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Original Article

Clinical Study of Phlebitis Migrans and Incompetence of the Leg's Superficial Vein in Buerger Disease

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Three of four (75%) vein biopsy samples from four patients (all male, mean onset: age 33.0, mean biopsy: age 59.7) of chronic phase phlebitis migrans showed positive periodontal bacteria DNA under the PCR (polymerase chain reaction) method.

Of the 24 cases of Buerger disease (22 males, 2 females, mean onset: age 31.9, mean examination: age 62.6) that were investigated in our vascular laboratory, 65% of the patients suffered from moderate to severe varicose veins. Eight cases had a history of phlebitis migrans and three had an active ulcer or uncontrollable erosion in the foot. The rate of incidence was significantly higher than that of the well-matched control group. Other findings included one instance of deep vein thrombosis, and one instance of deep vein reflux.

We could suggest that some intractable ulcer or erosion cases of Buerger disease may be complicated by superficial vein incompetence or other deep vein insufficiency. We also we need to check Buerger disease patients with duplex for vein reflux and other insufficiencies. Treatment of the varicose veins (including elastic stockings) was effective for all of the patients. (English Translation of Jpn J Phlebology 2011; 22: 25–31.)

Keywords: phlebitis migrans, buerger disease, foot ulcer, superficial vein incompetence, varix surgery

Introduction

In the early 1900s, Leo Buerger emphasized the presence of phlebitis migrans in Buerger disease in addition to arterial lesions.[1)] The phlebitis is defined as a characteristic finding for the diagnosis of Buerger disease. However, the long term results of the phlebitis or duplex examination of the superficial or deep vein have not been reported.[2)] In addition, it is not recognized that some of the chronic ulcers came from incompetence of the venous system.

Materials and Methods

1) PCR (polymerase chain reaction) Study: Four samples of the pigmentation portion of the phlebitis migrans or relatively fresh phlebitic vein near the ulcer were collected from four patients. A well-established PCR method was carried out for periodontal bacterial DNA. The patients were all male, and the onset age was 33.0 years. Symptoms and conditions included major amputation (2 cases), post-arterial reconstruction (1 case), and ischemic ulcer (1 case). The mean age at harvest was 59.7 years. The same examination was performed on the

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Table 1 Results of periodontal examination and PCR detection of phlebitis migrans in patients with Buerger disease

Age	Sex	Onset age	Main condition	Sample sites	Oral cavity bacteria	Vein bacteria
53	M	32	BK	foot	Pg, Tf, Td, Pn	Pg, Td
62	M	34	AK	thigh	Pg, Tf, Td, Cr, Pi	Pg, Td, Cr, Pi
59	M	41	bypass	foot	Pg, Tf, Td, Cr, Pi	none
65	M	25	ulcer	leg	Pg, Tf, Td, Cr, Pi	Cr

All patients adapted on Shionoya's criteria for Buerger's disease.[3)]
PCR: polimerase chain reaction; Pg: Porphyromanas gingivalis; Tf: Tannerella forsythus; Td: Treponema denticola; Cr: Campylobacter rectus; Pi: Prevotella intermedia; Pn: Prevotella nigrescens; BK: below knee amputation; AK: above knee amputation; lt: light; rt: right

oral saliva. The diagnosis was defined using Shionoya's criteria.[3)]

2) Duplex Study: About 24 Buerger disease patients (mean age 62.6 years, range of ages was 29–76, male/female ratio: 22/2, and onset average age of 31.9 years) were studied. We checked pigmentation along the lower limbs' superficial veins, ulcers, or erosion, and the presence of the valve incompetence and the deep vein thrombosis.

We utilized a colored duplex device (XarioXG Toshiba Medical Systems) in the inspection and searched for the presence of reflux of the great and small saphenous vein, the vein diameter, the presence of the main incompetent perforating vein, and the presence of deep vein thrombosis in a standing position. The diagnosis was equal to a Study 1) using Shionoya's criteria.

As a control, 58 males (average age 64 ± 10 years) were randomly selected and examined for the frequency of the varicosity using the above-mentioned methods.

Results

1) Oral bacteria DNA in 3 of 4 examples was detected (75%). All presented with bacteria in the oral cavity. We detected four kinds of bacteria; Pg (Porphyromanas gingivalis), Td (Treponema dentiocola), Cr (Campylobacter) and Pi (Prevotella intermedia). In two cases, Pg, Td, and Cr were all present. Pi was present in one case. From the oral cavity, other periodontal bacteria were identified as well as the above-mentioned bacteria. Refer to **Table 1** for details.

2) Eight patients (33.3%) had pigmentation of a leg or a foot and were judged to have a history of phlebitis migrans. An ulcer, or erosion, was observed in three cases. There was no acute phlebitis case that was accompanied by redness or pain.

Reflux in a branch or a saphenous vein trunk was observed in 15 cases by ultrasonic investigation in the standing position (62.5%). Other studies showed deep vein reflux in one case and deep vein thrombosis in one case (the patient underwent varicosity surgery in another hospital). A quick glance reveals that there was little meandering varicosity except in two limbs among the incompetent veins.

Subjects with significant reflux of the saphenous veins wore elastic stockings and vein ligation and/or sclerotherapy was performed on the subjects with an ulcer or erosion. All were healed.

In about 58 control normal males (average age 64 ± 10 years), the lower limbs varicosity rate was 22% (13/58). No deep vein thrombosis, deep vein reflux, or perforated vein incompetence were observed.

There was a significantly lower limb varicosity rate in comparison with the Buerger disease patients ($p < 0.01$, Z test $Z = 3.86$).

Case 1

59 year-old male. Chief complaint: ulcer of left dorsum of the foot.

His first symptoms, a pale and fatigued foot, appeared at the age of 22. It was diagnosed as Buerger disease when he was 25 years old.

He underwent various treatments before receiving a left lumbar sympathectomy at age 29. He smoked over 20 cigarettes per day from age 20 to 35 and then gave up smoking.

He observed pigmentation and phlebitis like changes on both sides of the foot and leg from about age 45. His chief complaint was of left foot ulcers for 12 years, which became intractable. The ulcer is 4 × 6 cm wide and 1 cm deep (**Fig. 1**). He lost eight teeth and had dentures made. During the time that he smoked, he had gingivitis.

The angiography showed that three below-the-knee vessels that are occluded in the left and peroneal artery have been replaced with corkscrew-type collateral.

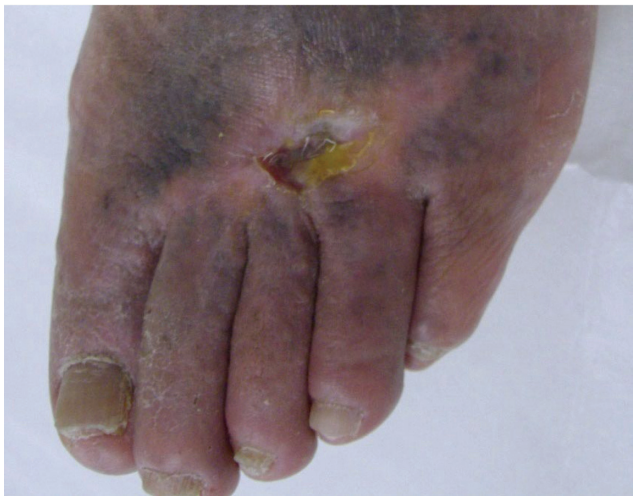
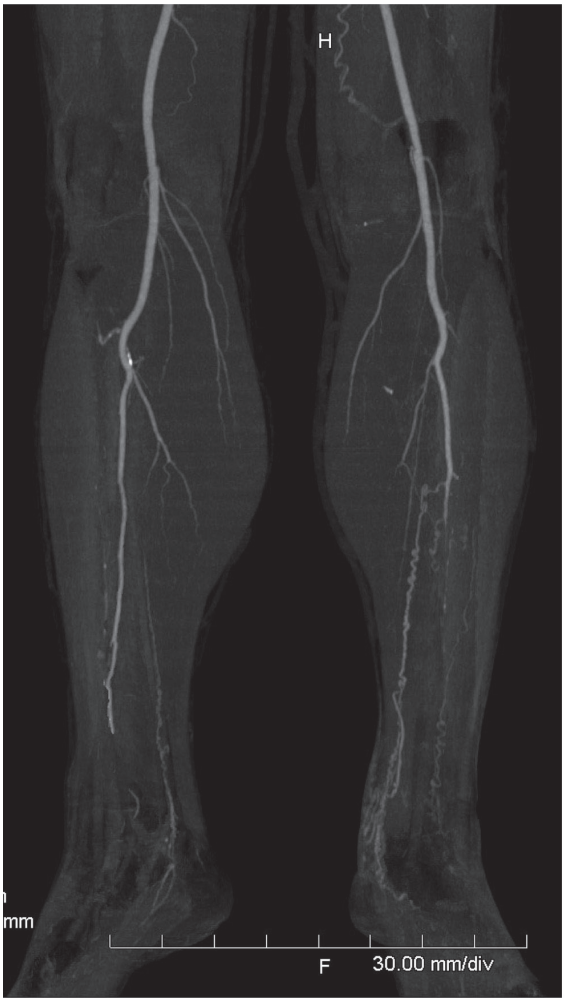


Fig. 1 A 59 year-old male complaining of ulcer on the dorsum of the left foot for 12 years. Skin pigmentation is remarkable. Photo taken in 2006.

In the right leg, posterior and anterior tibial arteries are occluded at the origin, and the peroneal artery is occluded at the ankle joint (**Fig. 2a**). The right and left ulnar arteries are occluded according to the Allen test. He has no diabetes, hyperlipidemia, or hypertension. The ABI is 1.38 on the right, and 0.73 on the left.

The color duplex findings on the right side reveal great and small saphenous vein reflux for the full length and in the left accessory, great saphenous vein reflux was demonstrated. The deep veins were normal (**Fig. 2b**).

The ulcer was reduced with the use of an elastic bandage and elastic stockings after the first examination by the vascular surgeon in April 2006. By August, the reflux had disappeared due to the combination of the great saphenous vein ligatures and sclerotherapy. The ulcer healed in September 2006 (**Fig. 3**). In 2007, he resumed hiking, his favorite activity, and continued to recover. He later was able to ski.



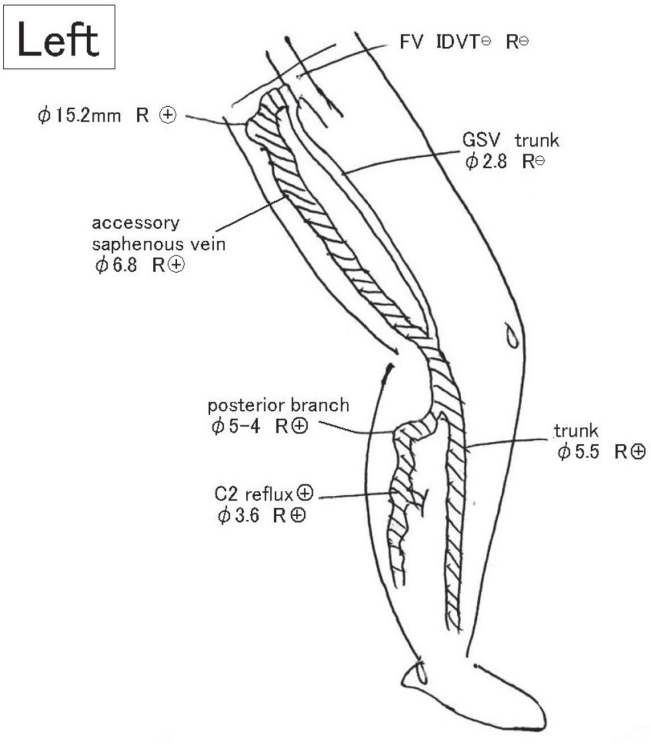


Fig. 2

a: Angiographyof the case showing typical Buerger disease.
b: Venous echogram showing reflux of the great saphenous vein.

a | b

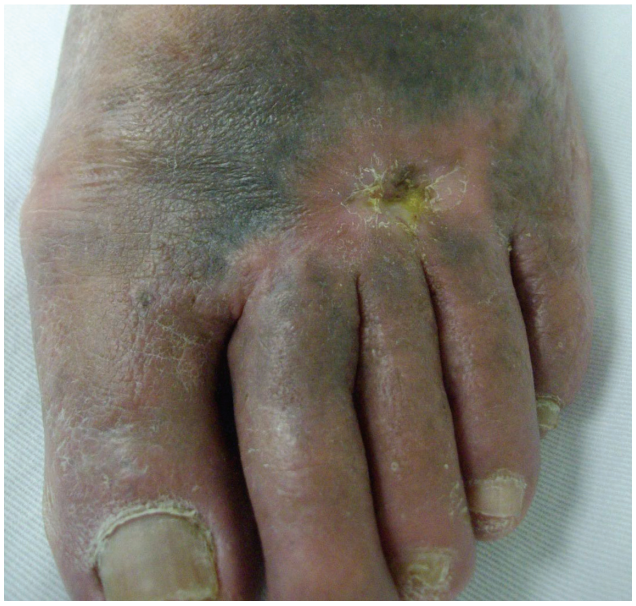


Fig. 3 Photo one month after saphenous vein ligation and sclerotherapy. The ulcer healed rapidly.

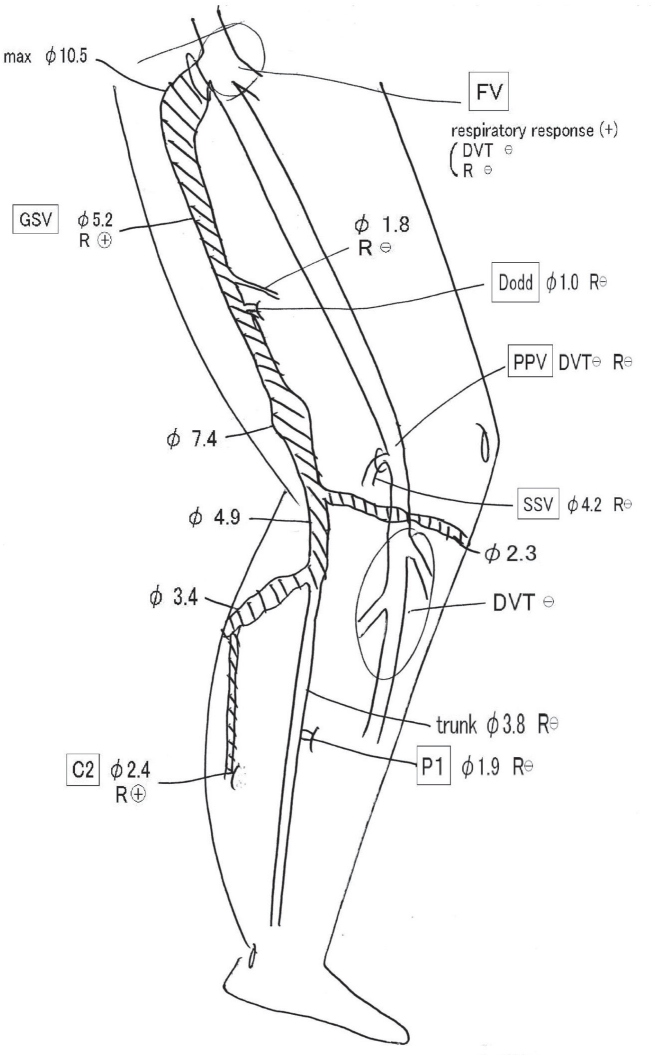


Fig. 4 A 29 year-old male. Arteriogram revealed typical Buerger disease and venous echogram showed severe reflux of great saphenous vein.

Lower limbs vein studies in three young Buerger disease patients (under age 55)

Case 2–1

A 29 year-old male diagnosed with Buerger disease at age 23. He smoked 80 cigarettes per day for five years. His chief complaint was intermittent claudication (100m).The ABI is 0.48 on the left, and the right is normal. The left superficial artery was occluded at the Hunter canal and the anterior tibial artery was occluded at the foot level. The duplex study showed left-side great saphenous vein reflux for almost the entire length and the saphenofemoral junction was 10.5 mm in diameter (**Fig. 4**). It rose to ABI0.79 with the use of elastic stockings and a 2 year ban on smoking from July 2010. He is on an anti-platelet agent. He had gingival bleeding while he smoked, but there was no damage to his teeth.

Case2-2

A 43 year-old male who developed Buerger disease, it is at age 28. He was a pack-a-day smoker for 10 years. His few symptoms stabilized after he stopped smoking in 2008. The ABI was in the normal range. As for the lower limb arteries, there is bilateral posterior tibial artery occlusion and anterior tibial artery narrowing with occlusion of the foot arteries.

The left ulnar artery is occluded. The trunk of the great and small saphenous veins showed no reflux, but a superficial branch vein revealed reflux. He can walk in the treadmill test for five minutes, but there is a feeling of wrongness in the big toe. He takes no medicine for the condition.

Case 2–3

A 55 years old male who developed Buerger disease, it is at age 23. He had a left below-the-knee amputation and amputations of the right big toe and third toe afterward. An angiography showed femoral and popliteal artery occlusion on the left and on the right, anterior tibial artery occlusion, and narrowing of the posterior tibial artery. He has few surviving healthy teeth in his lower and upper jaws (**Fig. 5**). There was right leg pigmentation and a 3 × 4 cm ulcer/erosion in the medial foot, and erosions

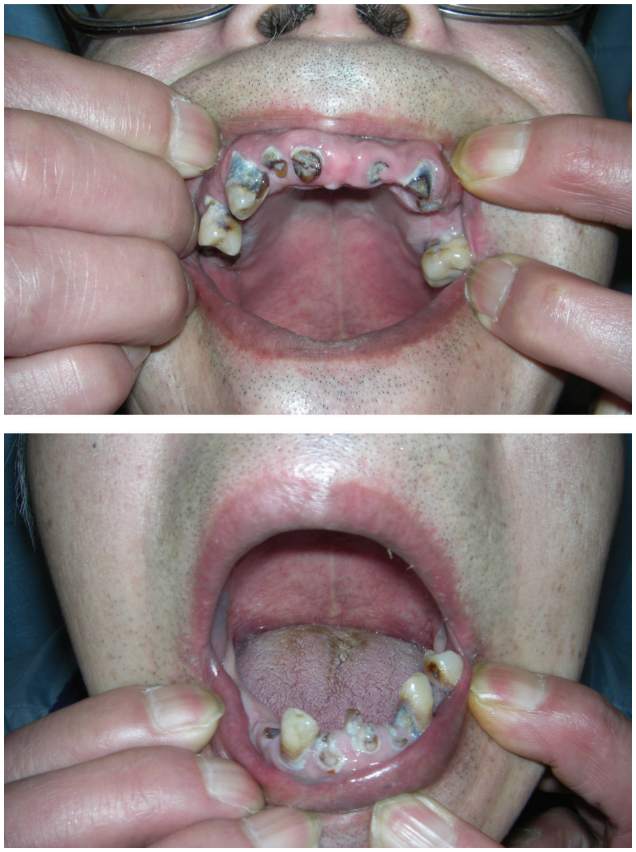


Fig. 5 A 55 year-old male showing severe dental condition since age 23 when his symptoms started. Venous reflux demonstrated in the great and short saphenous veins with wide wet erosion which healed quickly after venous ligation and sclerotherapy were performed.

between the second and third toe and the fourth and fifth toe. The duplex study showed reflux in the great and small saphenous veins. Saphenous vein ligations and sclerotherapy were performed in December 2009. The result was good, and the ulcer and erosion healed in January 2010. He is receiving oral care from a periodontal dentist.

Discussion

Phlebitis migrans is the characteristic finding that Buerger emphasized, for distinguishing Buerger disease[1] from juvenile arteriosclerosis. Furthermore, he reported that a thrombus is seen in high frequency in not only the superficial vein, but also in a deep vein. Shionoya regards the frequency of examinations for Buerger disease as around 40%, and because of the low frequency, either arterial occlusion of the upper extremity or/and phlebit's migrans determines it to be one of the diagnostic criteria. In his criteria, phlebitis is not an essential point for diagnosis.[3]

When the reddish phlebitis portion is removed surgically and is viewed under a microscope, inflamed cells and giant cells are seen. The phlebitis is seen below the knee and mostly around the ankle.[4] On the other hand, pigmentation can be from various causes, though it is not diagnosed as phlebitis in a Buerger disease patient.

It is not clear whether phlebitic veins are patent or occluded after the diagnosis of phlebitis.[5] Possibly related to the decrease of cases in developed countries, the report on the reflux of the vein examined by duplex or the color Doppler methods is not found in the literature. In examinations only by venography performed in the 1970s, abnormalities were reportedly observed in around 60% of the cases.[2] Still further, because the acute phase of phlebitis seemed to involve infection, Buerger doubted infection, but was unable to prove it.[1] Our results suggested that the presence of periodontal bacteria in the veins destroys the vein and lead to the venous valve dysfunction. However, a 41 year-old male patient showed phlebitis migrans on the great saphenous vein. The ultrasound examination revealed that the saphenous vein was occluded. This may mean that the pathogenesis of the venous reflux has two sources; namely direct damage or indirect valve damage by thrombus.

Sakaguchi suggested that the phlebitis lead to expression of the arterial lesion and thought it was connected to etiology discovery.[6]

In 2002, we found and reported that oral bacteria DNA is present in the occluded arterial part of Buerger disease for the first time and also reported elevation of IgG titer to periodontal pathogens.[7,8] Furthermore, when we discovered that oral bacteria enters platelets and forms lumps, we were able to show that oral bacteria are carried from the oral cavity into the circulating blood system safely.[9]

Our hypothesis is that the main cause is an embolism of aggregated mass in a platelet, including oral bacteria; young people, even heavy smokers, have healthy endothelial tissue, which makes it difficult to explain that the main cause is an adhesive or endothelial problem of a young man. Interestingly, the onset process of phlebitis or systemic occlusion of the entire body is easily explained using this hypothesis (**Fig. 6**).[9–14]

It is already well known that smoking causes great harm directly to the periodontal area. It is said there is no effective treatment for the diseased teeth of a smoker.[10,11,13,14] Smokers suffer from weak bacterial infections that keep bacteria around the teeth; the bacteria

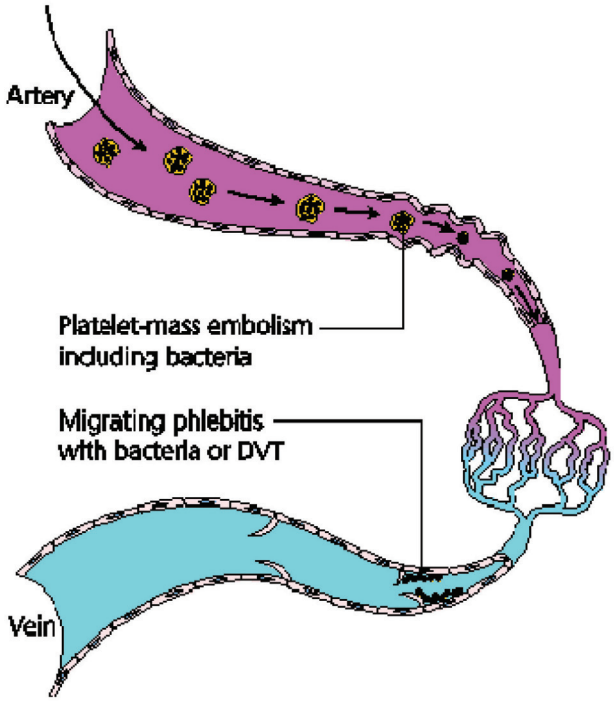


Fig. 6 Hypothesis for the development of Buerger disease, deep vein thrombosis, and phlebitis migrans.

enter the platelets and is transported around the body. It was not surprising to find extra-peripheral arterial involvement, such as cerebral, coronary, visceral arteries, and so on with Buerger disease-like occlusions.[5] It seems that fingers and toes easily become symptomatic and small embolisms occur in comparison with the other bigger organs containing phagocytes.

As a result, I can understand how oral bacteria, which passe through a capillary, may cause acute inflammation in a vein of the foot, and that the various kinds of inflammation reactions in the phlebitis migrans have been observed and reported.[15–17] It is thought that oral bacteria will move up the foot vein slowly, destroying the vein valve with an inflammatory reaction.[18] There were few cases this time for a DNA PCR study, but disease from oral bacteria was still found in 75% of the phlebitis migrans. By the way, Kurihara reported that the frequency of oral bacteria expression for the primary varicose veins is 48%.[15]

We would like to further discuss recent cases and also our results, in which we observed the valve function. The primary varicosity is developed when a valve is incompetent, but nobody knows how and when it progresses from which part. It is said that phlebitis migrans of Buerger disease appears in the leg or the ankle region. Our study suggested that saphenous vein incompetence is mainly observed but branch vein incompetence is also present. In addition, three cases showed an ulcer and erosion. One ulcer was deep, and in this case (**Fig.s 1** and **3**) was treated as an ischemic ulcer by his personal physician for a long time. Furthermore, even if there is reflux, the meandering of the vein seems to be characteristically unremarkable. The genetic differences that we examined, as well as the smoking frequency of males, will explain why men are so much more vulnerable than women.[19]

Generally, for ischemic lower limbs, elastic stockings are considered to be contraindicated. However, when the arterial condition becomes chronic, elastic stockings were effective in alleviating symptoms. And from personal experience, the ankle-brachial pressure index should be near or greater than 0.7 and there should be no acute ischemic signs or symptoms in the toes.

Ligation of the incompetent vein, and foam sclerotherapy are effective, too. However, our job is to sufficiently understand how to treat the ischemic limb and to provide an adequate explanation to the patient.

Conclusion

Three out of four venous samples of phlebitis migrans showed oral bacterial DNA by PCR. With 24 Buerger disease patients, moderate varicosity with vein incompetence by duplex was observed in 65%. Of those, three patients demonstrated a chronic ulcer or erosion. The ulcer or erosion was healed completely by the reflux treatment. As for Buerger disease, the subject of the treatment is utilized only for artery ischemia. However, in our hypothesis, the observation of a vein is necessary.

References

1) Buerger L. The association of migrating thrombophlebitis with thrombo-angeitis. Internat Clin 1909; **19**: 84-105.
2) Chopra BS, Zakariah T, Sodhi JS, et al. Thromboangitis obliterans: a clinical study with special emphasis on venous involvement. Angiology 1976; **27**: 126-32. [Medline] [CrossRef]
3) Shionoya S. Venous involvement. Edited by Shionoya S. Buerger's disease; Pathology, diagnosis, and treatment. Univ. of Nagoya Press 1990 Nagoya. pp 71–73.
4) Ishikawa K. History and future view of Buerger disease. Genndaiiryou 1976; **8**: 1285-9. (in Japanese)
5) Shigematsu H, Shigematsu K. Factors affecting the long-term outcome of Buerger's disease (thromboan-

giitis obliterans). Int Angiol 1999; **18**: 58-64. [Medline]
6) Sakaguchi S, Urano T, Watabiki H, et al. Coagulo-immunological study of Buerger disease—Special attention on the phase of the disease (4th report). 1984 Report for systemic vascular research project of the Ministry of Health and Labor. 1985: pp 202–206. (in Japanese)
7) Iwai T, Inoue Y, Umeda M, et al. Oral bacteria in the occluded arteries of patients with Buerger disease. J Vasc Surg 2005; **42**: 107-15. [Medline] [CrossRef]
8) Chen YW, Iwai T, Umeda M, et al. Elevated IgG titers to periodontal pathogens related to Buerger disease. Int J Cardiol 2007; **122**: 79-81. [Medline] [CrossRef]
9) Li X, Iwai T, Nakamura H, et al. An ultrastructural study of Porphyromonas gingivalis-induced platelet aggregation. Thromb Res 2008; **122**: 810-9. [Medline] [CrossRef]
10) Iwai T, Inoue Y, Li X, et al. Weak oral bacteria and vascular lesions. J Jpn Coll Angiol 2008; **48**: 185-91. (in Japanese with English abstract)
11) Iwai T, Inoue Y, Umeda M, et al. Buerger disease, smoking and periodontitis. Ann Vasc Disease 2008; **1**: 80-4. [CrossRef]
12) Iwai T. Buerger disease. Current Ther 2008; **26**: 785-9. (in Japanese)
13) Chen YW, Umeda M, Nagasawa T, et al. Periodontitis may increase the risk of peripheral arterial disease. Eur J Vasc Endovasc Surg 2008; **35**: 153-8. [Medline] [CrossRef]
14) Iwai T. Recent topics and treatment for Buerger disease. Rinsho to Kenkyu 2005; **82**: 1170-2. (in Japanese)
15) Kurihara N, Inoue Y, Iwai T, et al. Oral bacteria are a possible risk factor for valvular incompetence in primary varicose veins. Eur J Vasc Endovasc Surg 2007; **34**: 102-6. [Medline] [CrossRef]
16) Sayer GL, Smith PD. Immunocytochemical characterisation of the inflammatory cell infiltrate of varicose veins. Eur J Vasc Endovasc Surg 2004; **28**: 479-83. [Medline] [CrossRef]
17) Ono T, Bergan JJ, Schmid-Schonbein GW, et al. Monocyto infiltration into venous valves. J Vasc Surg 1998; **27**: 158-66. [Medline] [CrossRef]
18) Iwai T. Buerger disease: new evidence. Davies AH, Mitchell AWM, edit. Vascular and endovascular surgery highlights 2008–09, Health press 2009 Oxford pp 93–98.
19) Chen Z, Takahashi M, Naruse T, et al. Synergistic contribution of CD14 and HLA loci in the susceptibility to Buerger disease. Hum Genet 2007; **122**: 367-72. [Medline] [CrossRef]