CASE REPORTS

Severe Calciphylaxis Secondary to end Stage Renal Failure: A Case Report

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ABSTRACT

Calciphylaxis is a vascular calcification disease causing skin necrosis which contributes to high morbidity and mortality. Its exact pathogenesis is currently unknown but is commonly associated with chronic renal failure, hypercalcemia, hyperphosphatemia, secondary hyperparathyroidism and a variety of hypercoagulable state. It is relatively rare but may occur in 1-4% of patients with End Stage Renal Failure (ESRF).[1] We are reporting a case of young lady with underlying ESRF presented with vascular and skin calciphylaxis.

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Introduction

Calciphylaxis is an uncommon condition affecting 1-4% of ESRF population.[1] Calciphylaxis was first introduced in 1962 by Selye when he was able to precipitate systemic calcification in nephrectomised rat.[2] However, its exact aetiology and pathogenesis have remained obscured until now.

Due to poor understanding regarding the disease, there are currently no definite diagnostic and therapeutic guidelines which may prevent devastating outcomes in calciphylaxis patients. The prognosis is generally poor with mortality rate as high as 60% in patients with ulcerative disease.[3] Patients who do not die of sepsis frequently had to undergo amputation of the affected limbs.

Case(s)

We are reporting a case of 30-year-old lady with underlying Type 1 Diabetes Mellitus complicated with retinopathy, neuropathy and ESRF secondary to Diabetic Kidney Disease for 3
years. She was on regular hemodialysis for 1 year and subsequently converted to Continuous Ambulatory Peritoneal Dialysis (CAPD) for 2 years.

She was initially presented with worsening bluish discoloration of all her fingers and toes for over 1 month. It was associated with severe pain and warmness. Some of the fingers slowly became black in colour. There was worsening ulceration over the right middle finger associated with pus discharge. She also had intermittent claudication of bilateral lower limbs. She had no fever, chest pain and abdominal pain at that time. She had no recent

admission prior to the presentation. She is a non-smoker and her family history were unremarkable.

Initial assessment noted dry gangrene of all fingers and toes. There was presence of right middle finger ulceration with surrounding erythema. Other systemic examinations were unremarkable.

She was seen by orthopaedic colleague and the impression was wet gangrene of the right middle finger complicated with osteomyelitis and dry gangrene of bilateral fingers and toes. She had undergone Ray's amputation of the right middle fingers and planned for conservative management for the rest of her bilateral fingers and toes dry gangrene. She was noted to have Methicillin Resistance Staphylococcal Aureus infection from the bone cultures and had completed IV vancomycin for 2 weeks and planned for oral T Bactrim and T Rifampicin for 6 weeks. She was discharged relatively well.

She presented again 2 weeks after discharge with complaint of generalized abdominal pain for 2 days. It was persistent in nature with no specific aggravating and relieving factor. The pain score was 9/10. It was associated with nausea, vomiting and loose stools for 2 days. There were no mucus and bloods in the stool and no history of black tarry stool. There was no fever. She was still able to continue with her CAPD and her peritoneal dialysis effluent was clear.

Abdominal examination revealed generalized abdominal tenderness with normal bowel sound. Per rectal examination was normal. Other systemic examinations were unremarkable.

Her blood investigations revealed leucocytosis with white cell count (WCC) of $30x10^9$/L and increased CRP indicating inflammation. Her intact parathyroid hormone (IPTH) level was 414 pg/ml, calcium 2.64 mmol/L, phosphate 2.07 mmol/L, alkaline phosphatase (ALP) 331 u/L. Unfortunately, autoantibodies associated with collagen disease was not sent. Other investigations were unremarkable.

She was initially treated as Peritoneal Dialysis (PD) peritonitis and intraperitoneal (IP) Cefazolin and IP Ceftazidime were initiated however she responded poorly to the treatment. Her abdominal pain was so severe that Acute Pain Service was involved, and she was started on IV Fentanyl infusion and later was changed to SC Morphine.

Her blood cultures and PD fluid cultures remained negative. Her PD fluid cell count was less than 100 cells/uL therefore not suggestive of PD peritonitis. Her abdominal pain did not improve despite adequate analgesia and few days on antibiotic. Her PD fluids remained clear. Therefore, an urgent abdominal CT scan was arranged.

Her abdominal CT scan noted extensive dense circumferential calcifications of the wall of the abdominal aortas and its branches (hepatic artery, celiac axis, superior mesenteric artery and inferior mesenteric artery), common iliac artery, external iliac artery and femoral artery. There was segmental filling defect within distal middle colic branches of superior mesenteric artery with dilated fluid filled jejunal loops. However, there is no definite evidence of acute bowel ischemia like enhancing bowel thickening or intramural air.

Her final diagnosis was severe calciphylaxis secondary to ESRF and she was subsequently managed conservatively with pain management. She had eventually died of Hospital Acquired Infection due to prolonged hospital stay.

Results

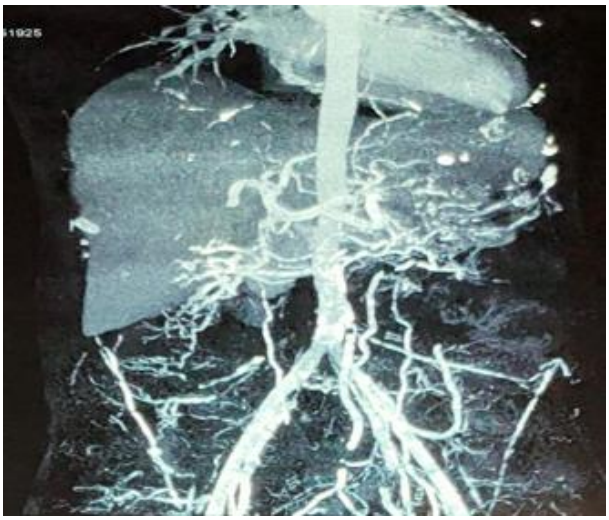

Figure 1. Coronal and sagittal view of abdominal CT scan showing extensive dense circumferential calcifications of the wall of the abdominal aortas and its branches (hepatic artery, celiac axis, superior mesenteric artery, inferior mesenteric artery), common iliac artery, external iliac artery and femoral artery.

Discussion

Calciphylaxis is a rare necrotizing calcifying arteriolopathy which is generally uncommon but may affect up to 1-4% of ESRF patient populations. It was first introduced by Seyes in 1962 when he was able to demonstrate formation of calciphylaxis in nephrectomised rats.[2]

Its exact pathogenesis is unclear, but it is characterized by calcification of tunica media of small and medial arteries causing blockage of the lumen subsequently causing skin necrosis. It was suggested that uraemia-induced defects in nuclear factor-Kb (RANK), RANK ligand and osteoprotegerin may cause skeletal and extra skeletal mineralization defect subsequently leading to calciphylaxis.[4] Therefore, its risk factors may include prolonged dialysis with abnormal metabolism of calcium and phosphate as a result from renal hyperparathyroidism. Other risk factor may include connective tissue disease, chronic liver disease, diabetes mellitus, systemic hypercoagulability, and concomitant vascular disease.[5]

Patients commonly presented with intense pain and refractory skin ulcers. Early lesion may manifest as nonspecific violaceous mottling or as erythematous papules, plaques or nodules and may progress to stellate purpuric configuration with central cutaneous necrosis.[6] Bullous may also be seen as a rare manifestation of calciphylaxis.[7] They are at constant risk of infections and this disease generally has very poor prognosis. Patients with internal involvement may develop gastrointestinal haemorrhage or organ failure.

Our literature search has shown that there are only 4 reported cases of systemic calciphylaxis presented with gastrointestinal involvement like what is presented in our patient.[3] Therefore, high level of suspicion is needed so that proper investigation with CT scan, can be done to determine the diagnosis and prognosis.[8]

However, due to its rarity, there is currently no high-quality evidence for a guideline on how to properly investigate and to treat calciphylaxis patients. Imaging studies may include plain radiography that show a netlike pattern of arterial calcification. Incisional cutaneous biopsy is usually diagnostic and typically demonstrate calcification within the media and intima of small and medium sized arterioles with extensive intimal hyperplasia and fibrosis, but biopsy may result in a nonhealing wound.

This patient was diagnosed with severe calciphylaxis based on presence of gangrenous of

all fingers and toes as well as from the abdominal CT scan findings on top of her risk factor as an ESRF patient and her high level of calcium, phosphate and parathyroid hormone.

General management may include identification of risk factor, correction of abnormal metabolism of calcium and phosphate, prevention of infection and local management of ulcers usually by debridement. In patients with elevated calcium and phosphate, the levels must be brought to low-normal levels as quickly as safely possible.

Recently intravenous sodium thiosulfate administration has been gaining attention and has shown dramatic improvement in signs and symptoms in an ESRF patient and even a complete resolution of the disease in a non-uremic calciphylaxis patient.[9,10] It is a potent antioxidant that may increase the solubility of calcium deposits.

Another case report has also shown a better control of calciphylaxis in a dialysis patient with cinacalcet which act by inhibiting parathyroid hormone production via negative feedback to normalize the calcium and phosphate metabolism.[11] Studies have shown its efficacy in decreasing PTH, calcium and phosphate levels. Bisphosphonates like pamidronate may also be helpful by inhibiting arterial calcification. Aggressive wound care may also be necessary to avoid wound infection and sepsis. Other than that, it is also important to manage the pain appropriately.

Conclusion

Calciphylaxis is an important complication of ESRF which has high morbidity and mortality and they may also manifest as gastrointestinal complication. A good management in calcium and phosphate metabolism as well as maintaining dialysis adequacy is important to prevent this complication.

Conflict of Interest

The author started there is no conflict of interest.

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