TRASH FOOT SYNDROME: A CASE REPORT

Gino Francis F. Baylon, MD
Ruperto O. Estrada Jr., MD, MHA, FPOA, FPCS

BACKGROUND

Trash foot syndrome (TFS), also known as blue toe syndrome (BTS) and occlusive vasculopathy, is the appearance of a bluish cyanotic discoloration of the forefoot caused by the occlusion of small- to medium-sized arteries of the ankle and foot by fibrino-platelet micro-emboli. The source of these micro-emboli is hypothesized to arise from an atherosclerotic plaque in the aorta or the large arteries distal to the aortic bifurcation. The term BTS is sometimes interchanged with cholesterol embolization syndrome (CES). TFS is one of several end-results of CES. TFS is rarely encountered by the orthopedic surgeon; the antecedent CES is commonly unrecognized. Here we discuss a 74-year-old hemodynamically-stable post-total hip arthroplasty (THA) patient at the Philippine Orthopedic Center (POC) who developed acute cyanosis and gangrene of the ipsilateral foot.

CASE REPORT

A 74-year-old female sustained a right femoral neck fracture due to a bad fall and was admitted at the POC. Her past medical history mentioned hypertension only. She denied a history of a previous cardio-aortovascular intervention, the use of anticoagulants, anti-thrombotic agents and other long-standing medications and current neoplastic and coagulation disorders. She entered the Emergency Department on a wheelchair in mild pain distress but otherwise was conversant and cooperative. Vital signs were normal except for mild hypertension. No cutaneous lesions were noted. Examination of the heart, lungs, abdomen and distal extremities were unremarkable. The right hip was moderately tender and was externally rotated. Blood tests results are summarized in Table 1.

	14 days pre-THA	1 day post-THA	Second admit	HD1	HD3	HD4	HD8
Hgb	125	94	75	118	108	102	101
Hct	0.39	0.27	0.22	0.36	0.33	0.29	0.3
RBC	4	2.89	2.36	3.9	3.58	3.12	3.25
WBC	7.8	11.39	8.81	10.66	15.91	12.37	8.78
PMN	0.6	0.84	0.58	0.63	0.76	0.73	0.65
LYM	0.4	0.08	0.28	0.27	0.13	0.17	0.22
MONO		0.08	0.12	0.08	0.08	0.07	0.1
EOS		0	0.01	0.02	0.02	0.02	0.03
BAS		0	0.01	0	0.01	0.01	0
ESR	61		67		62		99
CRP	37.83		99.2		62.7		48.1
PT	12.5		13.8		14.4		
PTT	25.6		26.7		25.9		
BT	2m 40s		1 30		2 0		
CT	4m 25s		10 0		9 0		
PC	243,000	228,000	480,000	457,000	403,000	459,000	495,000
TSH				0.991			
D-dimer				2.53			

Table 1. Blood tests results. Values in highlighted in orange signify elevated levels while those highlighted in bluish hues mean decreased values, as per in-hospital standards.

HD – hospital day
PC – platelet count
TSH – thyroid stimulating hormone

14 days pre–THA, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR were moderately elevated while serum globulin, cholesterol and Fasting Blood Sugar (FBS) were mildly elevated. Serum chemistries and electrolytes were within normal limits.

2-D echocardiography test was interpreted as normal left ventricle with good systolic function, grade 1 diastolic dysfunction, trivial mitral regurgitation and normal pulmonary artery pressure. Electrocardiography result was normal sinus rhythm with non-specific

Corresponding author: ROEJ, bodiestrada@gmail.com

ST-T wave changes. Her urine specimen revealed 5-10 pus cells/high power field. The THA was fairly straightforward and recuperation was uneventful; she was discharged without incident on the fourth post-operative (PO) day on pain reliever medication and aspirin 80 mg once daily. At post-operative (PO) day 8 she was brought to the Emergency Department because of blistering and discoloration of the ipsilateral right foot. The patient noted dusky appearance of her right foot at post-operative (PO) day 5. On assessment there was gangrenous desquamation of the devitalized epidermis over the whole foot dorsum up to the heel and 90% of the plantar surface, mild bluish hue of the second to fourth toes and the plantar forefoot, foot pain and non-appreciable dorsal pedal and posterior tibial pulsations. (Figure 1) The popliteal pulse was faint. Massive swelling, fever, foot and ankle pain and prominent superficial veins suggestive of deep vein thrombosis (DVT) were not elicited.

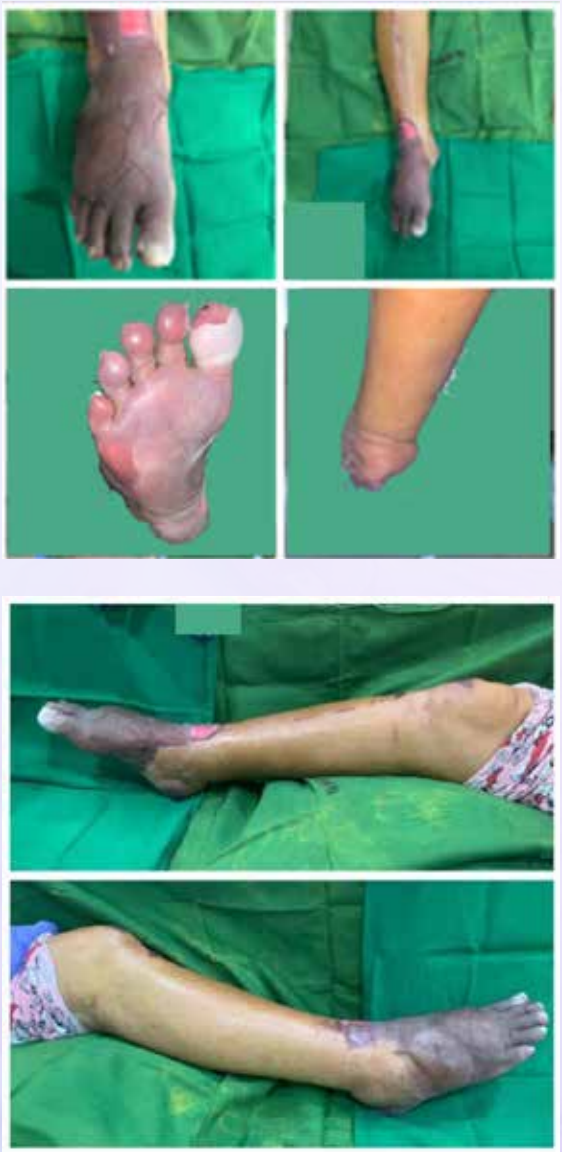

Fig. 1. Gangrenous desquamation of the skin was evident. The second, third and fourth toes and plantar forefoot manifested with a mild bluish hue at the tips.

Radiographs of the leg and foot were interpreted as diffuse osteoporosis and arthritic changes. The cemented total hip construct was in place. (Figure 2) TFS was the presumptive working diagnosis given by the vascular medicine service.

Fig. 2. X-rays of the foot and leg showed osteoporosis and arthritic changes compatible with her age.

She was confined again. The vascular surgeon put her on enoxaparin 40 mg every 12 hours subcutaneously for three days then to be re-assessed with an amputation as a probability. Blood count results were: Hgb 75 g/L, Hct 0.22, WBC 8.81 x 10^9/L, PMN 0.58, lymp 0.28, ESR 67 mm/hr, CRP 99.2 mg/L. Plate count was elevated. Two units packed red cells were transfused. Her lower extremity was placed on a Bohler frame. The infectious disease service started her on cefazolin IV every 12 hours. She was counseled by the psychology department and referred to the internist for pre-surgical clearance. Meanwhile the blisters were aspirated and un-roofed. Arterial and venous duplex ultrasound scan revealed total occlusion of the anterior tibial and dorsal pedal arteries, near total occlusion of the posterior tibial artery, arterial stenosis 50%-99% of the distal external iliac-, common femoral-, superficial femoral- and, popliteal arteries, arterial stenosis 1%- 19% of the rest of the arterial tree, no evidence of deep vein thrombosis (DVT) bilaterally, common femoral vein insufficiency and, rheologic stasis of bilateral common femoral and popliteal veins.

Packed red blood cell was transfused. On the second hospital day (HD) the majority of the dark discoloration has worsened and the forefoot was gangrenous. Hgb

was now 118 g/L but WBC was increased to 10.66 x 10^9/L. ESR and CRP were still elevated by the third HD. Without improvement the patient underwent above knee amputation on the fourth HD. (Figure 3) Her recovery was uneventful.

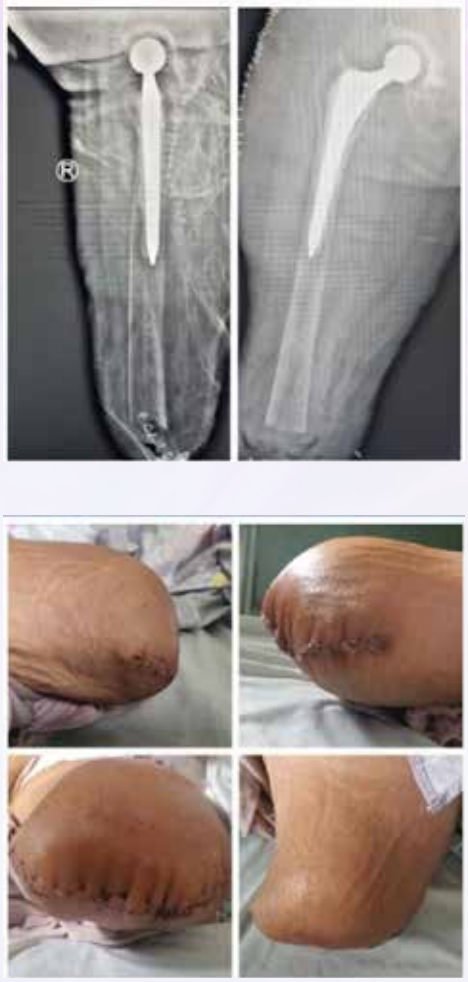

Fig. 3. Radiographs and Gross Photos of AKA Stump

DISCUSSION

TFS is commonly seen in, but not pathognomonic of, CES. The commonly unrecognized CES is a systemic embolization of a portion of an atheromatous plaque from a large proximal artery to more distal small arteries measuring 100-200 um in diameter [13] that will cause inflammation, mechanical luminal blockade, induce end-organ failure and vascular compromise of a lower extremity. TFS refers to scattered or geographic bluish or purple cyanotic lesions limited to the foot and caused by cholesterol emboli, among others which results in gangrene if attended to late. This acute condition needs to be differentiated from Raynaud's phenomenon which features more diffuse ischemic lesions occurring as a response to cold, stress or emotional upset, affects the fingers rarely the toes, nose, lips, ears and a return of normal blood flow up to 15 minutes after warm stimulation of the extremity Other etiologies for TFS are shown in Table 2

Table 2. General etiologies of trash foot syndrome and examples. (Adapted from Hirschmann and Raugi, J Am Acad Dermatol 2009) **[10]**

Decreased arterial flow	Decreased venous flow	Abnormal circulating blood
1. Embolism, e.g. cholesterol emboli, cardiac/aortic tumor, cardiac vegetations 2. Vasoconstrictive disorders, e.g., acrocyanosis, medication-induced (amantadine) 3. Thrombosis, e.g., antiphospholipid syndrome, thrombocytopenia purpura, warfarin skin necrosis, disseminated intravascular coagulation 4. Infectious and non-infectious inflammation, e.g. syphilis, other forms of vasculitis 5. Other vascular obstructions, e.g., calcific vasculopathy		

Examples of decreased venous flow are phlegmasia cerulea dolens and venous gangrene. Abnormalities in circulating blood include hyperviscosity disorders myeloproliferative disorders and cold-related agglutination.

The TFS begins with the dislodgment of portions of an advanced atheromatous plaque located in the tunica intima layer of the aorta and large arteries by 1) an unknown spontaneous mechanism 2) partial dissolution of the plaque by medical treatment, e.g. anticoagulation therapy, 3) an iatrogenic intraluminal mechanical procedure or 4) as a part of a concurrent illness. The plaque or fibrino-platelet microemboli and its component minute cholesterol crystals find their way into obstructing small- and medium-sized arteries in the lower extremity. It can also cause ischemia of an end organ and subsequent organ failure. The foot develops cyanosis-gangrene if it is not addressed promptly. Inflammation plays a large part in the pathogenesis of atherosclerosis. The dislodged plaque/s contain/s a big amount of inflammatory cells and these may cause TFS in the long term. Inflammatory markers e.g., C-reactive protein (CRP) levels may increase suggesting an increased inflammatory activity. **[9]**

By a process of elimination we arrived at a mechanism of decreased arterial flow caused by plaque, possibly cholesterol emboli, more or less in agreement with the vascular service impression. This raises the concern that the patient has CES. Computed tomography (CT) angiography was not available and musculoskeletal ultrasound imaging cannot locate the source of the plaque. Tartari et al stated that if it is CES and cutaneous lesions are mostly bilateral and early-onset with livedo

reticularis (LR; reddish-blue/purple spots distributed along a fishnet or lace pattern on the skin usually at the lower trunk and lower extremities), the origin of the emboli is proximal to the aortic bifurcation. **[30]** The patient's femoral artery is stenosed by 50%-99%. Khan stated that the lower extremities are involved if the origin of the atheroma is distal to the renal arteries while if the proximal aorta is the origin site then symptoms may occur in the central nervous system, abdomen and extremities. **[16]** The mother plaque in our patient was deduced to be somewhere in the common iliac-, external iliac- and proximal common femoral- arteries. She had a normal thyroid stimulating hormone value. The elevated D-dimer test result could be due to recent surgery, recumbency, old age and an elevated triglyceride level. **[2,29]**

There are no incidence reports of TFS. For CES Ozkok, citing several authors, compiled the incidence at 0.09%-2.9%. **[24]** In general autopsy reports the frequency of CES is at 0.31%-2.4% while in autopsies on individuals who died after aorto-cardiovascular procedures the frequency was 12%-77%. **[6,15,18,22,23]**

Trash foot syndrome is commonly caused by on-going CES which is often unrecognized by orthopedists and which needs to be addressed soonest. Khan and Jacobs state that the triad of LR, pain and intact pulses is pathognomonic of TFS. [16] The TFS patient needs to be examined upright and supine for the LR disappear on recumbency, [3] and as reported by Sheehan on a 64-year-old Filipino male in 1993. [28] Other authors disagree with the pathognomonic usefulness of livedo reticularis **[8,19,26]** because it also manifests in cold weather, stress, infections, diabetes and autoimmune disorders. It may blanch under moderate pressure. The orthopedist also has to extract useful information on the past medical history, e.g. tobacco use, hypertension, dyslipidemia, atherosclerosis, ischemic cardiovascular disease, cerebrovascular disease, diabetes, aortic aneurysm and peripheral vascular disease. **[11,20]**

Laboratory tests for TFS while in the early or reversible state may support the diagnosis but are non-specific. C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) levels are elevated due to the inflammatory state of the dislodged plaque/s. Eosinophilia varies from 14% to 80% in incidence. **[20,31]** Eosinophiluria and proteinuria can be detected in a third of patients with renal involvement (of CES). Other possible abnormal results include anemia, leukocytosis, thrombocytopenia, elevated amylase-lipase-lactate, elevated HbA1c, elevated serum creatinine (renal involvement) and elevated lactic dehydrogenase **[5,27]** Sawalhi and Hamad stated it is important to perform duplex ultrasound imaging and echocardiography to determine the location of the micro-emboli and to rule out a cardiac etiology, respectively. **[25]** An abdominal CT scan may locate plaques affecting the thoraco-abdominal and descending aorta **[3]** while computed tomogram angiography or ultrasound imaging may help in the diagnosis and differentiate the TFS from a thrombogenic etiology. Definitive diagnosis of TFS secondary to CES can only be made with biopsy of involved skin, muscle or kidney. Skin biopsy of the LR lesions may show cholesterol crystals or deposits **[8,16,17]** which is practical in the busy POC setting where scheduling for surgeries is at a premium.. Under polarized microscopy the crystals exhibit birefringence. **[19]** A challenge about skin biopsy of LR lesions is that it may be difficult to ascertain which lesion may give a good microscopic yield of the crystals; sometimes multiple thick punch biopsy cuts have to be performed. The patient did not undergo a biopsy due to the urgency of the situation. Overall the orthopedist has to balance the situation regarding the need and timeliness in performing and interpreting these tests against the backdrop of a rapidly progressing gangrene and a decision to amputate.

The prognosis of TFS for the wider elderly population is mostly poor because of the presence of co-morbidities as well as late diagnosis in low-income settings. Frank reported that up to 30% of individuals suffering from CES die within one year of diagnosis. **[8]** The treatment is essentially supportive for CES and non-gangrenous TFS; a more important goal is the prevention of more attacks by management of the patient's co-morbidities, e.g., achieving euglycemia, correction of dyslipidemia, avoidance of smoking and control of hypertension. Anticoagulation may be briefly beneficial but the respective studies involve small populations **[15,18,23]** Its opponents argue it may destabilize a plaque and cause further micro-embolism **[12,14,21,31]** Likewise the use of anti-inflammatory medications, e.g., corticosteroids and colchicine, involve small population studies and have not proven widely efficacious. **[8,31]** Statins inhibit HMG-CoA reductase which is the rate-limiting step in the production of cholesterol and may help in managing CES by limiting one of the latter's risk factors. Binnenmars reported on a 72 year old female on hemodialysis who developed CES five months after stopping statin intake. She was re-started on simvastatin-ezetimibe which diminished her pains and cutaneous lesions until it disappeared. **[1]** Woolfson and Lachmann described a patient with proven renal cholesterol emboli in whom increasing renal dysfunction was eventually arrested by simvastatin. **[32]** Finch and Ryatt reported on a 69-year-old male who had 3-month old LR lesions which deteriorated despite taking low-dose aspirin and a lipid-lowering diet. He was started on simvastatin 10 mg daily. After three months his serum cholesterol decreased significantly and the LR lesions diminished in extent and prominence.**[7]** Surgical procedures to treat CES are varied. Endarterectomy and bypass procedures

may be successful only if the obstructed small arteries can be localized. Interventional stent insertion may further destabilize a plaque. Kim et al was able to successfully treat TFS in only one patient with lumbar sympathectomy. **[17]** Medical treatment often cannot change the inevitable outcome of established TFS. In the POC setting a patient will be referred soonest to the vascular medicine section for co-management. Debridement of an ulcer and abscess, negative pressure wound therapy (NPWT) and antibiotics may be instituted as needed. The definitive treatment is an amputation. It seemed that our patient's TFS was in its late stage or the occlusion evolved rapidly. Moving forward, the best strategy for our patient is to continue management of her co-morbidities as well as to vigilantly monitor 1) for a recurrence and 2) the sterile and working condition of her THA.

SUMMARY

We have a 74-year-old female, post-right total hip arthroplasty, who developed acute ipsilateral foot gangrene less than one week later. The clinical presentation in the absence of extensive work-up was suggestive of TFS. One major cause of TFS is CES which is commonly unrecognized by the orthopedist . The diagnostic acumen lies in 1) having a high index of suspicion and 2) searching for clinical features. Elevated CRP and ESR, and foot pain were present in the patient but none of LR, eosinophilia, eosinophiluria and intact distal pulses. Duplex ultrasound imaging revealed total occlusion of the anterior tibial and dorsal pedal arteries, near total occlusion of the posterior tibial artery and arterial stenosis 50%-99% of the distal external iliac-, common femoral-, superficial femoral- and popliteal arteries. It also ruled out DVT. Biopsy to verify CES was not performed. She underwent above knee amputation on the fourth day of her second confinement. Prognosis of TFS is generally poor because of age-related co-morbidities.

DISCLOSURE

None

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