International Journal of Gerontology 5 (2011) 59–61

Contents lists available at ScienceDirect

International Journal of Gerontology

journal homepage: www.ijge-online.com

Case Report

Delayed Diagnosis in an Elderly Patient With Atypical Presentation of Peripheral Artery Occlusion Disease†

Yu-Ya Tseng [1], Lee-Ching Hwang [1], Wen-Han Chang [2]*

[1] Department of Family Medicine, Mackay Memorial Hospital, [2] Department of Emergency Medicine, Mackay Memorial Hospital, Taipei, Taiwan.

ARTICLE INFO

Article history:
Received 16 January 2009
Accepted 12 May 2009
Available online 9 March 2011

Keywords:
atypical presentations,
elderly,
intermittent claudication,
limb ischemia,
PAOD

SUMMARY

Peripheral artery occlusion disease (PAOD) is a clinical disorder with occlusion in the arteries of the limbs. PAOD is common but frequently overlooked because of subtle physical findings and a lack of classic symptoms, especially in the elderly. A 67-year-old female arrived at the emergency department with unconsciousness and progressive left lower leg cyanotic change. Her history revealed that she had felt severe left calf pain with foot numbness 3 weeks earlier. She visited a neurology clinic then, and only an analgesic was prescribed. At the emergency department, her left lower leg had cyanotic change with dry gangrene over the toes and a pulseless left dorsalis pedis artery was found. Septic shock with respiratory failure occurred, and intubation with fluid resuscitation was performed. However, emergent surgery was not arranged because of her unstable physical condition. After several days of antibiotics use, the sepsis persisted. Peripheral vessel ultrasonography revealed total artery occlusion in the left popliteal artery, and, consequently, above-the-knee amputation was performed. She then recovered smoothly and was discharged. We therefore report a case of PAOD that, through a delayed finding by clinicians, led to life-threatening infection and limb amputation.

1. Introduction

Peripheral artery occlusion disease (PAOD) is a manifestation of systemic atherosclerosis, which causes increased risk of death and ischemic events, yet it may be underdiagnosed in primary care practice[1]. The prevalence of PAOD increases sharply with age, from 3% in patients younger than 60 years to 20% in patients older than 75 years[2]. PAOD will become more frequent over the next few decades as the number of aged persons increases[3].

PAOD is common but frequently overlooked because of subtle physical findings and a lack of classic symptoms[4,5]. Atypical symptoms may be present because of comorbidities, alterations in pain perception, and physical inactivity[6], especially in the elderly. The risk factors for PAOD are similar to those that promote the development of coronary atherosclerosis (advanced age, diabetes, hypertension, and so forth)[7,8].

Early diagnosis and treatment of PAOD in the diabetic elderly is critically important to reduce the risk of cardiovascular events, to minimize the risk of long-term disability, and to improve quality of life. Delayed findings of PAOD may result in severe limb-threatening ischemia, leading to amputation.

We present a case of delayed finding of PAOD with an atypical presentation in an elderly female patient, which led to life-threatening infection and limb amputation.

2. Case Report

The 67-year-old female patient presented to the emergency department (ED) with unconsciousness. She had shown progressive cyanotic change and coldness to the touch in left lower leg over the previous 3 days. According to her clinical history, she had diabetes and hypertension, but they were poorly controlled. Past cerebrovascular disease led to right hemiparesis, and she also suffered from chronic renal insufficiency (CRI).

Three weeks earlier, she had felt severe left calf pain with foot numbness and had visited a clinic for treatment. However, only an analgesic and a nerve conduction velocity test were prescribed at that time, based on the common symptoms of musculoskeletal or neurologic disorders.

Five days before visiting the ED, superficial vein engorgement with bruising was noted over the left lower leg, and she became unable to walk. Two days later, progressive cyanotic change was

* *Correspondence to*: Dr Wen-Han Chang, Department of Emergency Medicine, Mackay Memorial Hospital, 92, Section 2, Chungshan North Rd, Taipei, Taiwan. Tel.: +886 2 2543 3535; fax: +886 2 2543 3642.
E-mail address: branden888@gmail.com (W.-H. Chang).
† All contributing authors declare no conflict of interest.

1873-9598/$ – see front matter
doi:10.1016/j.ijge.2011.01.012

found in her left lower leg and unconsciousness was also noted. Therefore, she was brought to our ED immediately.

At the ED, her body temperature was 36.6°C, with blood pressure at 130/55 mmHg, pulse rate at 91 beats/min, respiratory rate at 20 breaths/min, and a Glasgow Coma Scale of 10. Physical examination revealed cyanotic change in her left lower leg with dry gangrene over the toes, paralysis, paresthesia, poikilothermia, and paleness, but no pain (Fig. 1). She had a weak pulse at the left popliteal artery and no pulse at the left dorsalis pedis artery.

Her hemogram showed leukocytosis with a left shift (white blood cells [WBCs]: 32,400/μL, neutrophil: 89%). Her blood chemistry revealed elevated C-reactive protein (29.7 mg/dL), azotemia (blood urea nitrogen: 108 mg/dL, Cr: 4.2 mg/dL), hyperkalemia (7.9 mEq/L), elevated D-dimer (>10,000 ng/mL), and hyperglycemia (284 mg/dL). Urinalysis showed pyuria (urine WBC: numerous/μL). Arterial blood gas revealed metabolic acidosis with partial respiratory compensation; however, chest radiographs showed neither pulmonary edema nor a pneumonia patch.

Soon, metabolic acidosis with impending respiratory failure and septic shock occurred, and intubation with mechanical ventilation and fluid resuscitation was given. The case was presented as critical limb ischemia with severe sepsis. A cerebrovascular surgeon and an orthopedist were consulted regarding emergency surgery. They suggested performing amputation after the infection was controlled and her condition was stabilized. She was then admitted to the medical intensive care unit for further investigation and management.

After admission, empiric antibiotics (teicoplanin and imipenem) were prescribed. The urine culture yielded *Escherichia coli* and *Enterococcus faecalis*, neither of which showed growth in blood culture over 5 days. However, sepsis with leukocytosis persisted over several days of antibiotic usage. Peripheral vessel ultrasonography revealed total occlusion in the left popliteal artery.

Amputation above the knee was suggested by the orthopedist and was performed on the 12th day after admission. After the operation, her general condition improved gradually. Leukocytosis also subsided. Her WBC was 23,500/μL on Day 7 and 28,300/μL on Day 11. After amputation, WBC was 20,600/μL on Day 13 and 13,500/μL on Day 14.

A weaning program was performed smoothly without dyspnea or desaturation. Then, she was transferred to an ordinary ward and discharged in stable condition.

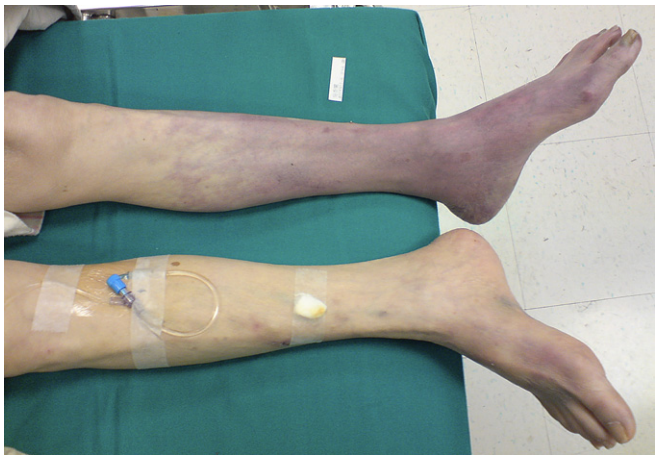

Fig. 1. Clinical picture of left lower leg showing cyanotic change, paleness, and dry gangrene over left toes.

3. Discussion

PAOD afflicts the elderly more commonly than it does younger patients because atherosclerosis is a continual process, and the symptoms generally develop late in this process[2]. The risk factors for PAOD are similar to those that promote the development of coronary atherosclerosis, including advanced age, diabetes, hypertension, hyperlipidemia, history of cardiovascular disease, CRI[9], sedentary lifestyle, and tobacco use.

Symptoms of PAOD are variable and, unfortunately, frequently lead to incorrect diagnoses.[10] PAOD is asymptomatic in almost 90% of patients.[1,8] Both symptomatic and asymptomatic PAOD lead to significantly increased risks of coronary and cardiovascular mortality, renal failure, intestinal angina, lower leg ulcers, and limb loss. Multiple aging factors increase susceptibility to infection[11] and risks for coexistent diseases in the elderly, raising the mortality and morbidity rates of PAOD.[12] Atypical symptoms as a result of comorbidities, alterations in pain perception, and physical inactivity may be present, especially in the elderly with complex arterial pathology[3].

Intermittent claudication (IC) is a common symptom of PAOD[7]. Classic IC is defined as having an exertional calf pain that does not begin at rest, causes the patient to stop walking, and resolves within 10 minutes of rest[6]. IC may progress to acute or critical limb ischemia (CLI), although the risk is less than 1% per year[13]. The clinical presentation of acute limb ischemia includes the five "Ps" that suggest limb jeopardy: pain, paralysis, paresthesia, pulselessness, and pallor, and sometimes includes a sixth "P," poikilothermia, indicated by a cold extremity[14].

CLI is the progression of symptoms of pain while at rest, night pain, tissue loss, and gangrene. CLI is of particular concern because it predicts poor outcomes: 30% of CLI patients will have amputations, and 20% will die within 6 months[11].

Atypical leg symptoms are classified by other complaints (numbness, weakness, giving way, aching, cramping, pain[15], and so forth) of the foot, thigh, or buttock with this ischemic pattern[8]. They may not stop the patient walking, or involve the calves, or resolve within 10 minutes while at rest.[6] Among those symptomatic PAOD patients, who have atypical IC symptoms are rather than classic[1,6]. The most reliable physical findings of PAOD are diminished or absent pedal pulses, presence of femoral artery bruit, abnormal skin color, and cool skin;[16] however, their absence does not preclude PAOD[7].

PAOD is frequently overlooked in elderly patients because of subtle physical findings and a lack of classic symptoms. The prevalence of IC is rather low in elderly PAOD patients[17]. With aging, the sensory systems gradually lose their sharpness. Moreover, the pain may sometimes be absent or diminished because of the recruitment of collaterals or because neurosensory loss interferes with perception, as in some elderly individuals with diabetes[18].

Clinicians who use a classic history of claudication alone to detect PAOD are likely to miss 85%–90% of the diagnoses[1]. It may be mistaken for a musculoskeletal or neurologic disorder because its symptomatology can mimic nonvascular etiology[3].

In this long-term diabetic patient, with left lower leg cyanotic change and dry gangrene over the toes, paralysis, paresthesia, pulselessness, poikilothermia, pallor but no pain, acute or CLI should be of grave concern despite the painless presentation.

People at high risk for vascular disease or presenting leg symptoms (as determined by the PAOD checklist, the Rose questionnaire[19], and the Edinburgh questionnaire, which is composed of a series of six questions and a pain diagram that are self-administered by the patient[20]) should be screened with an ankle brachial index (ABI) to confirm the diagnosis. Patients found to

have a low ABI (less than 0.9) should be aggressively treated for atherosclerotic disease, even if they look asymptomatic. Additional studies, such as duplex ultrasonography, magnetic resonance arteriography, and angiography are indicated for determining lesion localization and are best used when invasive or surgical intervention is required[21].

Because of the variable presentations and severe consequences of delayed findings, a high degree of alertness and screening procedures are important for early diagnosis[22].

In our case, this patient had diabetes, hypertension, CRI, long-term cerebrovascular accidents, and advanced age. These are atherosclerotic risk factors for PAOD. This kind of patient is more susceptible to arterial thrombosis and acute limb ischemia[23]. Vascular pathology in diabetes involves multiple organ systems, and it is a major risk factor for lower extremity amputation, particularly when combined with peripheral neuropathy and infection[24].

Hence, when this patient presented atypical leg symptoms with left calf pain while at rest and toe numbness a few weeks prior, PAOD should have been a great concern, despite the fact that these symptoms could have also been easily attributed to neurologic disorders or nonspecific musculoskeletal symptoms of aging and coexistent disease[25]. Further evaluations, such as an ABI, might have been performed. When we encounter such cases in the ED, acute or CLI should be considered even with the atypical presentation of painlessness because of diabetic neurosensory loss and aging. We should be on the lookout for the limb-threatening manifestations of PAOD, which require urgent intervention[26].

It is beneficial to intervene with medical management at an early stage of PAOD. The goal of treatment is to prevent its progression, to reduce the risk of major atherosclerotic events elsewhere, to improve function in symptomatic patients, and to prevent limb loss[3]. Medical management involves risk factor modification, exercise, and pharmacological therapy[4]. Patients must be recognized early and referred for revascularization before limb-threatening ischemia occurs. Indications for revascularization include claudication that is unresponsive to medications and CLI. Aggressive and early intervention can prevent limb amputation. In addition, amputation may be unavoidable if life-threatening infection or ischemia occurs[13].

Based on the presentation at the ED (capillary refill was absent, there was complete paralysis and sensory loss), our case might have been in the Class III, irreversible, category of the Rutherford Classification[18] of acute limb ischemia, and primary amputation would have been required.

Death caused directly by PAOD is rare. Mortality and morbidity are more often because of concomitant coronary or cerebrovascular disease. Elderly persons with PAOD are at increased risk for all-cause mortality, cardiovascular mortality, and mortality from coronary artery disease[11]. The relative risk of death for all causes of mortality is two to six times higher in PAOD patients than in the general population[23,27,28].

In conclusion, the evaluation and management of elderly patients with PAOD requires a multidisciplinary and individualized approach[3], especially for patients with underlying risk factors and atypical presentations. Delays in finding PAOD can lead to devastating limb ischemia and amputation, dramatically decreasing patients' mobility and independence. Early recognition and intervention to minimize morbidity and mortality are critical.

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