# The ATAK complex (Adrenaline, Takotsubo, Anaphylaxis, and Kounis hypersensitivity -associated coronary syndrome) in neurological conditions

Sir,

Takotsubo syndrome, transient left ventricular apical ballooning, takotsubo cardiomyopathy, apical ballooning syndrome, atypical apical ballooning, ampulla cardiomyopathy, broken heart syndrome, transient left ventricular dysfunction syndrome, and stress cardiomyopathy were named after a round-bottomed and narrow-necked fishing pot – takotsubo in Japanese – for trapping octopus because of its resemblance to left ventriculogram. In the interesting report published in *Indian Journal of Critical Care Medicine*,[1] a 48-year-old man with progressive loss of vision, hypotension, tachycardia, and acidosis was found to have takotsubo syndrome while the coronary arteries were normal. Computerized tomography revealed dense sellar–suprasellar mass lesion extending into the hypothalamus resembling pituitary adenoma with hypocortisolism suggesting hypopituitarism. With dobutamine, atenolol, and noradrenaline, his condition improved. This case raises some issues concerning neurological conditions, mental stress adrenaline, anaphylaxis, and Kounis syndrome.

Mental stress commences with impulses from high brain cortical centers that are relayed through the limbic system to hypothalamus resulting in the release of corticotropin-releasing hormone (main coordinator of the mental stress response) and norepinephrine, serotonin, acetylcholine, proopiomelanocortin, adrenocorticotropic hormone, glucagon, growth hormone, and homocysteine that stimulate sympathetic nervous system. These substances can induce heightened cardiovascular activity, endothelial injury, induction of adhesion molecules on the endothelial cells, to which recruited inflammatory cells adhere and translocate to the arterial wall and finally myocardial damage. An acute phase response is engendered, resulting in production of cytokines interleukin-1 (IL-1), IL-6, tumor necrosis factor-alpha, acute phase proteins, macrophage, mast cell, and platelet activation that eventually culminate in the development of Kounis syndrome.[2]

Stress-induced cytokine production has been incriminated for multivessel coronary artery spasm at epicardial or microvascular levels that induce takotsubo cardiomyopathy. Inflammatory mediators released during anaphylaxis can induce coronary spasm and takotsubo syndrome and adrenaline given for anaphylaxis might contribute to coronary spasm and transient takotsubo syndrome. Adrenaline and noradrenaline released by the renin–angiotensin–aldosterone system together with histamine stimulate the release of more catecholamines by direct action on the adrenal medullary cells. Administration of catecholamines for hemodynamic support of anaphylactic shock would also increase the plasma catecholamines. Catecholamine increase in patients with angina, renders blood platelets more sensitive and more prone to aggregation and thrombosis.

Therefore, measurement of anaphylactic inflammatory mediators including histamine, chymase, leukotrienes, thromboxane, and platelet activating factor or the use of corticosteroids or mast cell stabilizers for prevention and treatment may shed light on etiology and pathophysiology of takotsubo cardiomyopathy.

The concurrence of acute coronary syndromes with conditions associated with mast cell activation, involving interrelated and interacting inflammatory cells constitute the Kounis syndrome.[3] Inflammatory cells, such as mast cells, T-cells, and macrophages, activate each other via multidirectional stimuli and release mediators capable to induce coronary events. Experimental findings suggest that cardiac mast cell activation by acute stress may contribute to myocardial ischemia through the release of histamine or proinflammatory mediators.[4]

Therefore, takotsubo cardiomyopathy should be always considered in neurological conditions with prolonged addisonian crisis. Furthermore, Adrenaline, takotsubo, Anaphylaxis, and Kounis syndrome (ATAK) seem to constitute a challenging contemporary complex that needs inexorable "attack" to elucidate its etiology, pathophysiology, and treatment.[5]

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