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Lower Limb Pain Caused by Insufficient Muscular Microcirculation

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Abstract:	Lumbar spinal surgery is a common procedure to treat low back pain. To remark that lower limb perfusion insufficiency may induce the similar syndrome as neuropathic pain, it was surveyed 1,076 cases post spinal surgery within 5 years, in which 51 cases had no obvious improvement 3 months after surgery, 27 cases received second operation because of instability, inadequate decompression and wrong level, and the other 27 cases including 3 cases after twice spinal surgeries were enrolled. Physical examinations were presented with atypical neuropathic pain and muscle wasting at single lower limbs which deteriorated with long distance walking. Computed tomography or magnetic resonance imaging scan were studied including the neural structure and lower limbs angiography. The picture showed degenerative change without definite neural structural compression or vascular occlusion. There is also no significant finding of electrodiagnostic study. Rest radionuclide study of lower limb muscle and myocardium was performed in these 27 cases using Thallium-201. All patients presented 9 - 24% (avg. 14%) muscle perfusion difference compared with two legs. Most of peripheral arterial occlusion disease cases present the symptoms with ischemic pain and vascular claudication. In the study, the patients present not only ischemic limb but also the bizarre symptoms, such as low back pain with or without radiating root pain and sensory disturbance. Physicians should be aware of the possibility of lower limb pain caused by lower perfusion syndrome.
Response to Reviewers:	To: Professor Editor Indian Journal of Surgery E-mail: angie.malanday@springer.com Dear Professor Editor, Thank you for your letter dated on Feb. 27, 2012 regarding to our manuscript entitled “Lower Limb Pain Caused by Insufficient Muscular Microcirculation (Ms. No. IJOS-D-12-00166)”. Thanks for the Editors and Reviewers’ valuable comments. We have tried to revise our manuscript in response to the comments as attachment.

	Your further editorial consideration will be very much appreciated. Best regards, Yung-Hsiang Chen, Ph.D. Graduate Institute of Integrated Medicine China Medical University Taichung 40402, Taiwan E-mail: yhchen@mail.cmu.edu.tw Reviewer(s)' Comments to the Author: Reviewers' comments: The Indian Journal of Surgery is not a specialized Spine journal. Please modify your manuscript to include vascular component and exclude majority of spine content. We would appreciate a trim manuscript, with vascular focus. Response: Thank you so much for the comments, we fully agree with your opinion. We have tried to revise our manuscript in response to the comments as attachment. Your further consideration will be very much appreciated.

*Title Page

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Lower Limb Pain Caused by Insufficient Muscular Microcirculation

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Running Title: Lower Limb Perfusion Insufficiency and FBSS

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Abstract

Lumbar spinal surgery is a common procedure to treat low back pain. To remark that lower limb perfusion insufficiency may induce the similar syndrome as neuropathic pain, it was surveyed 1,076 cases post spinal surgery within 5 years, in which 51 cases had no obvious improvement 3 months after surgery, 27 cases received second operation because of instability, inadequate decompression and wrong level, and the other 27 cases including 3 cases after twice spinal surgeries were enrolled. Physical examinations were presented with atypical neuropathic pain and muscle wasting at single lower limbs which deteriorated with long distance walking. Computed tomography or magnetic resonance imaging scan were studied including the neural structure and lower limbs angiography. The picture showed degenerative change without definite neural structural compression or vascular occlusion. There is also no significant finding of electrodiagnostic study. Rest radionuclide study of lower limb muscle and myocardium was performed in these 27 cases using Thallium-201. All patients presented 9 – 24% (avg. 14%) muscle perfusion difference compared

with two legs. Most of peripheral arterial occlusion disease cases present the symptoms with ischemic pain and vascular claudication. In the study, the patients present not only ischemic limb but also the bizarre symptoms, such as low back pain with or without radiating root pain and sensory disturbance. Physicians should be aware of the possibility of lower limb pain caused by lower perfusion syndrome.

Keywords: Lower limb perfusion insufficiency; Microcirculation; Neurogenic claudication; Failed back surgery syndrome

Introduction

Lower limb perfusion insufficiency, the most common form of peripheral arterial occlusion disease (PAOD) [1], due to atherosclerosis is a clinical problem that has no effective medical therapy [2]. When significant atherosclerotic peripheral arterial disease and neurogenic claudication occur together in the lower limb, neuropathy may mask the typical symptoms and signs of lower limb ischemia, thus confounding diagnosis [3]. The diagnostic information gained from symptom enquiry, including claudication, as well as clinical findings (e.g. absent pulses and prolonged capillary refill times) can often be misleading in patients [4].

Failed back surgery syndrome (FBSS) is clinically defined as persistent or recurrent pain, mainly in the lower back and/or legs, even after previous anatomically successful spinal surgery [5]. Some of the anatomic pain source is unclear, but lower limb perfusion insufficiency may induce the similar syndrome as neuropathic pain [6]. Because the success can be measured in a variety of ways, reports of surgical failure rates vary widely. In many series, the overall success rate exceeds 80%. However, some degree of back pain can persist for years in up to 70% of patients after discectomy [7]. The success rates fall to around 30% after a second back surgery, 15% after the third, and to 5% after the fourth surgery [8]. It is a disabling condition that affecting approximately 30% of spinal surgery patients and it is difficult to treat these

patients with conservative therapy [5, 9]. Patients with FBSS typically suffer many associated problems, including operations of the lumbosacral area, depression and sleeping problems, family and economic problems, high-dose opioid dependence, and low probability that further surgery will result in pain relief [10]. Although FBSS involves many controversies, it defines a common and difficult clinical situation that deserves particular attention.

Many physicians have declared that pathophysiologic and anatomic diagnosis is critical to the success in FBSS [8, 11, 12], however, diagnostic algorithms generally fall into two integrated approaches including temporal and anatomic. Immediate failure or continuation of preoperative symptoms is ascribed to wrong diagnosis, technical error, or poor patient selection primarily because of psychosocial factors [13]. Temporary relief followed by pain recurrence within a few weeks of surgery suggests infection. Longer-term failures may be caused by loss of intervertebral stability or spinal stenosis, either at the previous surgical site or at adjacent levels [8]. Data on the causes of failed back surgery are limited. When applying these principles of diagnosis to the various reviews of causes of FBSS, it is clear that most of the time an exact diagnosis is unclear. Many authors have advised against a monolithic, solely anatomic diagnosis and favor a biopsychosocial assessment that includes anatomy with considerations of behavioral elements ranging from fear avoidance to secondary

gain [14].

There are few papers to remark that lower limb perfusion insufficiency may induce the similar symptom as neuropathic pain [15]. Patients and primary physicians now need a more sophisticated understanding of diagnostic possibilities, treatment options, range of surgical techniques, and expected results. The aim of this study is addressed on the symptom similarity between lower limb insufficient perfusion and neurogenic claudication for the prevention of following possible FBSS.

Methods

Patients

The study was approved by the Institutional Review Board of Chung Shan Medical University Hospital. All patients provided were informed the written consent before participating. 1,076 cases with post spinal surgery within 5 years were surveyed. 51 cases had no obvious improvement 3 months after surgery; 27 cases received second operation because of instability, inadequate decompression, or wrong level; and the other 27 cases including 3 cases after twice spinal surgeries were enrolled in this study. The mean age and body mass index (BMI) of these patients were 62.4 ± 10.0 (range 41 – 82) years and 27.9 ± 3.5 (range 23 – 39) kg/m^2, respectively. Males comprised 51.9% of these patients. The demographic data including mean age, gender, BMI, diabetes, smoking, other related diseases, and surgical area are shown in **Table 1**. Physical examination presented with atypical neuropathic pain and muscle wasting at single lower limbs which deteriorated with long distance walking. Computational tomography (CT) or magnetic resonance imaging (MRI) scan was utilized for studying the neural structure and lower limbs angiography. Radiographic measurements were made by technicians “blind” to treatment group status, with variability controlled via inter- and intra-observer comparisons [16].

Myocardial and Lower Limb Scintigraphy

Stress Thallium-201 myocardial scintigraphy was performed on all patients. Briefly, ECG was performed during graded exercise testing on a bicycle ergometer. The results of exercise ECG were interpreted as negative if there were no ischemic changes during exercise [17]. Single-photon emission computed tomography (SPECT) imaging was performed within 5 – 10 min after the injection of Thallium-201, with the patient in the supine position, using a single-head, wide-angle-lens gamma camera and a low-energy, high-resolution collimator.

Additionally, patients were instructed to remain in the supine position for lower limb Thallium-201 scanning in the same run after exercise myocardial SPECT imaging [18]. Three irregular areas of interest were drawn using a trackball around the entire buttock, thigh, and calf on one side. Symmetrical areas of interest were automatically generated. No correction was made for background activity. Total counts in each of the three levels were then determined by computer, and right-to-left ratios were calculated at each level. A ratio < 0.9 or > 1.1 at one or several levels defined an abnormal result of lower limb scintigraphy for the level considered, as reported previously [17, 19]. The perfusion defects were obvious in some patients, but counting was always performed.

Statistical Analysis

The statistical analyses were performed using SPSS software (SPSS, Chicago, IL). The data were expressed as *n* or means ± SD, and the correlations with the scintigraphy variable were tested by the Mann-Whitney nonparametric test. *P* values were two-sided; a value <0.05 was considered statistically significant.

Results

Table 1 presents the demographic data and clinical characteristics for patients with FBSS. The demographic data includes mean age, gender, BMI, diabetes, smoking, other related diseases, and surgical area. There is also no significant finding of electro-diagnostic electromyography (EMG) and nerve conduction velocity (NCV) study (Table 1). In the quantified rest radionuclide study of lower limb muscle and myocardium using Thallium-201, it was compared the muscle perfusion difference between two lower limbs each other. All patients presented 9 – 24% (average 14%) muscle perfusion difference compared with two legs. Table 2 shows the neuropathic and vascular features that were found from the patients.

Angiograms of the superficial femoral artery from a 61 years-old male (patient No. 11) with right lower limb pain were shown in Figure 1A. No vascular occlusion was found in Angiography. However, mean total counts of lower limb Thallium-201 scanning and regional right-to-left ratio were shown. The right-to-left ratio for perfusion difference of legs was 0.82/1. The test showed a defect of perfusion in the right calf (arrow) (Figure 1B). The lower limb scintigraphy Thallium-201 scanning was abnormal in almost 27 patients. Figure 1C shows degenerative change without definite neural structural compression or vascular occlusion.

Discussion

This present study addressed on the symptom similarity between lower limb insufficient perfusion and neurogenic claudication for the prevention of following possible FBSS. For the past two decades, researchers and practitioners have used the phrase FBSS to describe patients with chronic disabling lower back pain with or without leg pain after one or more spinal surgeries [5]. However, studies with relevant outcome are rarely diagnosis specific, and high level research studies comparing surgical and nonsurgical approaches to FBSS studies have not been published to date [20].

Most of PAOD cases present the symptoms with ischemic pain and vascular claudication [21]. However, these symptoms, usually, happen in the stage of significant loss of vascular patency. Sonogram and angiogram are good modalities for diagnosis of PAOD. The majority of patients with early stage atherosclerotic vascular change developed similar symptom as well, although blood circulation is normal. Skeletal muscle perfusion scan provides the information at the level of a microcirculation (in fact at tissue oxygenation). In the present study, the patients present not only ischemic limb but also the bizarre symptoms, such as low back pain with or without radiating root pain and sensory disturbance. These symptoms are hard to discriminate spinal problem from neuropathy. Many spinal surgeons try to

emphasize the discrepancy between two categories; nevertheless, the clear-cut separation is not so easy [22]. The peak incidence of patients with insufficient lower limb perfusion is 6^{th} - 7^{th} decay, but they probable have spinal disorder as well. Through the symptomatic expression and image finding even MRI or CT scan, surgeons might make incorrect diagnoses and subsequent wrong decisions. The cause of vascular stenosis even obstructs related systemic disorder such as hyperlipidemia, obesity, DM, hypertension or renal insufficiency. Neuropathic pain can happen in any age, it is not closed to systemic disease. Once aged patients suffer from lower limb disability and no sufficient evidence to support the lesion originated from neural structure, muscle perfusion assessment should be considered for study.

The FBSS label has been used primarily to connote poor prognosis and to warn patient and practitioner accordingly in making further treatment choices. In one review, initial success rates exceeding 50% fell to around 30% after the second surgery, to 15% after the third, and to 5% after the fourth [23]. From the nonoperative perspective, rehabilitation may have less success in reducing pain reports in postsurgical patients compared to their nonoperated peers, even when most physical capacities improve equally [8]. Although diminished prognosis after an unsuccessful operation may be conceded, some authors caution against inappropriate discouragement and even distraction from the critical clinical tasks of diagnosis and

treatment [24, 25].

Back surgery is not the final common pathway for everyone with persistent back pain. It offers specific therapy for specific anatomical derangements associated with specific complexes of symptoms [26], When surgery ranges beyond carefully defined situations, disappointed patients are likely to be expected. A generation ago, “back surgery” usually meant removing the offending portion of a herniated disk [10], Time has changed, and both the indications and the surgical techniques have expanded enormously. Indeed, clinical science has struggled to keep pace with innovation, creating uncertainties about the efficacy and safety of some new surgical techniques. Often, internists are asked for advice by these challenging patients but are unfamiliar with the conditions leading to back surgery, the types of back surgery, and the best approaches to diagnosis and management [13].

Conclusions

Muscle scan can demarcate the perfusion difference between two lower limbs. Many Spinal surgeons perform the spinal surgery according to the complaints from patients and the radiological finding. However, these symptoms are hard to demarcate from ischemic pain (Table 3). Physicians should be aware of the possibility of lower limb pain causing by lower perfusion syndrome.

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Conflict of interest statement

There are no conflicts of interest.

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Figure Legends

Figure 1. A 61 year-old male with right lower limb pain. (A) The angiography shows no vascular occlusion. (B) MRI shows the disc herniation at L4-5 and L5-S1. (C) Muscle perfusion scan shows lower perfusion of right limb.

Table 1

Table 1. Demographic Data of Patients with FBSS

No.	Age	Sex	BMI	DM	Smoking	Related diseases	Surgical area	EMG or NCV	Perfusion difference (R/L)
1	41	F	31	No	Yes	CAD	L5-S1	Non-specific	0.84/1
2	58	F	39	Yes	Yes	Hyperlipidemia	L2-3-4-5	Non-specific	0.76/1
3	82	M	27	Yes	Yes	Renal insufficiency	L3-4-5	L5 radiculopathy	1/0.88
4	74	M	31	No	Yes	Renal insufficiency	L3-4-5-S1	Non-specific	0.90/1
5	61	F	24	Yes	No	CAD	L5-S1	Non-specific	1/0.90
6	63	F	28	Yes	No	Hyperlipidemia	L2-3-4	Non-specific	1/0.82
7	63	M	34	Yes	Yes	Hypertension hyperlipidemia	L2-3-4-5	L5 radiculopathy	0.86/1
8	71	M	27	No	Yes	CAD, Renal insufficiency	L2-3-4-5	Non-specific	1/0.91
9	55	F	29	Yes	No	Hypertension Hyperlipidemia	L5-S1	Non-specific	0.77/1
10	47	M	25	Yes	Yes	CAD, Renal insufficiency	L3-4-5	Non-specific	1/0.86
11	61	M	32	Yes	Yes	CAD, Renal insufficiency Hypertension	L4-5-S1	Non-specific	0.82/1
12	60	F	23	No	No	CAD Hyperlipidemia	L5-S1	Non-specific	1/0.90
13	51	M	26	No	Yes	Hyperlipidemia	L4-5	Non-specific	0.89/1
14	67	M	25	No	Yes	CAD Hyperlipidemia	L2-3-4	L4 radiculopathy	1/0.90
15	74	F	28	Yes	No	CAD Hyperlipidemia Renal insufficiency	L2-3-4-5	Non-specific	1/0.85
16	43	F	23	No	No	Hyperlipidemia Renal insufficiency	L4-5-S1	Non-specific	1/0.90
17	66	M	30	Yes	Yes	CAD Hyperlipidemia	L3-4-5-S1	L5 radiculopathy	1.0/0.88
18	58	F	28	Yes	Yes	CAD Hyperlipidemia Hypertension	L4-5-S1	Non-specific	0.88/1.0
19	65	M	28	Yes	Yes	CAD Hyperlipidemia Hypertension	L3-4-5	Non-specific	1.0/0.86
20	73	M	26	Yes	Yes	CAD Hyperlipidemia Hypertension	L3-4-5-S1	Non-specific	0.83/1.0
21	64	F	25	Yes	No	CAD Hyperlipidemia Hypertension	L4-5	Non-specific	0.90/1.0
22	69	F	27	Yes	No	CAD Hypertension Renal insufficiency	L4-5-S1	Non-specific	1.0/0.90
23	54	M	30	No	Yes	CAD	L2-3	Non-specific	1.0/0.88
24	78	M	24	Yes	Yes	CAD Hypertension Renal insufficiency	L4-5-S1	Non-specific	0.81/1.0
25	62	F	28	Yes	No	Hypertension Renal insufficiency	L4-5	Non-specific L5 radiculopathy	1.0/0.83
26	66	F	26	Yes	No	Hyperlipidemia Hypertension CAD	L4-5-S1	Non-specific	0.89/1.0
27	58	M	28	Yes	Yes	Hyperlipidemia Hypertension CAD	L5-S1	Non-specific	1.0/0.90

Table 2. Neuropathic and Vascular Features in Patient with FBSS

Findings	Neuropathic Features	Vascular Features
Pain type and location	Lower limb pain and paresthesias (23/27) Except: 4,7,15,21	Calf muscle cramping (20/27) Except: 4,5,8,13,16,21,23
Radiation pain	Proximal to distal (12/27) 2,5,9,10,12,16,17,21,22,23,26,27	Distal to proximal (11/27) 1,3,6,7,8,11,13,15,18,20,24
Symptom worse		Exercise (27/27)
Walking distance		Constant (22/27) Variable (5/27) 4,5,8,12,27
Relief	Resting (16/27) Except: 1,2,3,6,9,15,17,18,19,20,22 Lumbar flexion (12/27) 1,2,4,6,7,11,15,17,18,22,23,27	Cessation of lower limb exercise (25/27) except: 2,7 Night resting pain (9/27) 1,2,3,6,7,9,15,19,20
Back pain		(19/27) Except: 4,5,10,13,14,16,21,26
Hill walking	Downhill walking (9/27) 3,5,9,11,12,15,19,21,25	Uphill walking (18/27)
Lower limb appearance		Normal
Pulsation		Diminished (1/27) 24 Normal (26/27)
Range of motion of lumbar spine		13 (diminished pain): 2,4,6,9,11,14,15,17,19,20,22,24,26
Non-invasive angiographic study (CT or MRI)		No occlusion of peripheral artery (27/27)

Table 3. Clinical Features Differentiating Neurogenic Claudication and Vascular Claudication

Findings	Neurogenic Claudication	Vascular Claudication
Pain type and location	Lower extremity aching, burning, paresthesias	Calf tightness and cramping
Radiation	Proximal to distal	Distal to proximal
Exacerbation	Lumbar extension including standing, and upright exercise	All lower extremity exercise
Walking distance	Variable	Constant
Relief	Lumbar flexion and rest	Cessation of lower extremity exercise
Back pain	Common	Rare
Bicycle/treadmill test	Bicycle generates minimal symptoms, treadmill generates symptoms	Bicycle and treadmill generate symptoms
Hill walking	Walking uphill generates minimal symptoms, walking downhill generates symptoms	Waling uphill and walking downhill generate symptoms
Lower extremity appearance	Normal	Vascular changes including hair loss, toenail atrophy, edema
Pulses lower extremity	Normal	Diminished
Lumbar range of motion	Diminished, painful	Normal

Figure 1
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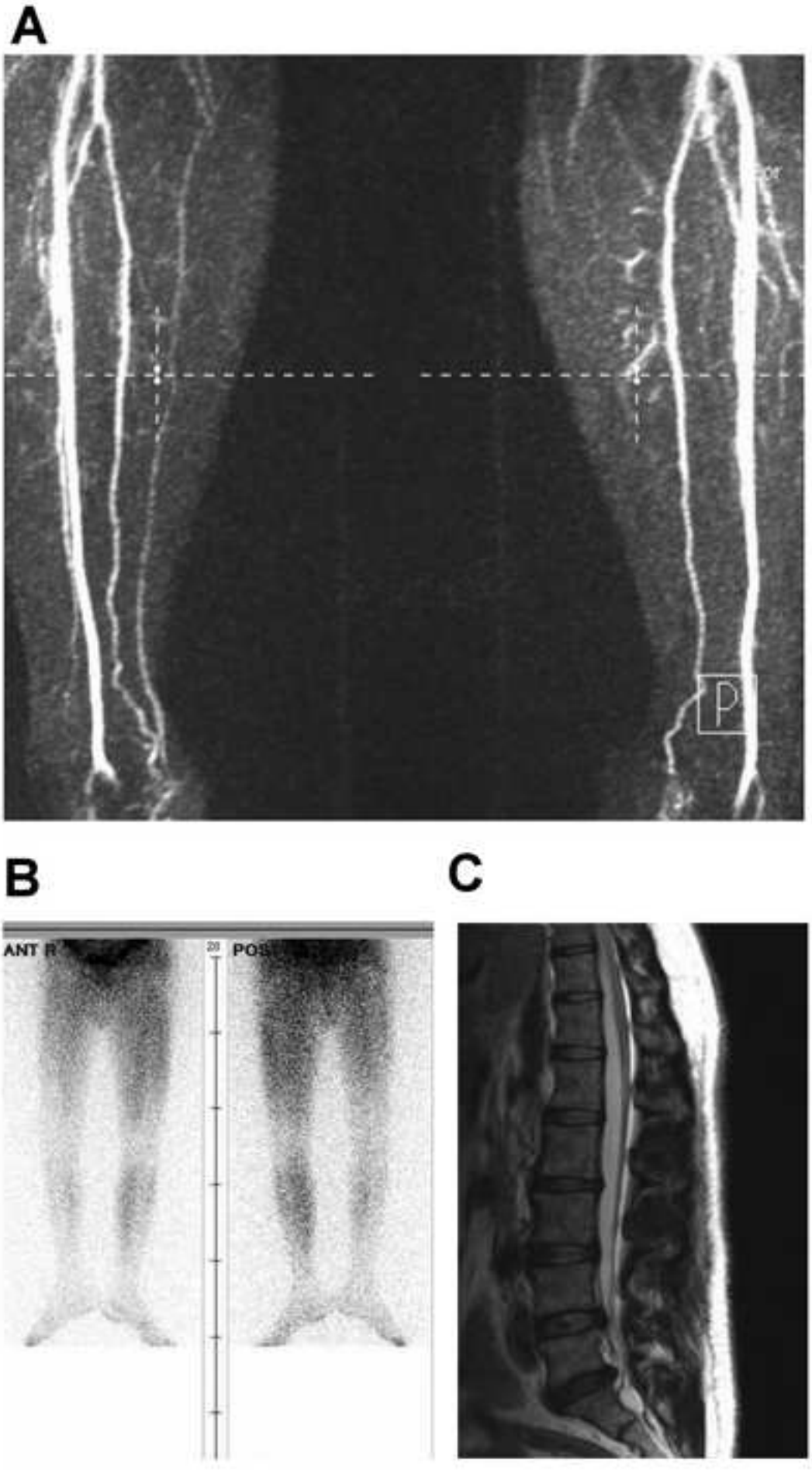

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