

# Complex Regional Pain Syndrome Following Transfemoral Catheterization

By *hmpeditor*

Created 10/26/2011 - 12:12

[November 2011](#) [1]

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- Wed, 10/26/11 - 12:12pm
- 0 Comments
- 

Section:

Online Exclusive

Issue Number:

[Volume 23 - Issue 11 - November 2011](#) [2]

Author(s):

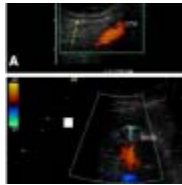
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**ABSTRACT:** Complex regional pain syndrome (CRPS) (previously reflex sympathetic dystrophy) is a chronic pain condition usually resulting as a consequence of trauma or surgery. Though described occasionally after vascular surgery, it is distinctly rare after percutaneous cardiovascular procedures. We report a case of CRPS following transfemoral catheterization-related groin pseudoaneurysm. To our knowledge, this is the first such report following transfemoral catheterization. A 36-year-old female underwent an electrophysiological study and AV node re-entry tachycardia ablation using the left femoral vein approach. One month later she presented complaining of numbness and tingling in her left foot with swelling and mild groin discomfort. A lower extremity duplex scan showed a left common femoral artery pseudoaneurysm that was partially thrombosed and subsequently resolved spontaneously. The patient had intractable symptoms of pain, temperature changes, color changes, and trophic changes of the left foot. Conventional angiography was done to rule out occlusive arterial disease but just showed very sluggish flow. Further evaluation with transcutaneous oxymetry and 3-phase bone scan was consistent with microvascular dysfunction and poor cutaneous blood flow suggestive of cold-type CRPS. In this case report, we also review the clinical features and the vascular changes associated with CRPS and discuss the pathophysiology of the syndrome from a cardiovascular specialist's perspective. Interventionalists should be aware that CRPS is a possible, albeit rare, condition that may follow many vascular procedures that they perform on a daily basis.

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Complex regional pain syndrome (CRPS) is a chronic pain condition characterized by chronic, continuous regional pain that is out of proportion to the severity of the injury. The pain is not limited to a specific nerve distribution or dermatome, and is typically associated with abnormal sensory, motor, vasomotor changes, and/or trophic findings.<sup>1</sup> Common inciting events for CRPS are soft tissue injuries, fractures, and strokes. It has also been reported rarely after microscopic trauma such as an insect bite, immunization, or even in the absence of an identifiable trigger.<sup>2,3</sup> Though described after vascular surgery procedures such as arteriovenous fistula (AVF) and arteriovenous graft<sup>4-6</sup>, CRPS is not usually associated with percutaneous vascular procedures. A detailed literature search resulted in identification of rare isolated cases of CRPS after transbrachial and transradial cardiac catheterization<sup>7-9</sup> but not after transfemoral catheterization. To our knowledge, this is the first reported case of CRPS following transfemoral catheterization. We also report the angiographic findings of cold-type CRPS, not previously well described.

## Case Report



[3]A 36-year-old previously healthy Caucasian woman with longstanding history of tachypalpitations underwent electrophysiological study and AV node re-entry tachycardia (AVNRT) ablation using the left femoral vein approach. Two large-gauge 8 and 10 Fr sheaths were used during the procedure. Her immediate postprocedure course was uneventful. She presented one month later complaining of numbness and tingling in her left foot, with local edema and mild groin discomfort. Pedal pulses were intact and no obvious abnormality was noted on examination of the foot. Lower extremity duplex scan revealed a left common femoral artery pseudoaneurysm (2.2 x 2.3 cm) that had almost completely thrombosed, with a small amount of residual to-and-fro flow (Figures 1A and 1B). It was decided to conservatively manage the pseudoaneurysm, expected to spontaneously thrombose. A few days later the patient presented to the office with complaints of worsening pain in her left leg and foot, which was elicited by even light touch, as well as continued localized swelling and cold sensation. On examination the patient's foot showed significant coolness, mottling of the skin most notable over the 3rd and 4th toes, mild edema, and normally palpable dorsalis pedis and posterior tibial pulses. We suspected distal embolization from the known femoral pseudoaneurysm. However, repeat duplex scan showed that the pseudoaneurysm had completely thrombosed with normal flow in the common and superficial femoral arteries (SFA) as well as the infragenicular arteries. The patient was started on aspirin and clopidogrel.



[4]Despite continuing antiplatelet therapy, the patient's pain continued to worsen and her left foot developed a slight cyanotic discoloration, with the distal leg and foot becoming

very cold to touch. She reported that the foot discoloration varied on a day-to-day basis (Figures 2A and 2B). Suspecting acute critical limb ischemia (CLI), she was admitted to the hospital and started on heparin. CT angiogram of the abdomen and pelvis was done, which did not show any proximal source of embolization. We then performed an abdominal aortogram with bilateral lower extremity runoff that did not show any aortic, iliac, or femoropopliteal abnormality. However, the patient had sluggish flow in the infragenicular arteries, the left significantly worse than the right. Slight improvement in flow was achieved by directed nitroglycerin injections intra-arterially, but it still remained sluggish. No discrete anatomic stenosis or occlusion was seen in the tibioperoneal arteries and arteries of the foot. Transcutaneous oxymetry revealed normal resting oxygenation but poor response to supplemental 100% oxygen in the foot, indicating microvascular dysfunction with poor cutaneous blood flow.

An extensive rheumatologic and hematological workup was negative for arteritis or hyperviscosity syndrome. The diagnosis of CRPS was considered. Clopidogrel was discontinued. A 3-phase bone scan was ordered, which exhibited diminished blood flow to the distal left lower extremity, suggestive of cold-type CRPS. Multiple treatments were tried without clinical improvement, including Neurontin, amitriptyline, vasodilators such as oral nitrates and amlodipine, and topical nitroglycerine paste. The patient was referred to Physical Medicine and Rehabilitation for further evaluation. She received ongoing physical therapy and underwent 3 treatments of sympathetic nerve block, but experienced only partial relief and continued to complain of debilitating pain. By this point the patient was unable to fully plantar or dorsiflex her left foot or bear any weight through the leg, and she mobilized with the assistance of crutches. Her distal lower extremity remained cold, mottled, and edematous, and she noted that she had not clipped her toenails on that side in 3 months because they had stopped growing. As a final treatment, the patient underwent a spinal cord stimulator trial that resulted in significant improvement in her symptoms. The pain subsided somewhat, swelling improved, and she was able to move her toes and cautiously begin to weight-bear again. Given her functional gains, a permanent spinal cord stimulator was implanted for long-term use. However, after the implantation she had suboptimal response and continued to have significant pain. With progressive atrophy of her left calf muscles, she was unable to participate in physical therapy due to pain. Her case was discussed in multidisciplinary conference and the patient was admitted to the hospital and epidural sympathetic block with aggressive physical therapy was pursued. While inpatient, she had repeat venous duplex and arterial duplex, which remained with no significant pathology. Patient underwent placement of epidural catheter and was started on bupivacaine 0.1% and hydromorphone 10 mcg/ml infusion, which improved her left lower extremity discomfort solidifying the diagnosis of CRPS. However, she was still unable to participate in an aggressive physical therapy program due to pain. Her left foot pain continued to get worse with overall decreased functionality. Due to her severe symptoms and inadequate response, the multidisciplinary team, including vascular surgeon, recommended amputation as it was thought that with very advanced and intractable CRPS and patient's extreme disability, she would be better rehabilitated with a below-the-knee prosthesis.

## **Discussion**

This case report describes a previously unreported complication following a transfemoral catheterization procedure. The goal is to familiarize the invasive cardiologist with the clinical

features of CRPS that may rarely be seen following vascular procedures. In the absence of a definite diagnostic test or biomarker, the diagnosis of CRPS can be challenging. CRPS is a diagnosis of exclusion and physicians should rule out other limb-threatening conditions such as critical limb ischemia, deep vein thrombosis, or arteritis before considering the diagnosis of CRPS. Since early recognition and diagnosis of CRPS is important for better clinical response, interventionalists should be aware that CRPS is a possible condition, which may follow the many vascular procedures that they perform on a daily basis.

The syndrome manifests itself in 3 distinct clinical phases<sup>10</sup>, and the patient in this case provides an apt illustration of the first two. The acute phase commonly presents in the first weeks to months following neurovascular insult with hyperalgesia and allodynia in a limb area not limited to one nerve distribution. *Hyperalgesia* refers to a lowering of the pain threshold and enhanced pain perception, while *allodynia* describes pain induction by non-noxious stimuli. Additionally, the acute phase is characterized by localized sweating and increased microvascular blood flow to the affected limb with resultant rubor, calor, and mild edema. The dystrophic phase typically occurs 3 to 6 months after the acute phase with decreased blood flow to the local area that results in atrophic skin changes, cooling, and a mottled appearance. Patients often describe reduction in growth of hair and nails in the affected limb, and persistent pain leads to reduced weight-bearing use and functional disabilities. Finally, several months to years after initial presentation, the atrophic phase of CRPS is characterized by atrophy and contracture formation from disuse and the patient's skin has become chronically cool and dry, with a glossy appearance.

The diagnosis of CRPS is primarily clinical in nature, as established by Harden and Bruehl.<sup>20</sup> There are 2 types of CRPS, the differentiation of which is made based on an identifiable inciting event. In this particular case, the patient most likely represents type I given her presentation following catheterization injury-related pseudoaneurysm. The following 4 criteria must be met for definitive clinical diagnosis of CRPS type I, which the patient met:<sup>1</sup>

1. Presence of an identifiable noxious event,
2. Allodynia, hyperalgesia, and continuous pain disproportionate to the inciting event,
3. Signs and symptoms of sensory, vasomotor, sudomotor/edema, and motor/trophic disturbances,
4. No other explanation.

CRPS is likely a very underrecognized condition. Data on the incidence of CRPS are scarce and mostly hospital-based. Sandroni et al reported the incidence of CRPS in the general population (Olmsted County, USA) to be 5.46/100,000 person years.<sup>11</sup> A more recent population-based study from the Netherlands reported a 4 times higher incidence rate; the estimated overall incidence rate was 26.2 per 100,000 person years, (95% CI: 23.0-29.7). Females were affected at least 3 times more often than males (ratio: 3.4). The highest incidence occurred in females in the age category of 61-70 years. The upper extremity was affected more frequently than the lower extremity and a fracture was the most common precipitating event (44%).<sup>12</sup>

The exact pathophysiology of CRPS remains unclear. Evidence suggests that N-methyl-D-aspartate (NMDA), which is implicated in CNS sensitization, may be overstimulated, as well as

microtrauma-induced cytokine release and glial cell activation are all implicated in the vasomotor and autonomic dysfunction.<sup>13,14</sup>

Regardless of the exact pathophysiology, vasomotor disturbances play a significant role in the natural history of CRPS and might even be of diagnostic value. Vascular disturbances mainly affect microcirculation in the distal part of the involved extremity, leading to vasoconstriction or vasodilatation in the different stages of CRPS. Wasner suggested that the interaction between different mechanisms underlying vasomotor disturbances (such as endothelial dysfunction, vascular hyper-reactivity, sympathetic vasoconstrictor activity, and neurogenic inflammation), is a major pathophysiological mechanism and has a great impact on the overall clinical picture in CRPS.<sup>15</sup>

Interestingly, multiple reports have suggested that non-neurogenic vascular factors (mainly endothelial dysfunction) contribute significantly to the clinical picture in patients with chronic cold-affected extremities related to CRPS. Stengel et al in 2006 examined endothelial function in 14 patients with the cold-type chronic CRPS using acetylcholine and sodium nitroprusside-induced vasodilation. On the affected side, acetylcholine-induced vasodilation was significantly reduced in comparison to controls and the unaffected extremity.

No significant differences were found after application of sodium nitroprusside. The results demonstrate impaired endothelial function in chronic CRPS.<sup>16</sup> Similarly, local concentrations of vasodilative endogenous nitric oxide were found to be reduced in patients with chronic CRPS, parallel with increased amounts of vasoconstrictive endothelin-1, which is derived from the endothelium and other tissues.<sup>17,18</sup> These suggest that endothelial dysfunction plays a role in chronic CRPS.

Our patient had the predominantly cold-type CRPS with microvascular vasoconstriction and she had evidence of slow flow in angiography, and transcutaneous oxymetry showing normal resting oxygenation but poor response to supplemental 100% oxygen due to poor skin microcirculation.

Numerous studies have documented the development of CRPS following distal upper extremity procedures, such as carpal tunnel release, Dupuytren's contracture release, and amputation. CRPS has also been described following minor trauma resulting in fractures;<sup>19</sup> rarely, vascular procedures have been reported as an inciting event for CRPS, such as arteriovenous fistula (AVF), arteriovenous graft,<sup>4-6</sup> transbrachial and transradial cardiac catheterization.<sup>7-9</sup> There are, however, no reported cases of development of CRPS in the lower extremity after transfemoral catheterization. Though uncommon, cardiologists should be familiar with this clinical entity.

**Acknowledgement.** The authors thank Dr. Stephen Paulus for reviewing the manuscript for grammatical accuracy and for making helpful suggestions.

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*Disclosure: The authors have completed and returned the ICMJE Form for Disclosure of Potential Conflicts of Interest. The authors report no conflicts of interest regarding the content herein.*

*Manuscript submitted April 14, 2011 and accepted May 9, 2011.*

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