A retrospective review of biopsy-proven calciphylaxis in a tertiary centre in Singapore: Clinical features and prognosis in a Chinese population

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Background
Calciphylaxis is a small vessel obliterator vasculopathy characterized by mural calcification resulting in painful ischaemic cutaneous ulceration². Mortality is high with a reported 1 year survival rate of 45.8% in Western populations¹. It is unclear if such high mortality is also present in other ethnic populations. We aimed to determine the epidemiological profile, clinical features and outcomes of patients with calciphylaxis seen at an academic medical centre in Singapore.

Methods
A retrospective review of all biopsy-proven calciphylaxis cases seen by the Department of Dermatology, Singapore General Hospital from January 2012 to May 2014 was performed. Clinical and follow up data were obtained from medical records.

Results
A total of 16 biopsy-proven cases of calciphylaxis were identified. 14 were uraemic while 2 were of non-uraemic calciphylaxis. All patients were Chinese with a mean age of 57 years and a marked female preponderance of 93.8% (n=15). Of the uraemic patients on dialysis, 8 (61.5%) were on haemodialysis while 4 (38.5%) were on peritoneal dialysis (mean duration = 107.5 months). All patients had multiple comorbidities such as diabetes mellitus, ischaemic heart disease and peripheral vascular disease. 2 patients with non-uraemic calciphylaxis had systemic lupus erythematosus and systemic sclerosis respectively.

In terms of clinical features, all patients presented with painful eschars and/or ulcers of the distal limbs with 2 (12.5%) also having proximal limb involvement. In addition, 8 (50%) had retiform purpura and 7 (44%) had induration suggestive of a panniculitis.

Discussion
Our study on calciphylaxis in a Chinese population shows that the demographics are similar to that reported in the Western and Japanese populations. The median age was 57 years compared to 59 years and 58 years in the studies by Weenig¹ and Hayashi² respectively. While all studies showed a female preponderance, it was most marked in our study with 93.8% being female.

Most cases were related to uraemia with 8 (61.5%) of patients being on haemodialysis in our study compared to Weenig¹ with 49 (76.5%). Interestingly, the mean duration of dialysis before diagnosis was only 9.2 months in the study by Weenig¹ with 12 (24%) of patient being newly commenced on dialysis within 1 month after diagnosis. This is in contrast to that reported in the Japanese population² with a mean duration of 107.5 months and our current study of 87.5 months.

Despite a lack of prospective randomized controlled trials, sodium thiosulphate is thought to be effective in the management of calciphylaxis by several mechanisms, including chelation of calcium, vasodilation and anti-oxidation³. Rapid relief of ischemic pain in days to weeks has been reported with wound healing taking 2 months or more³. However, of concern is that all-cause mortality in our study remained high at 61.5% at 1 year despite 81.5% of patients receiving sodium thiosulphate at standard doses of 25g thrice weekly. Possible reasons for this apparent lack of efficacy could be a delay in initial diagnosis due to late patient presentation, delayed dermatological referral as well as initial inconclusive biopsies. Sodium thiosulphate therapy was initiated within 1 month of diagnosis in our cases. However, an average delay of about 3 months from initial symptoms to diagnosis was noted.

Interestingly, all patients on peritoneal dialysis in our current study demised by 13 months post-diagnosis, suggesting that peritoneal dialysis may be a poor prognostic factor. However, this may be more reflective of the fact that patients selected for peritoneal dialysis are more likely to have multiple comorbidities such as advanced cardiac failure compared to those on haemodialysis, rendering them more susceptible subsequent septic and haemodynamic complications of calciphylaxis.

Conclusion
This study shows that mortality remains high despite routine use of sodium thiosulphate. Our data also supports previous studies that those on peritoneal dialysis may be associated with a poorer prognosis.

References

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