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# A 77-year-old woman with sudden onset of blue discolouration of right third toe

## 一名77歲女患者出現突發性右中趾瘀藍

We report on a 77-year-old woman with a history of peripheral vascular disease who presented with an acute-onset tender blue toe and deteriorating renal function. A clinical diagnosis of blue toe syndrome was made but the patient deteriorated rapidly and died. This case illustrates the rapidly devastating nature and fatality of blue toe syndrome. There is no effective treatment for this condition.

本文報告一名患有周邊血管疾病的77歲女性，突然出現腳趾瘀藍並感到痛楚，腎功能亦有衰竭跡象，經臨床診斷證實患有藍趾綜合徵。患者情況急速惡化，最終不治。病例說明了藍趾綜合徵的急速破壞性和致命性，唯現時仍未研究出有效的治療方法。

### Introduction

Blue toe syndrome is a clinical manifestation that describes acute digital cyanosis secondary to microembolism from a proximal atheromatous source, despite the presence of a palpable or Doppler positive distal pulse. No clinical data or information about blue toe syndrome are available in Hong Kong. We present a case of blue toe syndrome with suspected renal involvement.

### Case report

A 77-year-old woman, with a history of hypertension, paroxysmal supraventricular tachycardia, peripheral vascular disease, and Raynaud's syndrome with positive anti-nuclear antibody, presented with orthopnoea. Her regular medication included Adalat Retard (20 mg twice a day; Bayer AG, Germany), aspirin 60 mg daily, and flecainide 50 mg twice a day. Physical examination revealed pallor, bilateral ankle pitting oedema, and bilateral basal crepitations over the chest. Chest X-ray revealed cardiomegaly and congested lung fields. An electrocardiogram (ECG) demonstrated sinus rhythm with no ischaemic changes. Haematological investigations revealed slight anaemia that was normocytic and normochromic (haemoglobin level, 85 g/L; reference range, 110-160 g/L), and normal platelets and clotting profile. Renal function was slightly deranged: urea, 11.8 mmol/L (reference range, 3-8 mmol/L) and creatinine, 176 µmol/L (reference range, 53-97 µmol/L). She was diagnosed with congestive heart failure secondary to anaemia; she was prescribed diuretics and received a blood transfusion.

Her shortness of breath improved with treatment. Nonetheless, renal function was deteriorating with urea and creatinine levels raised to 23.8 mmol/L and 328 µmol/L, respectively. Her right third toe was incidentally noticed to be cyanotic and tender on palpation (Fig). Bilateral femoral and popliteal pulses were palpable and distal pulses were all Doppler positive. C-reactive protein was 181.1 mg/L (reference level, <5 mg/L) and erythrocyte sedimentation rate (ESR) was 65 mm/h (reference level, <30 mm/h) at that time. Blue toe syndrome was suspected in view of the cyanotic toe and acute-on-chronic renal failure. Zocor (10 mg at night; MSD, Australia) and dologesic (1 tablet, 4 times a day and as required) were given.

#### Key words:

Arteriosclerosis;  
Blue toe syndrome;  
Embolism, cholesterol

#### 關鍵詞：

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**Fig. The patient's acute cyanotic third toe**

#### Differential aetiologies of acute purplish toe discolouration

##### Intraluminal

##### *Thrombosis*

- Atherosclerosis
- Disseminated intravascular coagulation
- Antiphospholipid syndrome
- Polycythaemia rubra vera
- Thrombocythaemia
- Cryoglobulinaemia

##### *Embolism*

- Atheroemboli
- Cholesterol emboli
- Cardiac origin, eg atrial fibrillation

##### Intramural

- Vasculitis, eg connective tissue disease
- Raynaud's syndrome

Five days later, cardiac enzymes had increased: lactate dehydrogenase, 378 IU/L (reference range, 135-214 IU/L) and troponin T, 0.45 µg/L (cut-off value of acute myocardial infarction, >0.1 µg/L). Electrocardiogram showed atrial fibrillation and new T wave inversion in leads V1 to V3. Echocardiogram showed atrial fibrillation, left ventricular hypertrophy, and mild mitral, tricuspid, pulmonary, and aortic regurgitation. Left ventricle systolic function was normal and there was no blood clot in the heart chambers. She was commenced on digoxin, amiodarone, and low-molecular-weight heparin (LMWH) as treatment for atrial fibrillation and suspected acute coronary syndrome although she had no chest pain. Troponin T started to decrease in response to LMWH and ECG showed restored sinus rhythm. Nonetheless renal function was unchanged and her cyanotic toe showed no improvement.

Two weeks later she developed a high fever. She became drowsy and her previously stable blood pressure dropped from 150/70 to 76/45 mm Hg. Chest X-ray showed left-lower-zone haziness, and blood cultures were positive for *Staphylococcus aureus*. Fluid resuscitation with inotropic support was initiated and intravenous antibiotics were prescribed as treatment for septic shock. Her condition remained stable until the next day when she developed chest pain with shortness of breath and blood pressure again dropped to 80/50 mm Hg. Electrocardiogram showed atrial fibrillation, ST elevation over leads V1 to V3, and markedly raised troponin T. She died on the same day, 18 days after admission. Causes of death were documented as sepsis, acute coronary syndrome, congestive heart failure, and acute-on-chronic renal failure.

## Discussion

There are three main potential causes of acute purplish toe discolouration: thrombotic arterial occlusion, embolism, or intramural pathology (Box).<sup>1</sup> Under normal circumstances, a detailed history of the pattern of toe discolouration and

other associated clinical features, physical examination, and investigations should enable a diagnosis to be made, aetiology determined, and treatment planned.

In this patient, there was a pre-existing history of peripheral vascular disease when she presented with unilateral sudden onset of a painful blue toe and deranged renal function. Physical examination revealed no features of connective tissue disease and initial investigations showed no hypercoagulopathy or cryoglobulinaemia. Urinalysis revealed haematuria but no proteinuria, ECG showed sinus rhythm, and Doppler ultrasound of the lower extremities demonstrated positive distal pulses. The final diagnosis was blue toe syndrome with systemic manifestations of acute-on-chronic renal failure.

Blue toe syndrome, also known as purple toe syndrome or cholesterol emboli syndrome, was first described in 1976 as an event of acute digital cyanosis secondary to microembolism from a proximal atheromatous source, despite palpable or Doppler positive distal pulses.<sup>2</sup> Suspected causes included atheroemboli from dislodgement of an atheromatous plaque, or cholesterol emboli from ulceration of a plaque-releasing cholesterol crystals.<sup>3</sup> Both can occur spontaneously or following anticoagulation or endovascular manipulation, and result in vascular occlusion and subsequent tissue ischaemia.<sup>4</sup>

Apart from acute painful blue toe discolouration, local symptoms may include cutaneous manifestations such as livedo reticularis. Microembolisms may affect other organs, including neurological, cardiac, gastro-intestinal, and renal systems. The kidneys are the most often affected organs in multi-organ disorders (approximately 50% of the cases), and the prognosis is very poor, with mortality as high as 70%.<sup>5</sup>

Because of the lethal nature of this disease, a diagnosis should be established promptly and aggressive treatment promptly initiated. An increased ESR and eosinophil count

may be observed, but these findings are not specific.<sup>1</sup> The presence of abnormal renal function and cardiac enzymes may reflect systemic involvement of microembolism. Confirmation of the diagnosis is by skin or muscle biopsy that reveals characteristic lenticular clefts in small arteries, with reactive intimal thickening infiltrated by neutrophils. Later on the infiltrate is replaced by mononuclear and foreign body giant cells with prominent fibrosis in older lesions.

Establishing the source of embolism is vital. Echocardiogram and abdominal ultrasound can be used to evaluate cardiac and abdominal aorta sources of emboli, while non-invasive or invasive arterial studies of the lower extremities such as ankle brachial index or angiography can determine the presence of atherosclerosis or aneurysms of peripheral vessels.

Management of blue toe syndrome is initially supportive, with analgesics and careful positioning and protection of the foot. Organ support is indicated if there is multi-organ involvement. Medical treatment includes aspirin and lipid-lowering agent in view of the possible pathology of the lesion (fibrino-platelets and cholesterol emboli). The use of anticoagulants remains controversial because their use may promote atheroembolism.<sup>1,2</sup> Surgical treatment includes endarterectomy or bypass surgery aimed at removing the source lesion, or balloon angioplasty followed by stenting of the lesion. There are limited data with which to compare the outcomes of medical, surgical, or combined management of blue toe syndrome. Average mortality remains high at 20% regardless of management.<sup>2</sup>

## Conclusion

Blue toe syndrome is an acute peripheral vascular event, with possible systemic involvement and an associated high mortality. Careful history taking, physical examination, and investigations will help establish a diagnosis. Management is initially supportive, with subsequent medical and surgical therapy as indicated. The optimal treatment remains unclear. Experience of more cases and clinical trials may be useful in determining definitive recommendations.

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