

Availability of peripheral inserted central catheters in severe hemophilia patients with inhibitors

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= Abstract =

The most effective treatment strategy for patients with hemophilia is replacement therapy with FVIII or FIX concentrates, which usually requires long-term, uncomplicated venous access. However, central venous access device (CVADs, ports) insertion requires inpatient admission and general anesthesia, and presents some problems regarding health insurance coverage. Peripherally inserted central catheters (PICCs) were inserted in two severe hemophilia patients aged 7 and 11 years with high titers of inhibitors. They experienced frequent bleeding episodes and required replacement therapy, which eventually resulted in difficulty in acquiring venous line access. Factor VIII activity was below 1% and inhibitor titers were 160 and 26.3 BU/ml. In an outpatient setting, PICC lines are easily placed by radiological guidance and require local anesthesia alone. PICC has been feasible, in particular, for hemophilia patients with frequent bleeding episodes. (*Korean J Pediatr* 2008 51:1359-1362)

Key Words : Hemophilia, Peripherally inserted central catheter

Introduction

Hemophilia A and B are caused by deficient or defective blood coagulation factors VIII and IX, respectively. The most effective treatment strategy for the patients with severe forms of hemophilia is replacement therapy with FVIII or FIX concentrates. Irrespective of whether this is performed in response to a bleeding event or as a prophylactic infusion, replacement therapy requires long term, uncomplicated venous access. Especially, safe venous access is critical to hemophilic patients with inhibitors¹⁾. However, central venous access devices (CVADs, 'ports') insertions require inpatient admission and general anesthesia. Also it would be quite costly in Korea as port insertion are not be covered by health insurance.

Peripherally inserted central catheters (PICCs) are increasingly used as a medium to long-term intravenous access²⁾. PICCs were introduced to provide reliable vascular access for total parenteral nutrition in neonates³⁾. PICC utili-

zation has continued to increase because these catheters are easy to insert and have a low incidence of complications compared with other surgically placed central lines.

The author experienced safe and convenient insertion of PICC in hemophilia patients with inhibitors under local anesthesia in the outpatient setting.

Case report

The author performed PICCs insertions in two severe hemophilia A patients with inhibitors. It was critical to secure safe venous access because I planned to do immune tolerance therapy. However, they experienced frequent bleeding episodes and required replacement therapy daily or every other day, which led to difficulties in getting venous line access.

The ages of the two patients were 7 and 11. The vital signs were stable. On physical examination, one patient was found to have swelling and tenderness in the right knee. The other patient was slightly obese, but otherwise unremarkable. The results of laboratory test except the coagulation tests were within normal range. Factor VIII activities were all below 1% and their inhibitor titers were 160 and 26.3 BU/mL, respectively.

PICCs were inserted via cannula into cephalic vein of upper antecubital fossa for convenience of daily activities.

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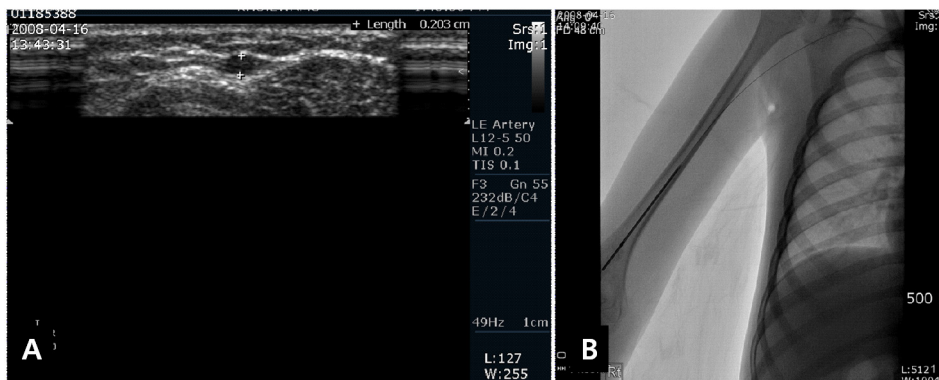


Fig. 1. Image of peripherally inserted central catheter (PICC) insertion. A) The cephalic vein was punctured at distal 1/3 of the upper arm under ultrasound guidance. B) Hairwire was inserted to the superior vena cava. 5 French PICC was inserted following the wire to meet with the superior vena cava and the right atrium.



Fig. 2. Photograph of peripherally inserted central catheter (PICC) in a patient. PICC was inserted into the cephalic vein of the upper antecubital fossa for convenience of daily activities.

Cephalic vein was punctured with a micropuncture needle at distal 1/3 of the right upper arm under ultrasound-guided and regurgitated blood to confirm venous blood (Fig. 1A). Hairwire was inserted to the superior vena cava and the needle was removed (Fig. 1B). Five French PICC was inserted following with the wire to junction with the superior vena cava and the right atrium and the microwire was removed. Following a final fluoroscopic check, the line was sutured into place (Fig. 2).

The author administered factor VIII inhibitor bypassing activity (FEIBA[®]; Baxter healthcare, Vienna, Austria) 75 IU/kg before the procedure, and experienced no bleeding complications. After the procedure, one patient had some bleeding and required recombinant activated factor VII (Novoseven[®]; Novo nordisk, Bagsvaerd, Denmark). There were no issues

in getting health insurance coverage, and the cost was relatively less than CVAD insertion. There were no specific problems in using PICC with immune tolerance therapy and injection of factor concentrates three or four times per week. One patient experienced phlebitis, and the PICC was removed five months after insertion. The other patient is still using a catheter without apparent problems for more than 7 months. We provided education on catheter management to them and their parents. They replaced factor concentrates for bleeding with home therapy combined with immune tolerance therapy.

Discussion

Safe venous access is a very important issue for hemophilic patients. It is exceptionally more difficult for patients with bleeding events or inhibitors to have safe venous access. Central venous access can be considered in patients requiring long-term replacement therapy. For such cases, CVAD insertions are commonly used in other countries¹⁾. In a recent survey, centers that routinely start primary prophylaxis at an early age needed CVADs in about 20–30% of cases, indicating that peripheral venous access is possible even for frequent dosing in most of the children^{4, 5)}. There are various kinds of available catheters and catheter-related complications are frequently reported. In Korea, CVAD insertions were performed on two hemophilia patients⁶⁾, but there were health insurance problems.

In other countries, two types of CVAD insertions are mainly performed to hemophilia patients¹⁾. The two most common CVAD designs used in hemophilic patients are tunnelled fully implantable (commonly termed ports) and

tunnelled with an external catheter hub (commonly known as Hickman or Broviac catheter). Infections are the most frequent complications associated with the use of central venous lines (CVLs) in children with hemophilia. Several retrospective studies that include data from a substantial number of patients have reported approximately 0.203 infections per 1,000 catheter-days (mainly Port-A-Cath)^{7, 8)}. According to meta-analysis of CVADs in hemophilia, the expected life span of CVADs prior to removal was 578 days (CI, 456-733 days per CVAD)¹¹⁾.

The two patients discussed in this case were severe hemophilia patients with high titer inhibitors, and also required factor infusions more than three times per week because of frequent bleeding episodes and immune tolerance therapy. So it was necessary that PICC insertions were performed on those patients for prolonged and safe venous access.

PICCs are frequently used to provide prolonged intravenous access in both acute and home care settings. PICCs offer an attractive alternative to other available indwelling CVL and CVADs. Shaw³⁾ described PICC use in 1973 as a method of providing reliable vascular access for total parenteral nutrition (TPN) in neonates.

The major advantages of PICCs are longer time compared to other peripheral catheters, fewer venous punctures for prolonged administrations⁹⁾.

Additional benefits of PICCs include easier insertion and removal than CVADs. PICCs are inserted in outpatient setting, requiring local anesthesia only. For each drug infusion, patients undergo pain driven by invasive needle insertion to Ports.

Duration of PICCs was reported to be inconsistent: One study about PICCs for cancer patients concludes that 351 PICCs were in place for a mean 30 days (range, 1 to 487 days)⁹⁾. In another study about PICCs in children with cancer the median catheter life was 161 days (range 5-390 days)¹⁰⁾. These reports show that catheter life varies.

Complications associated with PICC insertion are infrequent, but include bleeding, tendon or nerve damage, cardiac arrhythmias, chest pain, catheter malposition, and catheter embolism^{11, 12)}. Catheter-associated sepsis requires removal of the catheter and appropriate antibiotic therapy. The incidence of catheter-associated sepsis with PICCs ranged from 0 to 2.2% in several studies^{9, 10, 12)}. Also, the rate of catheter removal because of phlebitis has ranged from 2.2% to 3.3% in several reports^{11, 13, 14)}.

Several measures for hemophilic patients can be taken to

diminish the risk of complications associated with an implantable venous access system^{15, 16)}. The single most important preventive measure is strict adherence to hand washing, aseptic technique, and education and re-education of the family or patient¹⁷⁾. To prevent thrombosis, flushing with saline and heparin-lock are also important, along with the introduction of urokinase or recombinant tissue plasminogen activator into the catheter when infusions become less smooth^{16, 18)}.

Similar efforts are required for prolonged use of PICCs. One patient with PICC experienced phlebitis, and the PICC was removed. We should pay attention to the possibility of infections and occlusion of the catheter. If patients want home therapy for factor replacement, additional education and caution are necessary.

In summary, PICCs are easily placed in outpatient setting without general anesthesia, and there is also a higher possibility of insurance coverage because there is little chance of bleeding thus necessitating less amount of factor infusion. PICCs are thought to be helpful for hemophilia patients who need frequent, long-term factor replacement. Special attention is needed for prolonged use of PICCs.

한글 요약

중증 혈우병 항체 환자에서 시행한 말초삽입 중심혈관 카테터의 유용성

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박영실

혈우병 환자에서 가장 효과적인 치료 방침은 응고 인자의 보충으로, 그를 위해 안전하고 오래 사용할 수 있는 정맥 확보가 필요하다. 그러나 중심 정맥으로의 port는 전신 마취와 일정한 입원이 필요하고, 혈우병 환자에서 시행할 경우 보험 삭감의 문제도 있다. 본 저자는 두 명의 중증 혈우병 항체 환자에게 말초 삽입 중심 정맥관을 삽입하였다. 환자들은 잦은 출혈 소견 때문에 응고 인자를 투여 받았으며, 그로 인하여 혈관 확보에 어려움이 있었다. 환자 나이는 7세와 11세였다. 제 8 응고 인자 활성도는 모두 1% 이하였으며, 제 8 응고 인자 항체 수치는 각각 160과 26.3 BU/mL였다. 말초 삽입 중심 정맥관은 초음파 인도 하에, 외래에서, 국소 마취로 쉽게 삽입되었다. 말초 삽입 중심 정맥관 삽입은 잦은 출혈을 보이는 혈우병 환자에게 사용해 볼 수 있는 방법이다.

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