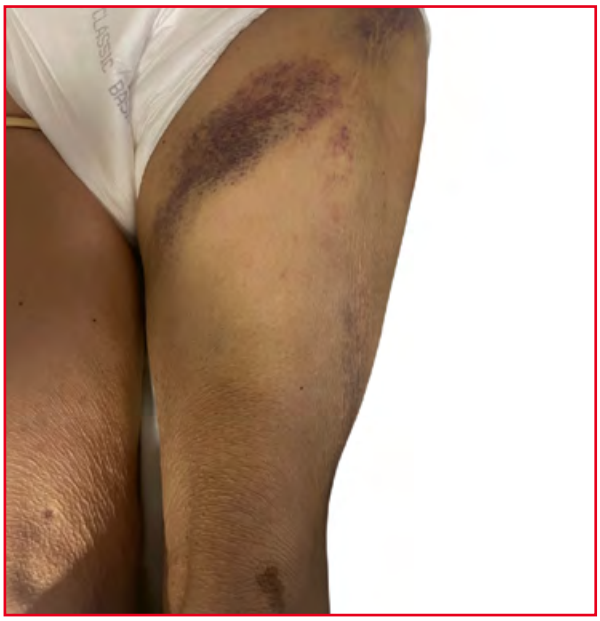

Figure 3. Echymosis of the lower limb

-Inhibitor Coagulant Complex (Feiba) was applied. The treatment eradicating the inhibitor was also extended with cyclophosphamide, and then with rituximab, resulting in the elimination of the inhibitor and an increase in the value of factor VIII.

Discussion

The administration of rFVIIa using an infusion pump is a novel but promising method. There are studies presenting the favorability of hemostatic effects in patients who are administered factor products, such as factor VIII or rFVIIa in infusion instead of intermittent bolus injections [9]. The dosage of rFVIIa is more precise when it is administered through an infusion pump. While administering a bolus injection, the dosage of rFVIIa is rounded to the closest number. Whereas through the pump, patients can be provided a precise fixed dose [6]. The precision of a dosage enables reduction of the expenses related to patient's treatment. It is also more convenient for the patient who is not woken up at night for bolus injection [6].

Fixed doses and intervals do not only offer more accurate, efficient and reliable administration but can also reduce burden on nursing staff and thus minimalize the risk of human error [5]. According to study conducted by Pollard et al., the overall nursing time involved in reconstituting and administering rFVIIa can be reduced from 3–6 hours a day to 1–2 hours per day just by switching the rFVIIa administration method from bolus to pump infusion [6].

In terms of nursing time, an infusion pump of rFVIIa is also more favourable in comparison to recombinant porcine factor VIII (rpFVIII), which is a relatively new bypassing agent [3]. The dosage of rpFVIII should correspond to the FVIII levels, which ought to be closely monitored throughout the treatment. Therefore, in order to adjust the dosage of rpFVIII, patients require multiple factor VIII measurements [10]. rFVIIa is physically and chemically stable for over 24 hours when administered in an infusion pump, thus only one factor measurement daily is required in those patients [11].

We have conducted a survey among 10 nursing staff members working at the Department of General Hematology in Łódź with the aim to assess their preferences of rFVIIa administration. 80% of interviewees pointed to rFVIIa in infusion pump as more comfortable treatment method than 4h interval boluses. Half of the surveyed nursing staff members assessed infusion pump administration of rFVIIa as very easy (1 out of 5 points) while only 10% evaluated it as very difficult (5 out of 5 points). Amongst the advantages of the bolus administration over pump infusions, the majority defined lack of patient's permanent connection to the infusion pump. While as the greatest advantage of the infusion pump, 60% pointed to the administration of the drug at precise time intervals (Fig. 4–5).

Intravenous infusion of rFVIIa can be administered through peripheral venous catheter. However in situation of prolonged intravenous treatment or difficult-to-access peripheral vasculature, patients are eligible for MC insertion [7]. MCs have favourable dwell times and failure rates against other types of catheters. They can be inserted at the patient's bedside and require no radiological verification [8]. They have a high rate of first-attempt placements as well as low complication rate. The risk of catheter-related bloodstream infections was proven not to be significantly different between MCs and PICCs (peripherally inserted central catheters) [12]. They have favourable dwell times and failure rates while maintaining the same risk of infection as other PICCs. This technique has potential to reduce the costs as well as risk to the patients [13–14].

Conclusions

Administration of rFVIIa in infusion pump outweighs bolus intermittent injections in terms of accuracy and reliability. It is favoured amongst

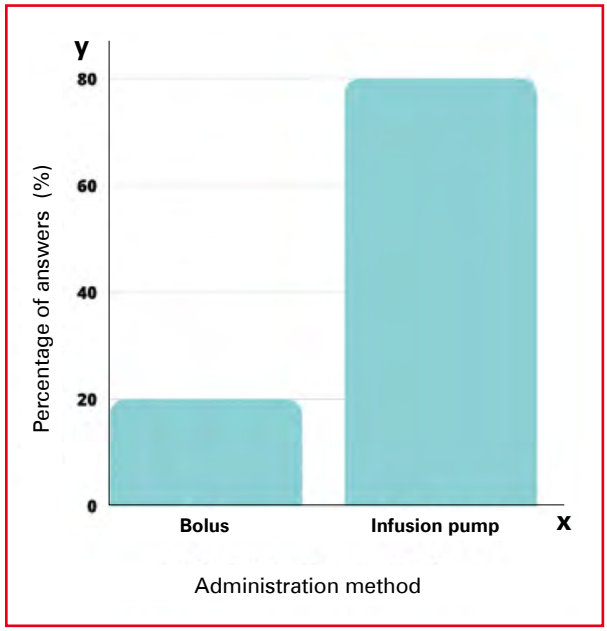

Figure 4. Graph presenting the nursing staff's preferences regarding the way of recombinant factor VIIa administration. The x axis corresponds to the administration method. The y axis indicates the percentage of answers

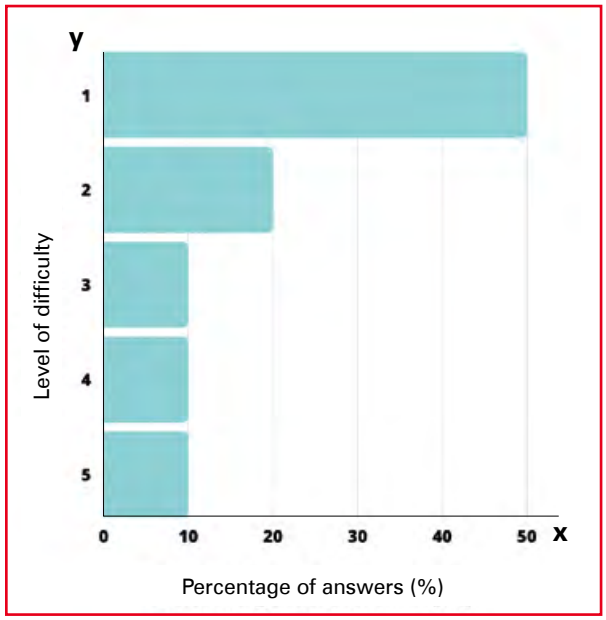

Figure 5. Graph presenting the nursing staff's assessment of level of difficulty recombinant factor VIIa administration by infusion pump. The x axis corresponds to the percentage of answers. The y axis indicates the level of difficulty (from 1 — very easy to 5 — very difficult)

nursing staff and can have significant influence on minimizing the risk of human error. In patients with prolonged intravenous treatment or difficult-to-access peripheral vasculature, MCs are an interesting alternative.

Conflict of interest: none declared

Authors contributions: MW and TR proposed the idea of the case report. MW managed the patient. WR, MW contributed to writing the article. All authors (WR, MW, TR) contributed to revising and editing the manuscript.

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