Successful Treatment of Severe Ischemic Foot Ulcer with Sterile Maggots: The First Case in This Country

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Abstract: This is a report on a patient with severe ischemic ulcer of the lower limb (diabetic gangrene) in whom it was determined that amputation of the lower limb was unavoidable because of the spread of infection to the whole foot. However, treatment of the patient with sterile maggots was successful to control the infection, and the foot was preserved. The case was a 65-year-old woman with ischemic gangrene of the left foot. As arterial reconstruction to the foot was diagnosed impossible by angiography, transplantation of bone marrow and peripheral mononuclear cell into the left calf muscle was conducted. Then, amputation of the first and second left toes and debridement were conducted, but gradually the infection spread to the whole foot. Such being the case, starting on March 26, 2004, treatment with sterile maggots was carried out three times on the locus of ulcers of the left foot as a result of which infection of the wounds was controlled and epithelialization of the left foot progressed rapidly, attaining a complete healing of the wounds after 3 months. This is the first case of successful treatment with sterile maggots to be reported in this country. (Jpn. J. Vasc. Surg., 14: 653–657, 2005)

Key words: Maggot debridement therapy (MDT), Diabetic foot, Gangrene, Severe ischemic ulcer

Introduction

Although effectiveness of maggot debridement therapy (MDT) for leg ulcers (especially for diabetic gangrene) has been established in Europe and United States, MDT for diabetic foot has not been tried so far in this country. The following is a report on the first attempt at MDT in this country that resulted in a good result.

Case Report

Patient: A 63-year-old woman.

Chief complaints: Left foot gangrene and severe pain.

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Received: December 24, 2004
Revision accepted: May 18, 2005

Past history: Diabetes mellitus (self injection of insulin for the past 8 years), hypertension, chronic renal insufficiency (blood dialysis has been carried out three times a week for the past 6 years), smoking (–), coronary artery bypass surgery (left anterior descending artery) in June, 2002.

Family history: Non-contributory.

History of the present illness: Experienced a sense of coldness in the left foot beginning some time in January, 2002. Wounds developed at the inner aspect of the left first toe, but were thought to be due to ingrowing toenails. Beginning some time in June, 2002, pain at rest appeared in the left foot (especially during blood dialysis). As conservative treatment (intravenous injection of prostaglandins) started at some time in January, 2003 failed to induce improvement, the patient was introduced to the Division of Cardiovascular Surgery.

Status at the time of admission: Slight anaemia, no jaundice and no abnormalities in heart and pulmonary sounds.

Blood test: Number of leucocytes 9800; haemoglobin 9.3 g/

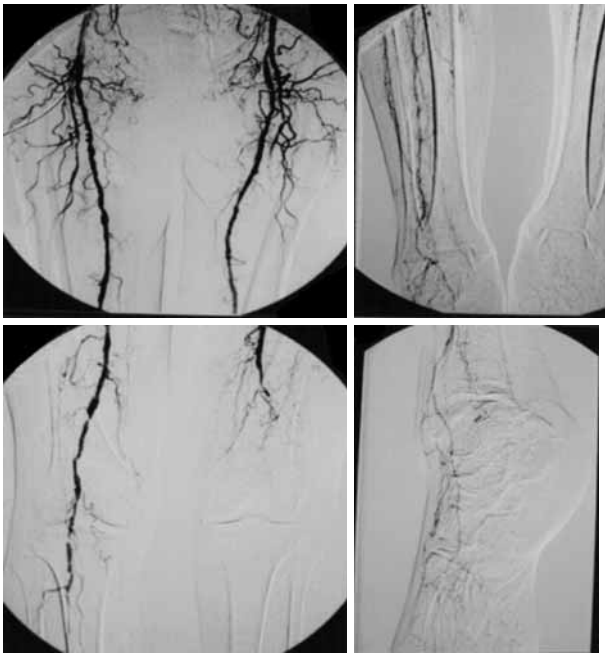

Fig. 1 Contrast arteriogram shows only small collateral vessels in the left lower extremity and no vessels suitable for use in a distal bypass procedure.

dl; number of platelets 18×10^4; BUN 48 mg/dl; creatinine 2.4 mg/dl; sHba1c 15.3%.

ECG: Left ventricular hypertrophy; sporadic supraventricular premature contractions.

Echo test of the cervical artery: Left, no significant stenosis; right, 70% stenosis of the internal carotid artery.

ABI: 0.15 (left), 0.61 (right).

Ultrasonic echo test of the heart: Good left ventricular function.

Aortography (**Fig. 1**): Left common iliac artery: 50% stenosis. Left superficial femoral artery occluded, left popliteal artery occluded. Left peroneal artery: multiple stenosis. Decrease in arterial blood flow was observed in the anterior tibial artery and in the lower leg. Blood flow of the left foot was extremely deficient, especially at the inner part surrounding the ulcers.

Findings in the retina: Diabetic retinopathy was found in both eyes (already treated with light coagulation).

Thermography: Lowering of the temperature was observed at the toes of the left foot. The temperature of the left foot was 1.5˚C lower than that of the right foot.

Transcutaneous oxygen pressure of at toes of the left foot: 20 mmHg (right toe: 75 mmHg).

Microbial examination of pus that came from ulcer: Methicillin-resistant staphylococcus aureus (MRSA).

Course of the disease after admission: Transplantation of bone marrow mononuclear cells (1×10^9) to the left lower leg was conducted in September, 2003 and transplantation of peripheral mononuclear cells (1×10^9) was conducted in October and November of 2003. Following these procedures, the API of the left lower leg improved from 0.2 to 0.3. However infection of the foot become aggravated and the wounds enlarged. Finally the infected 1st and 2nd toes had to be surgically debrided and amputated on February 6, 2004 (**Fig. 2**). Although morphine hydrochloride 200 mg/day was administered for pain at rest, control of the pain was difficult. The pain at the time of blood dialysis conducted three times a week was so strong that continuous subcutaneous injection of narcotic analgesics (morphine hydrochloride) was necessary to control it. As the infection was found to extend to the whole foot, amputation under the knee was indicated. At this point the patient and her family were informed of the ineffectiveness of the conventional treatment of diabetic gangrenes and ulcers and that amputation was the only method remained. At the same time all the methods reported at that moment in the whole world as regards the treatment were explained to the patient herself. As the patient expressed a strong desire to

receive the treatment with sterile maggots, application for implementation of the therapy was presented to the Committee of Standards of Official Conduct of Okayama University School of Medicine and approved. Maggots were kindly provided from Dr. R. Russel (Director, Medical Entomology, Institute of Clinical Pathology and Medical Research, Westmead Hospital, Westmead, NSW, Australia). Transport and medical application of maggots to patients in our University are granted by the Bureau of Drug and Medical Safety, Department of Health and Social Welfare, Okayama Prefecture Government Office. Safety to use those imported maggot to patients was assured by Dr. R. Russel. He reported every batch of second instara larvae of Lucilia sericata had been checked "disinfected" and had passed a microbiological check-up as described by R. A. Sherman et al. and were suitable for use in wound debridement. Second instara larvae of Lucilia sericata (maggot) were placed on the wounds of the patient (3–4 larvae/cm^2). The wound was covered with a plastic board with small holes (0.2 mm) to enable the respiration of larvae. The time needed for larvae to become pupae (about 5 days) was set as 1 course and 3 courses were repeated in succession (**Fig. 3**). The area of the wound before treatment of 38 cm^2 decreased markedly to 15 cm^2 after 1 week and 6 cm^2 after 3 weeks. Granulation tissue at the bottom of the wound exhibited a good scarlet colour and became liable to bleeding. After 3 months the ulcer became completely epithelialized and the patient was discharged from the hospital (**Fig. 4**). Rehabilitation was started 3 weeks after the treatment and walking with a stick became possible after 5 months.

Fig. 2 Before maggot debridement therapy.

Fig. 3 After maggot debridement therapy (2 weeks).

Fig. 4 After maggot debridement therapy (3 months).

Discussion

The fact that maggots are useful for the treatment of ulcers has been recognized from ancient times.[1-3] It is reported that the natives of Australia and doctors of traditional medicine of Burma used maggots to treat ulcers thousands of years ago. In Europe and the United States famous medical scientists such as Ambroise Pare (1510–1590) in France, and Baron Dominique-Jean Larrey, a French army doctor, described in their books the effectiveness of maggots for treatment of ulcers. W. S. Baer, Professor of Orthopaedics of Johns Hopkins University, who participated in the World War I as an army doctor and observed in the field the healing of wounds of the arms and legs with bred maggots, used maggots after coming home for treatment of patients with chronic infection of the bone (osteomyelitis) and reported on the effectiveness of the therapy. Thereafter, the therapeutic method has been used continuously in hospitals of Europe and United States and more than 100 papers were published during the period between 1930 and 1940. However, after the discovery of penicillin by A. Fleming in 1928, the therapeutic method using maggots was considered obsolete and gradually lost

popularity. This therapeutic method became rapidly forgotten by people after World War II as a result of the development of surgical operations during the war, appearance of various kinds of antibiotics and resultant decreases in various kinds of infectious diseases.[4] However, ulcers resistant to antibiotics developed in the 1990's due to excessive use of the agents and diseases that were prone to lead to diabetes mellitus, arteriosclerosis, ischemia and so forth increased and the state of these diseases became more and more serious. Increased occurrence of nonhealing ulcers brought about by such changes put the treatment of ulcers with maggots again on the stage as a therapeutic method.[1, 3] As the usefulness of the method was proved in 1995, the treatment established a firm position in the medical treatment of today with stress on evidence based medicine (EBM).[5] Maggots are now used widely all over the world in around 2000 medical institutes as maggot debridement therapy (MDT).[6-8]

The following 4 mechanisms have been reported to explain the effectiveness of maggots. However, precise mechanisms remain to be clarified.

1) Necrotic tissues of the wounds are liquefied by a large amount of digestive fluids maggots secrete and become absorbed and digested. As a result, the wounds become cleaned (debridement action).[9]

2) As ammonium compounds, calcium carbonate and allantoin secreted by maggots keep the wounds alkaline, the proliferation of bacteria is prevented and, as a result, the infection is controlled.[10]

3) Proteolytic enzymes secreted by maggots prevent the proliferation of bacteria.[11]

4) Growth of granulation tissues at the site of wounds is promoted due to the strengthening of local immune reactions.[12, 13]

Treatment with maggots is advantageous in that 1) anaesthesia is not necessary, 2) there are no apparent contraindications, 3) the treatment is cheap as compared with conventional methods of treatment (administration of antibiotics, surgical treatment and so forth)[8] and 4) simultaneous use of other methods of treatment is possible. Furthermore, the treatment has a long history of use in Europe and in United States and is used widely.[14] It is to be expected that the treatment will become widely used in Japan.

Drawbacks of the treatment with maggots are:

1) Danger that the maggots become settled in the site of treatment (myiasis) cannot be denied.[15-17]

2) As the maggots move around the site of ulcers, patients sometimes feel a sense of discomfort that something is creeping.[18]

3) Sometimes ulcers do not improve with the use of sterile maggots.[17]

In such cases it is necessary to stop the treatment at once and switch to conventional methods. It seems necessary to increase clinical experience in this country. At the same time, it is necessary to continue to study the mode of life of maggots/flies further.

It seems possible that the treatment mentioned above devised for treatment of nonhealing ulcers may become a new standard method also in Japan for treatment of serious cases of ulcers in the four extremities.[19] Furthermore, the treatment may possibly be useful 1) for treatment of ulcers caused by other diseases such as post-deep venous thrombosis,[20] collagen diseases and autoimmune diseases,[21] 2) for ulcers of the body other than the extremities such as the trunk, the buttocks,[22] the head,[23] and so forth, 3) for control of infection with bacteria resistant to ordinary antibiotics such as MRSA and so forth. Thus, further investigations and studies are needed.[24, 25]

While this represents the first case in which this treatment was carried out in Japan, a system has already been established in Europe and in the United States in order to make it possible for public institutions to supply sterile maggots.[26] The present study was made possible by obtaining sterile maggots from Australia. It is necessary to make a system in this country in order to make domestic supply of maggot possible.[27]

Conclusion

The treatment with sterile maggots was conducted for a patient of severe ischemic ulcers of the lower leg with progressed infarction (diabetic gangrene). The ulcers healed completely after 3 months. Although the method is already established for the treatment of severe ischemic ulcers of the arms and legs (diabetic gangrene) in Europe and in the United States, this is the first time that the treatment was performed in this country with good results. Thus, it was decided to report the present case in some detail.

We would like to express sincere thanks to Professor R. A. Sherman (University of California, Irving), Professor R. Russel and Ms. Merilyn J. Geary (Westmead Hospital, ICPMR, University of Sydney) for advice in conducting this project.

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