A rare presentation of calciphylaxis in normal renal function

Parin Rimtepathip, David Cohen

ABSTRACT

Introduction: Calciphylaxis is a rare and life-threatening condition in which extensive microvascular calcification in arterioles and occlusion of vessels lead to painful non-healing ulcers with high mortality rate. Calciphylaxis is mainly associated with end stage renal disease or hyperparathyroidism, with rare cases reported in cirrhosis patient.

Case Report: A 55-year-old Caucasian male with significant history of porphyria cutanea tarda and Hepatitis C complicated by cirrhosis with normal renal function presents with history of non-healing ulcers on both of his hands. The diagnosis of calciphylaxis was made by X-ray. Due to rapid progression of the ulcers to tissue necrosis and gangrene with no definite underlying pathology, the patient's hands were eventually amputated due to the inability to withstand pain.

Conclusion: Patients presenting with painful ulceration of their fingers with history of cirrhosis and normal renal function should be worked up for calciphylaxis as part of the differential diagnosis, especially with low serum albumin level. Site of calciphylaxis also matters as there is a great difference between mortality rates of proximal versus distal. We postulate the idea of pathophysiological mechanism with further research needed. This case report should alert physicians that calciphylaxis does occur in patients with cirrhosis and normal renal function.

International Journal of Case Reports and Images (IJCRI)

International Journal of Case Reports and Images (IJCRI) is an international, peer reviewed, monthly, open access, online journal, publishing high-quality, articles in all areas of basic medical sciences and clinical specialties.

Aim of IJCRI is to encourage the publication of new information by providing a platform for reporting of unique, unusual and rare cases which enhance understanding of disease process, its diagnosis, management and clinico-pathologic correlations.

IJCRI publishes Review Articles, Case Series, Case Reports, Case in Images, Clinical Images and Letters to Editor.

Website: www.ijcasereportsandimages.com

CASE REPORT

PEER REVIEWED | OPEN ACCESS

A rare presentation of calciphylaxis in normal renal function

Parin Rimtepathip, David Cohen

ABSTRACT

Introduction: Calciphylaxis is a rare and life-threatening condition in which extensive microvascular calcification in arterioles and occlusion of vessels lead to painful non-healing ulcers with high mortality rate. Calciphylaxis is mainly associated with end stage renal disease or hyperparathyroidism, with rare cases reported in cirrhosis patient. **Case Report:** A 55-year-old Caucasian male with significant history of porphyria cutanea tarda and Hepatitis C complicated by cirrhosis with normal renal function presents with history of non-healing ulcers on both of his hands. The diagnosis of calciphylaxis was made by X-ray. Due to rapid progression of the ulcers to tissue necrosis and gangrene with no definite underlying pathology, the patient's hands were eventually amputated due to the inability to withstand pain. **Conclusion:** Patients presenting with painful ulceration of their fingers with history of cirrhosis and normal renal function should be worked up for calciphylaxis as part of the differential diagnosis, especially with low serum albumin level. Site of calciphylaxis also matters as there is a great difference between mortality rates of proximal versus distal. We postulate the idea of pathophysiological mechanism with further research needed. This case report should

alert physicians that calciphylaxis does occurred in patients with cirrhosis and normal renal function.

Keywords: Calciphylaxis, Cirrhosis, Porphyrria Cutanea Tarda, Hepatitis C

How to cite this article

Rimtepathip P, Cohen D. A rare presentation of calciphylaxis in normal renal function. Int J Case Rep Images 2015;6(6):366–369.

doi:10.5348/ijcri-201563-CR-10524

INTRODUCTION

Calciphylaxis is a rare and life-threatening condition in which extensive microvascular calcification due to calcium deposition in arterioles and occlusion of vessels lead to painful, violaceous, mottled skin lesions, which progress to non-healing ulcers, tissue necrosis, gangrene, sepsis, and potentially death [1]. Two years mortality rates from sepsis ranges from 50–80%. Patients with skin involvement over the trunk or proximal extremities have a poorer prognosis and higher mortality rate when compared to distal extremities. The lack of understanding the pathophysiology of the disease and numerous postulation result in unsatisfactory answer to why there is a difference in mortality rate. Biopsy of the calciphylaxis ulcer would reveals calcium deposits lining the vascular intima, while tissue calcification may also be seen on plain radiographs [2]. Risk factors for calciphylaxis are female gender, hyperphosphatemia with elevation of calcium phosphate axis, elevated parathyroid hormone, high alkaline phosphatase, and low serum albumin [3]. Many of the risk factors can be seen in patients on hemodialysis from chronic renal failure especially if the chronic renal failure is the complication of diabetes

Parin Rimtepathip¹, David Cohen²

Affiliations: ¹MS III, Mercer University School of Medicine; ²MD, Dermatologic Surgery Specialists, Macon, Georgia.

Corresponding Author: Parin Pearl Rimtepathip, 1385 Highlands Ridge Rd. ste. D. Smyrna 30082, Georgia; Ph: 4043941099; Email: pearl12j@uga.edu

Received: 06 March 2015

Accepted: 15 April 2015

Published: 01 June 2015

with 61% had acral gangrene compared to 34% of the non-diabetic calciphylaxis [4]. Calciphylaxis is therefore most common in hyperparathyroidism secondary to chronic renal impairment and rarely occurs in the setting of normal renal function [2]. However, these risk factors are not set in stone or fundamental in diagnosing patients with calciphylaxis. We report an extremely rare case of calciphylaxis in a 55-year-old Caucasian male with significant history of porphyria cutanea tarda and hepatitis C complicated by cirrhosis with normal renal function that presents with non-healing ulcers on both of his hands, with rapid progression to tissue necrosis and gangrene.

CASE REPORT

A 55-year-old Caucasian male with significant history of hepatitis C, porphyria cutanea tarda (PCT), and cirrhosis presents with non-healing ulcers on both hands. The patient was referred to the dermatological center for the evaluation of both hands as a possible complication of PCT. The clinical examination showed a cachectic patient with lesions shown in Figure 1. The patient noticed the new skin lesions on his hands to be different from the lesions of PCT several years ago. Even though PCT caused pain, the new onset of the non healing ulcers were far more painful. The patient described the ulcer as they first appeared as shallow eroding of the skin. Then the ulcers would accompanied by extreme pain and the tissue in the area would started to necroses. Some of the differential diagnoses for the patient's painful ulceration of the fingers were Raynaud syndrome, scleroderma, peripheral vascular disease, and vasculitis. During the course of treatment, patient denied any skin biopsied due to the existence of severe pain. Therefore, we decided to perform X-ray of his left hand. The finding of his left hand (Figure 2) showed mildly increased soft-tissue density and stipple calcification of the vessels. Calciphylaxis was diagnosed.

Due to the unknown pathogenesis which makes good clinical treatment extremely difficult, labs were ordered in an attempt to exclude any risk factors. All labs including CBC and biochemistry were normal except the low albumin level of < 3 g/dL. The patient was given analgesic for his pain but increase dosage did not alleviate his condition. Patient's fingers were ultimately amputated due to unbearable pain and unsalvageable tissue necrosis and gangrene.

DISCUSSION

Calciphylaxis (synonym calcific uremic arteriolopathy) results from calcification of the arterioles and subsequent thrombosis which lead to skin ischemia. Calciphylaxis is associated with high morbidity and mortality resulting primarily from infections. According to Mazhar et al.,

Figure 1: Presentation of calciphylaxis on patient's left hand with characteristic of ulceration, tissue necrosis, and gangrene.

Figure 2: Presentation of calciphylaxis on X-ray showing mildy increased soft-tissue density and stipple calcification of the vessels.

elevated parathyroid hormone levels, elevated serum phosphate and calcium-phosphate products especially in renal failure patients, elevated alkaline phosphatase, high serum levels of iPTH, low serum albumin, female, Caucasian origin, ESRD, medications such as warfarin, prednisone, calcitriol, and calcitriol salts are associated with risk factors at the time of diagnosis of calciphylaxis. Since most calciphylaxis typically occurs in patients with end-stage renal disease undergoing dialysis or patients who have secondary hyperparathyroidism, patients without these underlying risk factors are often misdiagnosed at presentation [3]. An important postulated

pathophysiologic mechanism is proposed by Danziger and Demer about the increase risk for calciphylaxis in patient with hepatic disease, like our presenting patient. A possible reason is that vitamin K is reduced in liver disease, which is required for post-translation gamma-carboxylation of matrix gamma-carboxyglutamic acid protein, fetuin, or growth arrest-specific gene 6. These are calcifications inhibitors produced by vascular smooth muscle cells. Warfarin, which inhibits vitamin K-dependent carboxylation of these calcification inhibitors, is thought to encourage vascular calcification in this way [5-6]. Another propose mechanism by Goli, Shah, Byrd, and Roy, is the deficiencies in protein C and S from cirrhosis as the cause of calciphylaxis as low levels of these anticoagulant factors may be an important etiologic factor [7].

Low serum albumin level is one of the main interests as a risk factor for our patient since all lab values were normal except the albumin level. Bleyer et al. reported a 17-fold increase in the risk of developing calciphylaxis with each decrease in albumin by 1 g/dL (OR= 16.9, 95% CI, 5.25 to 54.5) [8]. This finding is later supported by Coates et al., who reported a loss of 10 % body weight over six months preceding the diagnosis of calciphylaxis in 7 out of 16 patients in their series [9]. As mentioned earlier, two years mortality rates from infections and eventually sepsis for these patients might be due to underlying poor wound healing as a result of low albumin. Correcting albumin level in patients with calciphylaxis with no other risk factors might enhance their survival rates by enhancing the wound healing process, which would lead to less infection and less mortality rate. However, further research concerning the possible role of albumin level should be pursued. Suyin and I.H. Coulson proposed a summary of recommended investigations in Table 1 [2].

Why do patients with skin involvement over the trunk or proximal extremities have a poorer prognosis and higher mortality rate when compared to distal extremities which occurs below the knee? Is the fact that our patient beat the two years mortality rates of 50–80% because only his distal extremity was involved? The lesions of calciphylaxis typically develop suddenly and progress rapidly. However, does this concept apply

to distal calciphylaxis with better prognosis? According to Mazhar et al., eleven patients with calciphylaxis and seven controls died during the follow-up period. Seven out of ten patients who died of complications related to calciphylaxis had proximal lesions and died of infections [3]. Proximal lesions have been observed in many studies to be one of the worst prognoses, but none of the articles postulated the underlying pathophysiologic mechanisms. A raising question surrounding this area: Is it because proximal type of calciphylaxis involves major arteries while distal type involves arterioles? In humans, vascular calcification is an active process and is not sufficient to produce skin necrosis. Vascular calcification and thrombosis are both required to produce lesions of calciphylaxis [10]. According to Rayz, V. L., et al., in addition to biochemical factors, hemodynamic factors that are governed by luminal geometry and blood flow rates likely play an important role in the thrombus formation and deposition process [11]. Arteries and arterioles have different luminal geometry and blood flow rates, therefore, calcification and thrombus formation can possibly formed much faster and much more aggressive in the proximal calciphylaxis. Also, the proximal arteries increase the chance of infections developing into sepsis because they are closer to many important organs. The idea behind this theory stimulates further research concerning the difference between mortality rates in proximal versus distal calciphylaxis.

CONCLUSION

In conclusion, patients presenting with painful ulceration of their fingers with significant history of porphyria cutanea tarda and Hepatitis C with cirrhosis with normal renal function should be worked up for calciphylaxis as part of the differential diagnosis. Calciphylaxis is a very rare disease with approximately 160 case reports worldwide. This case report should alert physicians that calciphylaxis does occurred in patients with cirrhosis and normal renal function.

Table 1: Summary of Recommended Investigations [2]

Full blood count
Urea and Creatinine
Liver function
Corrected calcium
Phosphate
Calcium-phosphorus index (<55 mg ² /dL ²)
Parathyroid hormone
Coagulation profile
Thrombophilia screen (factor V Leiden, anti-cardiolipin Ab, lupus anticoagulant, protein c, protein s, homocysteine)
Skin biopsy
Plain radiographs
Technetium-99 scintigraphy to exclude visceral calcification

Author Contributions

Parin Rimtepathip – Substantial contributions to conception and design, Drafting the article, Final approval of the version to be published

David Cohen – Substantial contributions to conception and design, Drafting the article, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

Copyright

© 2015 Parin Rimtepathip et al. This article is distributed under the terms of Creative Commons Attribution License which permits unrestricted use, distribution and reproduction in any medium provided the original author(s) and original publisher are properly credited. Please see the copyright policy on the journal website for more information.

REFERENCES

1. Budisavljevic MN, Cheek D, Ploth DW. Calciphylaxis in chronic renal failure. *J Am Soc Nephrol* 1996 Jul;7(7):978–82.
2. Ong S, Coulson IH. Diagnosis and treatment of calciphylaxis. *Skinmed* 2012 May-Jun;10(3):166–70.
3. Mazhar AR, Johnson RJ, Gillen D, et al. Risk factors and mortality associated with calciphylaxis in end-stage renal disease. *Kidney Int* 2001 Jul;60(1):324–32.
4. Hafner J, Keusch G, Wahl C, Burg G. Calciphylaxis: a syndrome of skin necrosis and acral gangrene in chronic renal failure. *Vasa* 1998 Aug;27(3):137–43.
5. Danziger J. Vitamin K-dependent proteins, warfarin, and vascular calcification. *Clin J Am Soc Nephrol* 2008 Sep;3(5):1504–10.
6. Demer LL, Tintut Y. Vascular calcification: pathobiology of a multifaceted disease. *Circulation* 2008 Jun 3;117(22):2938–48.
7. Goli AK, Goli SA, Shah LS, Byrd RP Jr, Roy TM. Calciphylaxis: a rare association with alcoholic cirrhosis. Are deficiencies in protein C and S the cause? *South Med J* 2005 Jul;98(7):736–9.
8. Bleyer AJ, Choi M, Igwezie B, de la Torre E, White WL. A case control study of proximal calciphylaxis. *Am J Kidney Dis* 1998 Sep;32(3):376–83.
9. Coates T, Kirkland GS, Dymock RB, et al. Cutaneous necrosis from calcific uremic arteriopathy. *Am J Kidney Dis* 1998 Sep;32(3):384–91.
10. Bhambri A, Del Rosso JQ. Calciphylaxis: a review. *J Clin Aesthet Dermatol* 2008 Jul;1(2):38–41.
11. Rayz VL, Boussel L, Lawton MT, et al. Numerical modeling of the flow in intracranial aneurysms: prediction of regions prone to thrombus formation. *Ann Biomed Eng* 2008 Nov;36(11):1793–804.

Access full text article on
other devices

Access PDF of article on
other devices

Edorium Journals: An introduction

Edorium Journals Team

About Edorium Journals

Edorium Journals is a publisher of high-quality, open access, international scholarly journals covering subjects in basic sciences and clinical specialties and subspecialties.

Invitation for article submission

We sincerely invite you to submit your valuable research for publication to Edorium Journals.

But why should you publish with Edorium Journals?

In less than 10 words - we give you what no one does.

Vision of being the best

We have the vision of making our journals the best and the most authoritative journals in their respective specialties. We are working towards this goal every day of every week of every month of every year.

Exceptional services

We care for you, your work and your time. Our efficient, personalized and courteous services are a testimony to this.

Editorial Review

All manuscripts submitted to Edorium Journals undergo pre-processing review, first editorial review, peer review, second editorial review and finally third editorial review.

Peer Review

All manuscripts submitted to Edorium Journals undergo anonymous, double-blind, external peer review.

Early View version

Early View version of your manuscript will be published in the journal within 72 hours of final acceptance.

Manuscript status

From submission to publication of your article you will get regular updates (minimum six times) about status of your manuscripts directly in your email.

Our Commitment

Six weeks

You will get first decision on your manuscript within six weeks (42 days) of submission. If we fail to honor this by even one day, we will publish your manuscript free of charge.

Four weeks

After we receive page proofs, your manuscript will be published in the journal within four weeks (31 days). If we fail to honor this by even one day, we will publish your manuscript free of charge and refund you the full article publication charges you paid for your manuscript.

Mentored Review Articles (MRA)

Our academic program "Mentored Review Article" (MRA) gives you a unique opportunity to publish papers under mentorship of international faculty. These articles are published free of charges.

Favored Author program

One email is all it takes to become our favored author. You will not only get fee waivers but also get information and insights about scholarly publishing.

Institutional Membership program

Join our Institutional Memberships program and help scholars from your institute make their research accessible to all and save thousands of dollars in fees make their research accessible to all.

Our presence

We have some of the best designed publication formats. Our websites are very user friendly and enable you to do your work very easily with no hassle.

Something more...

We request you to have a look at our website to know more about us and our services.

We welcome you to interact with us, share with us, join us and of course publish with us.

Edorium Journals: On Web

Browse Journals

CONNECT WITH US