

Takotsubo Syndrome in the Dialysis Patient - Challenging Diagnosis in a Unique Population

Dialysis patients suffer excess heart failure, present in up-to 33%, associated with high mortality; and high sudden cardiac death rates, 6.5% per year; mostly due to coronary artery disease and autonomic dysfunction.^[1] Left ventricular cardiomyopathy and hypertrophy have been well described in dialysis patients^[2] but specific descriptions of Takotsubo syndrome (TS) in this population are rare, with only a few case studies, as described in manuscript in the present issue of journal.^[3] This is perhaps suggestive of the fact that TS, as a cause of chest pain or heart failure in the dialysis population, will be far less common than that caused by coronary artery disease (CAD), a leading cause of death in chronic kidney disease (CKD) and dialysis patients.^[1] Previous studies have suggested CKD as a risk factor in patients with TS. A systematic review of 1109 patients quoted that CKD was present in 7% (range 2-27%).^[4] TS has been described in acute kidney injury, CKD, kidney-transplantation, haemodialysis and peritoneal dialysis patients. However, there are no prospective cohort studies in dialysis patients and hence exact incidence, prognosis and causative mechanism are unknown.^[5]

Clinical Characteristics of Takotsubo's Cardiomyopathy, Diagnosis in Dialysis Patients

TS is a diagnosis of exclusion, described in post-menopausal females, often precipitated by emotional and physical stress. As suggested by the 'International Takotsubo Diagnostic Criteria', diagnosis of TS hinges on a specific set of results seen from investigations including serial troponins, electrocardiograms, echocardiogram and coronary angiography.^[6] The reversibility of the specific changes as well as the absence of culprit atherosclerotic disease is the key to a correct diagnosis. A patient presenting with acute chest pain on dialysis will require prompt investigations to rule out the more likely diagnosis of acute coronary ischaemia; as described in the case report. Whilst making a timely diagnosis of TS is important, the initial focus should be to ensure there is no cardiac ischaemia requiring immediate treatment in this high-risk population. It is particularly important to differentiate between TS and CAD in patient with cardiogenic shock due to the possible harm with the use of certain inotropes in TS.^[7]

Mechanism of Takotsubo's Syndrome

The prevalent catecholamine theory for TS, as outlined in the accompanying article, is supported by the specific cardiac dysfunction seen following a sudden sympathetic surge with depression of parasympathetic activity.^[7] However, catecholamine release and response in a dialysis patient may well be different from the non-dialysis population. Substantial

evidence exists demonstrating the sustained heightened sympathetic tone with suppressed parasympathetic tone in dialysis patients.^[8] It is unclear whether the acute stressor event triggering a decline in myocyte contractility seen in TS would be triggered in a cohort of patients with already chronically heightened catecholamine levels.

The trigger mentioned in most literature is usually an acute emotional event, hence the "broken heart" syndrome label. However, in the accompanying article, there was no single precipitating event. It seems unlikely that the chronic emotional stress associated with living with a chronic condition, in this case renal failure, has the same biochemical response as the acute events described that result in the high catecholamine release.

Intradialytic Myocardial Stunning and Takotsubo Syndrome

Previous studies have described repeat episodes of myocardial dysfunction during dialysis shown by echocardiogram and other imaging modalities. Such episodes may happen due to excess myocardial oxygen demand during dialysis, necessary to maintain higher cardiac output, in the presence of stable CAD. The 'demand myocardial ischaemia' occurring during dialysis patients causes temporary left ventricular remodelling or myocardial stunning, which reverses post-dialysis and its long-term effects are unknown. These changes have been compared to TS.^[9] However, the mechanism of intradialytic myocardial dysfunction is likely to be due to ischaemia and different from mechanism of TS, i.e. sudden sympathetic surge, though sympathetic overactivity during dialysis may happen. Moreover, intradialytic myocardial stunning is common, happens repeatedly, but TS is rarely reported in dialysis patients. Though very rare, TS has been reported in peritoneal dialysis patients, and it may be interesting to compare the incidence and nature of TS in peritoneal dialysis patients compared to haemodialysis patients. Such a comparison may generate new ideas for possible mechanism of TS in CKD and ESRD patients.

Other Reversible Causes of Heart Failure in Dialysis

There may other causes of reversible congestive heart failure in dialysis patients, such as coronary spasm and transient coronary artery occlusion due to a clot which disintegrates rapidly and not seen on angiography. Such cases may be misinterpreted as sympathetic surge related TS.

Conclusion

Takotsubo syndrome (TS) is a sudden, severe cardiac dysfunction with chest pain, precipitated by stress. It is

reversible in nature but often difficult to diagnose and rarely reported in dialysis; the mechanism of which is largely unknown. Dialysis patients with significant autonomic dysfunction, which makes them more prone to sudden cardiac arrhythmias, may be at risk. However, raising awareness of this condition among dialysis physicians is necessary to establish the diagnosis in dialysis patients and better understand the mechanism causing this devastating illness.

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