Hirosaki Med. J. 72 : 62—67, 2022

CASE STUDY

# Treatment of intractable infected giant skin ulcer on a leg by continuous intra-arterial infusion of antibiotics, using a tunneled catheter technique without a port and final skin graft, avoiding recommended amputation of the leg

Shoichi D. Takekawa[1], Hiraku Yodono[2], Masaki Takahashi[3], Junji Tanaka[4], and Mitsuo Sugawara[5]

**Author Notes**

**This paper is dedicated to the memory of the late Prof. Mitsuo Sugawara and the late Prof. Sydney Wallace.**

**Abstract**

The purpose of this paper is to report the usefulness of continuous intra-arterial infusion of antibiotics for the treatment of intractable skin infection, using a tunneled catheter technique without a port.

An elderly woman presented with pain in the left leg with a chronically infected intractable giant skin ulcer, for which amputation was recommended by former doctors to avoid the occurrence of skin cancer, because she had multiple (five times in 14 years) skin grafts and the skin ulcer continuing for so many years. The patient requested an alternative and interventional radiological treatment was selected.

The pus in the ulcer yielded numerous *Pseudomonas aeruginosa* and *Proteus vulgaris*. She was treated by continuous intra-arterial infusion of an antibiotic, Sulbenicillin, using a tunneled catheter technique without a port for 18 days. The organisms in the ulcer were completely eradicated, and the ulcer gradually healed with decreased size. When the size of the ulcer became minimal a skin graft completed the treatment, avoiding amputation. No local or subcutaneous infection relating to the procedure was noted during or after the treatment.

In a follow-up two years after the treatment, she was found to be living well without any complications.

Hirosaki Med. J. 72 : 62—67, 2022

**Key words:** Chronic infection; infected skin ulcer; Infusion of antibiotics; tunneled catheter technique; Amputation.

## Introduction

Chronic skin ulcers may be treated by injection of antibiotics or a skin graft. However, if subsequent care after a skin graft is not sufficient or vascular blood supply is insufficient, the wound may become infected and necrotic.

We report favorable results in treating an intractable chronically infected giant skin ulcer on the leg by continuous intra-arterial infusion of an antibiotic in a case in which the former attending doctor, fearing occurrence of skin cancer, felt amputation of the leg was necessary.

Continuous intra-arterial infusion of an antibiotic was carried out, by using a tunneled catheter technique without a port.

Generally, a port is recommended to be connected to an indwelling catheter when continuous intravascular infusion of drugs is contemplated, especially in the treatment of cancer by chemotherapy. The reasons why a port is recommended are to relieve the patient's discomfort from repeated injection and also to prevent infection relating to the catheter, which will be indwelling in the vessel for a long period.

A tunneled catheter technique without a port for infusion therapy may be thought as an old and pre-century technique, but we consider it to

[1] Research Institute of Diagnosis and Therapy of Vascular Diseases, Southern TOHOKU Research Institute for Neuroscience.
[2] Narumi Hospital.
[3] Fujita Health University.
[4] Saitama Medical University.
[5] (deceased), Hirosaki University Graduate School of Medicine.

Correspondence: S. D. Takekawa, M.D., M.S., PhD
Received for publication, January 21, 2021
Accepted for publication, February 6, 2021

be useful for relatively short-term use (approximately within one month).

A case in which such a technique without a port was employed for short-term use (for 18 days) with good results will be introduced.

## Case History

An old woman presented with pain in the left leg with chronically infected intractable giant skin ulcer for which amputation was recommended by her former attending doctors to avoid the occurrence of skin cancer.

Her past history of the disease revealed multiple skin grafts (five times in 14 years).

She refused amputation and looked for another treatment by interventional radiological treatment.

The infected giant skin ulcer on the left leg is a sequela of multiple skin grafts after a low-temperature burn due to contact with an Anka (foot warmer) in 1963.

In 1987 she was admitted to Dokkyo Medical University Koshigaya Hospital. She was well nourished, but she could not walk well due to the swollen leg. She had a giant skin ulcer, measuring 30 x 15 cm, over the anteromedial aspect of the left leg. She had multiple operative scars and deformed skin on the left leg due to the previous multiple skin grafts (Fig. 1A).

The skin ulcer was foul smelling and covered with light greenish pus and much secretion. A culture of the pus yielded numerous *Pseudomonas aeruginosa*, a moderate amount of *Staphylococcus aureus* and a small amount of *Proteus vulgaris*, all of which showed considerable sensitivity to Sulbenicillin.

Treatment and clinical course:

To begin with, it was necessary to treat the mixed infection of the giant ulcer.

On January 26, 1987, a 3F infusion catheter (C00k SKS) was inserted percutaneously into the left common femoral artery, and the tip of the catheter lay in the distal superficial femoral artery. The proximal catheter was pulled out through a tunnel under the skin and the catheter was fixed by strings of skin suture at about 20 cm above the inguinal ligament (Fig. 2 A, B). The proximal end of the catheter was connected to a stopcock and a port was not used.

She was treated by continuous intra-arterial slow infusion of Lillacilin 1.0 gram in 50 ml of normal saline/12 hours, that means 2.0 grams per day. This treatment was continued for 18 days. LiIacillin (trade name) contains Sulbenicillin, a synthetic penicillin.

One ampule of Solcoseryl (Ciba, Basel) in 100 ml of 5% glucose venous drip infusion daily and oral administration of Ferogradumet 1T, 3 times a day for hypochromic anemia, were added. Disinfectant and Gentacine ointment were applied locally.

The bacteriological study (culture) of the pus in the infected ulcer revealed negative results after the completion of the continuous intra-arterial infusion of antibiotics. Local disinfection was continued, and the ulcer healed gradually (Fig. 1 B, C, D).

The patient was transferred to Hirosaki University Hospital 5 months after the beginning of treatment. The local disinfection was continued thereafter in Hirosaki University Hospital.

The initial size of the ulcer was 30 x 15 cm, and the decrease of the size reached a plateau eight months later. The final size was 5 x 1.5 cm at 12 months after the initiation of the treatment (Fig. 3).

The blood supply to the ulcer region was studied by arteriography, which revealed the absence of the lower half of the anterior tibial artery of the left leg, probably due to previous multiple skin grafts (Fig. 4).

The ulcer became further smaller, measuring about 3.7 x 0.7 cm on April 13, 1988.

Since further healing of the ulcer could not be expected, the remaining ulcer was treated by


**Fig. 1.** 72-year-old woman with a giant skin ulcer on the left leg.

A: Infected giant skin ulcer at the initial visit.
B: Decreased ulcer 5 months later.
C: Further decrease of ulcer size, 8 months from first visit
D: Remaining small ulcer, 12 months from the first visit.

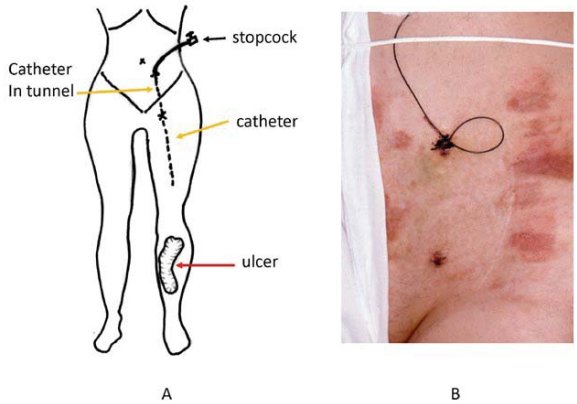


**Fig. 2.** 72-year-old woman with a giant skin ulcer on the left leg.

A: Schema of tunneling catheter technique. No port is used.
B: Local photo of the puncture site and exit site of a catheter.

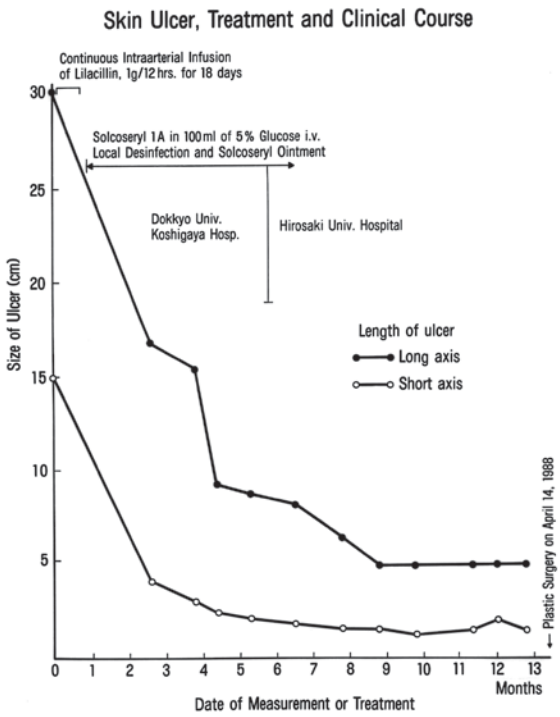


**Fig. 3.** 72-year-old woman with a giant skin ulcer on the left leg.

Time dependent change in the size of skin ulcer after treatment.

**Fig. 4.** 72-year-old woman with a giant skin ulcer on the left leg.

Left leg arteriography reveals absence of the lower half of the anterior tibial artery for a distance of 8 cm.


**Fig. 5.** 72-year-old woman with a giant skin ulcer on the left leg.
Post-operative skin graft (3 months after surgery)

**Fig. 6.** 74-year-old woman after treatment of a giant skin ulcer on the left leg.
Follow-up of skin graft (Two years after the initiation of the treatment with intra-arterial infusion of antibiotics, local disinfection and skin graft.)
Grafted skin is well adapted.

skin graft at the Department of Plastic Surgery, Hirosaki University Hospital,

On April 14, 1988 she was treated by free latissimus dorsi muscle flap transfer with mesh skin graft. The subscapular artery of the flap was anastomosed to the proximal anterior tibial artery and the vein of the flap was anastomosed to the comitant vein. Upper abdominal skin was used for the mesh skin graft. The grafted skin was well adapted (Fig. 5).

The post-operative course was uneventful, and the grafted skin was confirmed to be well adapted to the left leg two years later (Fig. 6).

She was able to walk well with her own legs after whole treatment (Fig. 7).

Her left leg was saved from amputation.

**Fig. 7.** 74-year-old woman after treatment of a giant skin ulcer on the left leg.
2-year-follow-up photograph of the leg after completion of treatment.
She was able to walk well with her own legs and her usual life was restored.

## Discussion

The technique of placement of tunneled catheters is used for both intravenous and intra-arterial infusion of drugs.

The proximal end of the catheter exiting from the tunnel is connected to either just a stopcock or to an embedded port.

For a long-term intravascular infusion of drugs, the port is used to ease the patient's discomfort and to protect against infection. The catheter-port system is often used for cancer infusion chemotherapy.

For a short-term infusion of drugs only a stopcock could be utilized.

There is a concern about the complication of infection for the tunneling catheter technique without the use of a port.

However, there are complications such as

infection in both simple technique without a port and also in the catheter-port system as described by Strecker and his associates[1], Clarkson et al[2], Clouse et al[3], Matsumoto et al[4] and others.

Shaul et al[5] found that neutropenia and failure to administer prophylactic antibiotics are risk factors for the development of early central venous catheter infection in pediatric patients.

Black et al[6] studied the risk factors of tunneled central venous catheters by multivariate analysis and stated that the only risk factors were time to catheter removal and a history of tunneled central venous catheters.

We have left the tunneled catheter in place for 18 days, but no local or subcutaneous infection was noted during or after the procedure.

We would like to emphasize the practical usefulness of tunneled catheter technique without a port for short-term infusion of antibiotics for a local infection.

There seem to be at least two reasons for the absence or low occurrence of infection from the tunneled catheter technique without a port in this case. One is diligent local disinfection. Second is the circulation of antibiotics originating from the catheter tip and spreading around the catheter in the subcutaneous tissue at the first pass of the drug via the venous route. Therefore, there was continuous infusion of the antibiotics to the entire body.

Sulbenicillin is a synthetic penicillin. According to Seki[7], it is effective against both Gram-positive and Gram-negative organisms. It is noteworthy that Sulbenicillin is effective against *P. aeruginosa* and *P. vulgaris*. The effective minimal concentration of Sulbenicillin is 0.39-12.5 μg/ml for Gram-positive bacteria, 0.20-100 μg/ml for Gram-negative bacteria and 3.12-100 μg/ml for *P. aeruginosa*.

The concentration of Sulbenicillin in the blood reaches 38-39 μg/ml at 30 minutes when 500 mg of the drug is injected intravenously.

The initial concentration of Sulbenicillin in the arterial catheter in our case was 20 mg/ml (1,000 mg/50ml).

According to Nadai[8] the time dependence of concentration of a drug (Ct), when administered by continuous intravenous infusion, is expressed by the equation 1.

$$Ct = K_0 / CLsys \cdot (1 - e^{-kel \cdot t}) \quad (1)$$

Where Ct: concentration of a drug at time "t",

$K_0$: Speed of injection of a drug,

CLsys: systemic clearance,

kel: drug disappearance constant.

The systemic concentration (Css) at equiliblium after long-term infusion ($t=\infty$) would be expressed by equation 2.

$$Css = K_0 / CLsys \quad (2)$$

Nadai also explains that the effectiveness of a drug in the penicillin line requires concentration of drug in blood be maintained above the minimal inhibitory concentration (MIC) for over 40 to 50 % of infusion time.

The concentration of a drug given by continuous intravenous infusion becomes 50% of the maximum concentration at equilibrium for the duration of twice of the half-life, and 97% of the maximum concentration at equilibrium for the duration of five times of the half-life.

This phenomenon would tell us that a considerable long-term infusion therapy would lead to much effectiveness for the treatment of infection.

In fact, our result of continuous intra-arterial infusion therapy for 18 days was successful to eradicate the bacteria.

The diluted solution of Sulbenicillin in the initial arterial blood was 1 g/50 ml (20 mg/ml), therefore the concentration of 20,000 μg/ml should have been sufficient to inhibit the very resistant *P. aeruginosa*.

The diluted Sulbenicillin will circulate in the veins, and in turn soak the soft tissue around the catheter and subcutaneous tunnel via arterial circulation.

The concentration of Sulbenicillin in the circulating blood at 30 minutes would be 76-78 μg/

ml in our case, if Seki's results (38-39 μg/ml by the dose of 500 mg) are applied. This concentration would be sufficient to control the organisms like *S. aureus*. However, further evaluation is needed regarding the concentration of drug in the circulating blood after long-term intra-arterial infusion, because we must know the systemic clearance.

## Conclusion

Successful use of a tunneled catheter technique without a port to treat incurable chronically infected giant skin ulcer was reported. No infection in the skin other than the ulcer or soft tissue relating to the catheter was noted.

Amputation of the leg was avoided by the cooperative efforts of radiologists and plastic surgeons.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

## Funding

The whole expenses of the patient's hospitalization in Hirosaki University Hospital was supported by the Research Fund for "Special patient for medical research" provided by the Ministry of Education of Japanese Government, including diagnosis, treatment and hospital fee for important cases (During the period of June, 1987 through July, 1989). For this arrangement the authors are grateful. (学用患者としての入院治療)

## Acknowledgements

We thank our former colleagues. Taisuke Sasaki, Koji Tarusawa, Manabu Miura, Naoko Nishi, Yoshiaki Yokoyama, Tamaki Kimura, Yasushi Mariya, Isao Kudo, Satoshi Komai, Hideaki Saeki and William G. Childs for editing. We also thank Prof. Shingo Kakeda, M.D., PhD for reviewing.

Presented in part at the Joint Meeting of Cardiovascular and Interventional Radiological Society of Europe and Japanese Society of Angiography and Interventional Radiology, during the time of ICR'89, June 30-July 2, 1989, Paris, France.

## References

1) Strecker EP, Boos IB, Ostheim-Dzerowycz W, Herber R, Vetter SC. Percutaneously implantable catheter-Port system: Preliminary technical results. Radiology. 1997;202:574-7.

2) Clarkson B, Young C, Dierick W, Kuehn P, Kim M, Berrett A, Clapp P, et al. Effects of continuous hepatic artery infusion of antimetabolites on primary and metastatic cancer of the liver. Cancer. 1962;15:472-88.

3) Clouse ME, Ahmed R, Ryan RB, Oberfield RA, McCaffrey JA. Complications of long term transbrachial hepatic arterial infusion chemotherapy. AJR Am J Roentgenol. 1977;129:799-803.

4) Matsumoto T, Yamagami T, Yoshimatsu R, Morishita H, Kimura N, Sato O, Hasebe T. Hepatic arterial infusion chemotherapy by the fixed-catheter-tip method: Retrospective comparison of percutaneous left subclavian and femoral port-catheter system implantation. AJR Am J Roentgenol. 2014;202:211-5.

5) Shaul DB, Scheer B, Rokhsar S, Jones VA, Chan LS, Boody BA, Malogolowkin MH, et al. Risk factors for early infection of central venous catheters in pediatric patients. J Am Coll Surg. 1998;186:654-8.

6) Black JR, Coker MA, Li Y, Sung J, Moawad S, Aal AKA, Gunn AJ. Infection of Small-Bore tunneled central venous catheters. AJR Am J Roentgenol. 2019;213:458-63.

7) Seki T. Introduction of a new drug: Sulbenicillin (Lilacillin). Kyorinmed. 1973;4:195-7. (in Japanese)

8) Nadai M. Foundation of drug pharmacokinetics and application to dosage regimen. Jpn J Pediat Nephrol. 2006;19:111-23. (in Japanese)