

Unilateral, Episodic, Transient Blanching of Nipple With Pain in a Male: A Case Report

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ABSTRACT

Introduction: Causes of nipple pain include trauma, vasospasm, malignancy, Paget's disease, inflammation secondary to blockage of the ducts, infection, and medications. Raynaud's phenomenon (RP) of the nipple is reported more often in women and typically presents bilaterally.

Case Presentation: A 63-year-old man presented with episodic, stabbing pain and blanching of the left nipple, worsening over 3 years. Symptoms began insidiously during military service. Examination revealed no abnormalities, but blanching was observed during a painful episode. Laboratory and imaging studies were unremarkable. Conservative measures and pharmacologic agents, including nitroglycerin ointment and amlodipine, provided minimal relief. Intercostal nerve blocks and cervical sympathetic blocks did not provide lasting relief. Ultrasound-guided paravertebral sympathetic block with local anesthetic provided temporary relief lasting week. Botulinum toxin injection around the areola resulted in sustained pain relief lasting more than month.

Discussion: The patient's presentation is consistent with primary RP of the nipple, a rare and underrecognized condition. While it typically affects distal extremities, it can involve other areas, including the nipple. Diagnosis is clinical, often requiring documentation during episodes. Management is challenging and largely anecdotal. Botulinum toxin has shown promise in RP, though evidence remains mixed.

Conclusions: This case highlights a rare presentation of unilateral, vasospastic nipple pain resembling primary RP, with partial response to botulinum toxin injection.

INTRODUCTION

Causes of nipple pain include trauma; inflammation, sometimes secondary to blockage of the ducts; infection; medications, including hormones; vasospasm; malignancy; and Paget's disease of the nipple.¹ Unilateral nipple pain accompanied by eczematous skin changes is also a feature of Paget's disease.² Secondary

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causes of nipple pain are often identified during physical examination, laboratory testing, and imaging studies. An idiopathic primary cause of nipple pain, particularly when associated with color changes such as blanching, may indicate Raynaud's phenomenon of the nipple.³ Nipple pain with color changes can be an early presenting symptom of connective tissue disorders and is usually identified through further investigation or as the disease progresses.⁴ Nipple pain is more commonly reported in women.⁴

We report an unusual case of unilateral nipple pain with associated color changes in a man and describe its subsequent management.

CASE PRESENTATION

A 63-year-old man sought treatment at the pain clinic for persistent left nipple pain lasting more than 30 years, which had

intensified over the past 3 years. He described prodromal symptoms, with the pain gradually moving from the lateral chest near the axilla to the nipple. He described the pain as beginning with an ache lateral to the nipple-areolar complex and, at its peak, feeling like a "16-gauge nail poking out through the nipple from the inside." Occasionally, the pain extended laterally and cephalad from the left nipple toward the axilla. He reported that his nipple also turned white and became erect during these painful episodes, which lasted about 15 to 60 minutes and occurred 1 to 6 times a day, with numeric rating scale (NRS) scores ranging from 3 to 7. He obtained some relief during these episodes by applying pressure lateral to the nipple.

The patient's past medical history included type 2 diabetes man-

aged with insulin, essential hypertension treated with losartan and amlodipine; fibromyalgia managed with pregabalin, and chronic lumbar radiculopathy treated with periodic epidural steroid injections. He also recalled painting army vehicles with chemical agent resistant coating (CARC) and exposure to burn pits during the Gulf War. He denied any family history of similar conditions or connective tissue disorders.

On examination, both nipples appeared normal, with no redness, color change, excoriation, discharge, retraction, inversion, or swelling. During a painful episode that occurred during a clinic visit, a small area of whitish discoloration with slight blanching of the nipple was observed (Figure). There was no tenderness to palpation or palpable mass in the breast or axilla. Laboratory values, including C-reactive protein and sedimentation rate, were within normal limits. Hormone levels—including testosterone, luteinizing hormone, follicle stimulating hormone, prolactin, cortisol, and aldosterone—were also normal. Mammography and breast ultrasound examination revealed no abnormalities. Chest computed tomography (CT) was unremarkable.

A trial of lidocaine patches and pregabalin did not provide relief. Fluoroscopically guided left T4-T5 intercostal nerve steroid injections resulted in 50% reduction in frequency and severity of pain for approximately 6 weeks. Because the pain originated more laterally, an intramuscular injection of 1% lidocaine was administered, providing approximately 60% pain relief for a week. Given blanching and nipple pain, Raynaud's phenomenon of the nipple was considered. As the patient was already taking amlodipine and losartan for hypertension and sildenafil for erectile dysfunction—agents traditionally used to treat Raynaud's phenomenon—he was started on nitroglycerin 2% ointment, applied 4 times a day as needed. This appeared to decrease the intensity and frequency of episodes, but he was unable to tolerate the staining and difficulty of application while at work.

An ultrasound-guided cervical sympathetic block with local anesthetic at the level of C7 did not provide relief. Subsequently, an ultrasound-guided thoracic paravertebral sympathetic block with 10 ml of 1% lidocaine was performed, resulting in almost complete pain relief lasting a week. He received these injections every 2 to 3 weeks, but each provided only a week of complete pain relief. Therefore, botulinum toxin injection was administered around the nipple—80 units divided among the 4 quadrants of the areola. This continues to provide significant pain relief lasting more than a month.

DISCUSSION

Our patient exhibited features suggestive of primary Raynaud's phenomenon of the nipple, including pain and blanching without any inciting event, underlying pathology, or family history of similar conditions. Maurice Raynaud first described an episodic, transient, painful vasospastic disease of the digits in 1862, following cold exposure and sometimes resulting in gangrene, in a case

Figure. Left Nipple Showing Blanching in the Nipple During a Painful Episode



series of 25 patients.⁵ Initially named Raynaud's disease, it has since been reclassified as Raynaud's phenomenon (RP). Two forms of RP have been described: primary RP, with no detectable underlying disease, and secondary RP, which is associated with systemic diseases such as scleroderma and other connective tissue disorder, including lupus, dermatomyositis, Sjögren syndrome, and undifferentiated connective tissue disease.⁵

Although RP is most commonly reported in the distal extremities, RP of the lips, nose, ears, and nipples also has been reported.⁶ Continuing confusion regarding its definition and diagnostic criteria has resulted in a reported prevalence of primary RP ranging from 2% to 22%, with an incidence of 3% to 5% in the general population.⁵ Primary RP is often a familial, symmetrical vasospasm affecting both hands (typically sparing the thumbs) and is more common in women younger than 30 years, often triggered by cold exposure or stress.⁵ In contrast, secondary RP is usually associated with a connective tissue disorder—occurring in approximately 90% of patients with systemic sclerosis—and is more common in women older than 40 years. Secondary RP may also be occupational, associated with use of vibratory tools (more common in men), playing slap bass, or exposure to chemicals such as vinyl chloride monomer and certain solvents.^{5,7,8}

Use of certain medications— β -blockers, interferon- α and - β , and cytotoxic agents—has also been linked to RP. Other reported associations include hormones—specifically estrogen, which increases expression of α_2 C-adrenoceptors and leads to vasoconstriction, as observed in premenopausal women—and certain cancers, including breast, ovarian and colorectal cancers.^{5,9-11}

CARC paint contains various chemical compounds, including, isocyanate, toluene diisocyanate, and solvents. These agents have been reported to cause skin and respiratory irritation, as well as kidney damage. Although dry CARC is considered inert, sanding, grinding, or exposure to extreme heat can release CARC dust or fumes. Gulf War veterans may have been exposed to CARC

paint fumes, which was used to prevent corrosion and penetration by chemical warfare agents. It is unclear whether our patient's exposure to CARC during the Gulf war—which coincides with symptom onset—is related to his condition, although multiple unexplained symptoms have been attributed to CARC exposure.¹²

RP is primarily a clinical diagnosis, classically described as a triphasic color change: white (vasospasm), blue (cyanosis due to de-oxygenation of the static venous vasculature), and red (reactive hyperemia). However, current definitions do not require all three phases. According to the European Society for Vascular Medicine guidelines, blanching alone or as part of a triphasic color change is required for the diagnosis.⁵ Due to the episodic and transient nature of RP, features are often self-reported and maybe missed, necessitating photographic documentation of the affected area during episodes.⁹

Investigations are warranted only to identify secondary causes of RP, including connective tissue disorders, with systemic sclerosis being common. Tests usually include complete blood count, C-reactive protein, erythrocyte sedimentation rate, thyroid functions tests, and antinuclear antibody titers.⁵ Capillary microscopy of the nail bed is a sensitive method for detecting early connective tissue disorders.⁵

Management of RP includes lifestyle modifications, such as smoking cessation, avoiding cold, wearing extra layers of clothing in cold weather, stress and anxiety reduction, avoiding caffeine and vasoconstrictive medications (eg, nonselective β -blockers).¹³ Dietary supplements—including evening primrose oil, fish oil, vitamin B6 (pyridoxine), and L-arginine—have shown some effectiveness, although evidence is limited.⁷ Pharmacologic management remains challenging, especially in complex cases. Calcium channel blockers are considered first-line agents for RP management. Other options include angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers, nitroglycerin paste, and selective serotonin reuptake inhibitors (SSRIs). If ineffective, phosphodiesterase type-5 inhibitors (eg, sildenafil) may be considered.¹³ Cervical sympathetic blocks have shown limited success, while digital sympathectomy has demonstrated some benefit.⁹

A systematic literature review of 42 clinical studies involving 425 patients treated with botulinum toxin reported positive outcomes in 96% of cases.¹⁴ However, a recent multicenter, randomized, double blind, placebo-controlled trial found no significant difference between botulinum toxin and placebo in RP treatment.¹⁵

The features and management of RP of the nipple are similar to those of RP in other locations. In 1970, Gunther reported a patient with nipple pain and color changes, attributing the symptoms to psychosomatic nipple soreness.¹⁶ RP was later identified as a cause of nipple pain with triphasic color changes in lactating women.^{17,18} Triphasic color change and pain are now considered characteristic features of RP of the nipple. For a diagnosis, at a

minimum, blanching of the nipple should be present. Pain is typically described as intermittent, throbbing, stabbing, lancinating, or piercing, lasting for a few seconds to minutes. Sensitivity to cold is common and thought to result from vasospasm of the vessels supplying the nipple. Reports of correlation to breast-feeding are mixed.^{17,18} RP of the nipple is typically bilateral. Use of labetalol for preeclampsia has also been associated with RP of the nipple.^{19,20} Treatment options for RP of the nipple are not well described in the literature and are mostly anecdotal. One report described the use of botulinum toxin for thelalgia of bilateral nipples in a man, resulting in complete remission of symptoms, although without associated blanching.²¹

CONCLUSIONS

We report a case of man with features of Raynaud's phenomenon of the left nipple. Various interventional and medical treatments—including calcium channel blockers and sympathetic blocks—provided only minimal and transient relief. Botulinum toxin injection resulted in significant and sustained pain relief lasting more than a month.

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REFERENCES

1. Douglas P. Re-thinking lactation-related nipple pain and damage. *Womens Health (Lond)*. 2022;18:17455057221087865. doi:10.1177/17455057221087865.
2. Adams SJ, Kanthan R. Paget's disease of the male breast in the 21st century: A systematic review. *Breast*. 2016;29:14-23. doi:10.1016/j.breast.2016.06.015.
3. Moreira TG, Castro GM, Gonçalves Júnior J. Raynaud's phenomenon of the nipple: Epidemiological, clinical, pathophysiological, and therapeutic characterization. *Int J Environ Res Public Health*. 2024;21(7):849. doi:10.3390/ijerph21070849.
4. Pereira M, Thable A. Raynaud's phenomenon of the nipple: Ensuring timely diagnosis. *J Am Assoc Nurse Pract*. 2020;33(4):271-277. doi:10.1097/JXX.0000000000000407.
5. Belch J, Carlizza A, Carpentier PH, et al. ESVN guidelines - the diagnosis and management of Raynaud's phenomenon. *Vasa*. 2017;46(6):413-423. doi:10.1024/0301-1526/a000661
6. Haque A, Hughes M. Raynaud's phenomenon. *Clin Med (Lond)*. 2020;20(6):580-587. doi:10.7861/clinmed.2020-0754
7. Nawaz I, Nawaz Y, Nawaz E, Manan MR, Mahmood A. Raynaud's phenomenon: reviewing the pathophysiology and management strategies. *Cureus*. 2022;14(1):e21681. doi:10.7759/cureus.21681
8. Jepsen JR, Simonsen JA. Raynaud's phenomenon in a slap bass player: a case report. *Med Probl Perform Art*. 2016;31(1):51-53. doi:10.21091/mpa.2016.1009
9. Pauling JD, Hughes M, Pope JE. Raynaud's phenomenon—an update on diagnosis, classification and management. *Clin Rheumatol*. 2019;38(12):3317-3330. doi:10.1007/s10067-019-04745-5
10. Aqodad Z, Bachir H, Alaoui H, Hamaz S, Serraj K Sr. Raynaud's phenomenon: beware of cancers!. *Cureus*. 2021;13(3):e14009. doi:10.7759/cureus.14009
11. Lai TS, Shim MR, Shin D, Zakhour M. Paraneoplastic Raynaud phenomenon

associated with metastatic ovarian cancer: a case report and review of the literature. *Gynecol Oncol Rep*. 2020;33:100575. doi:10.1016/j.gore.2020.100575

12. Public health: CARC paint. U.S. Department of Veterans Affairs. Updated April 16, 2025. Accessed March 12, 2024. <https://www.publichealth.va.gov/exposures/carc-paint/index.asp>

13. Ramahi A, Hughes M, Khanna D. Practical management of Raynaud's phenomenon - a primer for practicing physicians. *Curr Opin Rheumatol*. 2022;34(4):235-244. doi:10.1097/BOR.0000000000000877

14. Lawson O, Sisti A, Konofaos P. The use of botulinum toxin in Raynaud phenomenon: a comprehensive literature review. *Ann Plast Surg*. 2023;91(1):159-186. doi:10.1097/SAP.0000000000003603

15. Senet P, Maillard H, Diot E, et al. Efficacy and safety of botulinum toxin in adults with Raynaud's phenomenon secondary to systemic sclerosis: a multicenter, randomized, double-blind, placebo-controlled study. *Arthritis Rheumatol*. 2023;75(3):459-467. doi:10.1002/art.42342

16. Rothman LR. Comment on: "Skin disease of the breast and nipple". *J Am Acad Dermatol*. 2019;81(4):e111-e112. doi:10.1016/j.jaad.2019.06.021

17. Quental C, Brito DB, Sobral J, Macedo AM. Raynaud phenomenon of the nipple: a clinical case report. *J Family Reprod Health*. 2023;17(2):113-115. doi:10.18502/jfrh.v17i2.12876

18. Jansen S, Sampene K. Raynaud phenomenon of the nipple: an under-recognized condition. *Obstet Gynecol*. 2019;133(5):975-977. doi:10.1097/AOG.0000000000003219

19. Avila-Vega J, Urrea-Mendoza E, Lee C. Raynaud's phenomenon of the nipple as a side-effect of labetalol: case report and literature review. *Case Rep Womens Health*. 2019;23:e00135. doi:10.1016/j.crwh.2019.e00135

20. Humane A, Singh S. Labetalol-associated Raynaud's phenomenon of the nipple: a rare case report with review of literature. *J Obstet Gynaecol India*. 2022;72(6):533-535. doi:10.1007/s13224-022-01708-w

21. Eigelshoven S, Kruse R, Rauch L, Hanneken S, Ruzicka T, Neumann NJ. Thelalgia in man: successful treatment with botulinum toxin. *Arch Dermatol*. 2006;142(9):1242-1243. doi:10.1001/archderm.142.9.1242

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